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Honors Program
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TESIS O PROYECTO DE CREACIÓN
APROBADA COMO REQUISITO PARCIAL DEL
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RECINTO DE RÍO PIEDRAS

NOMBRE DE ESTUDIANTE: Alondra M. Díaz Díaz

NÚM. ESTUDIANTE: 801-16-2320 **FACULTAD:** Ciencias Naturales

TÍTULO DE LA TESINA O PROYECTO DE CREACIÓN: Prevalence and Clinical Course of Critically ILL Pedriatic Patients Infected with Mycoplasma Pneumoniae in a Community Hospital in Puerto Rico

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FECHA: 12 de diciembre de 2019

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Prevalence and Clinical Course of Critically Ill Pediatric Patients Infected with *Mycoplasma pneumoniae* in a Community Hospital in Puerto Rico

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December 18, 2019

Declaration

I hereby declare that this mini thesis titled **"Prevalence and clinical course of critically ill pediatric patients infected with *Mycoplasma pneumoniae* in a community hospital in Puerto Rico"** is the outcome of a research study carried out by me under the supervision of my mentor Dr. Anabel Puig and that it has not been submitted to any institution to the award of any recognition before. I further declare that I have acknowledged the sources used by me in the preparation of this work.

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December 18, 2019 Alondra M. Díaz Díaz

Abstract

Introduction: In some instances, *Mycoplasma pneumoniae* (MP) can be cause for hospitalization. An increase of MP admissions to hospitals has been reported in the pediatric community in Puerto Rico. Nonetheless, no study has been published concerning the prevalence of this condition in patients admitted to the Pediatric Intensive Care Unit (PICU) in Puerto Rico. This study evaluated the prevalence of MP in pediatric patients and its clinical course of patients who required admission to PICU.

Methods: In this retrospective cohort study, 50 electronic medical records of patients (0-21 years old) were evaluated. The patients were admitted to the PICU of a community hospital in San Juan, Puerto Rico from July 2015 to June 2018 with a confirmed diagnosis of *Mycoplasma pneumoniae*. Patients were divided into two groups: <5 years old and ≥5 years of age and the following variables were evaluated: hospital length of stay, clinical, laboratory and radiographic findings. Data were expressed as medians ± 95% Confidence Interval (CI) or percentiles as appropriate. Comparison between two groups were conducted with a Mann-Whitney test with a significant level of $p < 0.05$.

Results: There was an average hospital length of stay of 11.66 days with a mean of 5.22 days on PICU. From the admissions to PICU, 72% were straight from the emergency room. No significant difference was found between admitted children younger than five years old and the school-age children. There was no significant association between the age group and the length of stay, need for mechanical ventilation nor the presence of lung infiltrates. In addition, the admissions were year-round and cannot be described as seasonal, yet there was a significant increase in admissions during the 2017-2018 season, when Hurricane María hit Puerto Rico.

Conclusions: This study confirmed a rise in admissions to PICU of patients with MP during the study period. Since the increase was seen in the season when Hurricane María hit Puerto Rico, the impact of a hurricane may be described as a contributing factor for the increase and severity of MP cases. Unlike several studies that report a higher prevalence of MP in school age children, the present study found no association between the age groups and the prevalence of MP. Valuable information for physicians and children caregivers was provided and should be addressed to prevent and diminish the number of children admitted to PICU. Similar studies are recommended that evaluate a longer study period, patients who were admitted to the hospital without requiring intensive care, and more hospitals around Puerto Rico.

Keywords: Mycoplasma pneumoniae, PICU, community, children, Hurricane María.

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List of Abbreviations

CAP	Community-acquired pneumonia
CT	Computed Tomography
EBV	Epstein-Barr virus
ELISA	Enzyme-linked Immunosorbent Assay
ICD10	International Classification of Diseases, Tenth Revision
ICU	Intensive Care Unit
Ig	Immunoglobulin
LOS	Length of Stay
MP	Mycoplasma pneumoniae
MRMP	Macrolide-resistant MP
MSMP	Macrolide-sensitive MP
MVS	Mechanical Ventilation Support
PA	Particle Agglutination
PCR	Polymerase Chain Reaction
PICU	Pediatric Intensive Care Unit
RSV	Respiratory Syncytial Virus
SOB	Shortness of breath

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My sincere thanks to the San Jorge Children and Women's Hospital for allowed me to perform this study in their Pediatric Intensive Care Unit and allowing me access to the electronic medical record. Without their contribution, this study would not be possible.

I would also like to thank the Honors Studies Program of the University of Puerto Rico, Río Piedras Campus for their assistance in the process of developing and defending my research proposal and thesis.

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Chapter 1: Introduction

Background

Pneumonia is one of the main causes of death by a respiratory disease in children. The pathogen that causes most of the community-acquired pneumonia (CAP) in children is Mycoplasma pneumoniae (MP) (Chen, 2014). MP was identified in 1944 by Eaton and colleagues. Nowadays, MP is known to produce various diseases that vary in severity and, although in rare cases, can be fatal. Although most cases of MP can be managed by primary-care physicians, 25% of patients require hospitalization. Moreover, some patients with MP infections may require admission to an Intensive Care Unit (ICU) and some require mechanical ventilation support (Khoury et al., 2016). Besides respiratory tract infections, MP is responsible for numerous extrapulmonary manifestations, which includes skin, hematological and gastrointestinal manifestations among others (Kashyap and Sarkar, 2010). Although MP can infect people from any age, it is more common among school-age children (Huang, 2016). Because the pathogen lacks a cell wall, the more effective treatment requires macrolide antibiotics (Kumar, 2018). Nonetheless, a macrolide-resistant MP has a prevalence of 90% in Asia and it has been reported in the United States as well (Diaz et al., 2015).

Problem

The problem being investigated arises from the lack of information regarding the prevalence of a pathogen as contagious as MP in pediatric patients in Puerto Rico. Some authors like Dash et al. (2017) clarify that pneumonia caused by MP can be attributed to 15%-20% of cases of CAP and other authors such as Chen and colleagues (2014) reported that MP is attributed to 20%-30% of cases. Both authors reported that MP could be a major concern. A local newspaper

published an article in October 2018 about an outbreak of MP in a school in Humacao where 12 preschoolers were infected among a class of 24 students. The pediatrician Víctor Ramos, president of the Puerto Rico College of Physicians and Surgeons, stated that there has been a raise in MP cases in pediatric patients, and an increase in admissions to the Intensive Care Unit in the hospital where he works due to MP (Parés Arroyo, 2018). Moreover, a second newspaper article was published in February 2019, for which doctors where interviewed, addressing this issue. Doctor Gerardo Tosca, president of the Puerto Rican Pediatric Society, affirmed an increase of MP cases. Similarly, Doctor Ricardo Fontanet mentioned that tests to identify MP are not routinely done, unless the patient is admitted to the hospital. Moreover, it was noted that the Puerto Rico Health Department has no protocol concerning MP cases at schools (Parés Arroyo, 2019).

Given the concerning rise in hospital and Pediatric Intensive Care Unit (PICU) admissions of patients with MP and the lack of studies published regarding this matter, this study was designed to evaluate the prevalence of MP in pediatric patients and the clinical course of patients who require admission to the PICU. In order to accomplish this, a retrospective descriptive study was conducted evaluating medical records of patients admitted to PICU between July 2015 and June 2018 due to MP.

Hypothesis

This study had two hypotheses. First, that MP is seasonal and PICU admission peak during fall season. Second, that the prevalence of MP in patients in PICU is higher in patients 5 years of age and older.

Justification

MP is an important pathogen in the pediatric community. No similar study regarding the prevalence of MP in clinically ill pediatric patients in Puerto Rico was found during the process of literature review. Given the contagious nature of the disease and the increase of cases reported, it is important to conduct research to better comprehend different aspects of the clinical course among pediatric patients. Also, to diagnose MP, the doctor needs to request specific tests that are time-dependent and not routinely made based on the clinical manifestations, which are diverse. If the prevalence and severity of MP is not evaluated and the physicians do not consider it properly, the MP infection might complicate the patient's condition. Moreover, most MP patients, are 5 years old or older, but there has been an increase of reports of MP in patients under five years old (Huang, 2016). For this reason, the admissions to PICU with a diagnosis of MP were studied and divided into groups of age to study if the trend found in literature of higher prevalence in children 5 years and older was the same in Puerto Rico. The results of this study contributed for a better understanding of the clinical management in patients infected with MP.

Theoretically, this study provided additional data related to the manifestations, treatment, and clinical information of MP and its prevalence in a Hispanic community such as the one in Puerto Rico. The recent increase in outbreaks of MP in Puerto Rico, particularly in the pediatric community, make the study period convenient to recruit a good sample size. Providing information about the clinical profile of patients at the time of admission might present physicians with key information that guide them to make an earlier diagnosis and improve treatment of patients.

Chapter 2: Literature Review

Clinical symptoms:

Kashyap and Sarkar (2010) described in detail the clinical features and management of MP. Among clinical features, it is described that younger children are more likely to present wheezing while children under the age range of 5-15 years are more likely to develop bronchopneumonia. Extrapulmonary manifestations include dermatological manifestations (25%), gastrointestinal manifestations (25%), muscle-skeletal manifestations (14%) and more. In addition, Huang et al. (2016) emphasizes cough, tachypnea, fever and wheezing as the main clinical features. The injuries to the pulmonary tracts due to MP are attributed to the inflammatory response of the host. The authors concord with literature when stating that 25% of cases present with extrapulmonary manifestations. They add that the more common ones are presented in the nervous system, such as encephalitis which is more common in children under 10 years old (Chaudry et al., 2016).

This evidence suggested that the diagnosis of this condition based on clinical symptoms alone is not enough. This is because the most common symptoms can be found in other diseases and for some, will not require immediate medical attention. Moreover, a percentage of cases of MP, which primarily affects the respiratory system, present with extrapulmonary conditions that can be misleading.

Yun-Ju Ma and colleagues (2015) developed a study with hospitalized children under 18 years of age in Taiwan. They enrolled 127 patients with CAP and found that children younger than 5 years of age had a worse clinical course including longer hospital stay and more complications. These complications resulted in more admissions to the intensive care unit and a more frequent

need of oxygen (47.5% less than five years vs. 28.8% in patients over 5 years of age) and ventilation support (9.8% vs. 1.5%).

Radiographic evidence:

Despite clinical symptoms, patients with MP show pulmonary symptoms that may be evaluated with radiographic evidence. An example of these radiographic findings is atelectasis. A study conducted in China by De-Qua, S. and colleagues (2019) included 122 patients hospitalized from December 2015 to December 2018 with MP and atelectasis. The authors stated that this combination may cause various complications including systemic damage. Concerning radiographic findings, Gong et al. (2016) evaluated the value of CT as a diagnosis tool for pediatric MP. They conducted a prospective study with a sample of 1280 children over the course of 4 years. The patients were in the age group range between 3 months to 10 years old. The average length of stay (LOS) was 8.9 ± 2.1 days compared to 10 days of Chen's et al. (2015) study. Regarding the radiographic evidence, the most common lesion distribution was a unilateral lobe with a 53.8% of the children presenting it, followed by bilateral lesions on a 46.3% of the cases studied. This can be compared to a 20% of cases with bilateral involvement in Kashyap and Sarkar study (2010). Gong emphasized that, pediatric pneumonia should be diagnosed based on clinical manifestations and radiographic evidence using CT scans.

On the other hand, Shu-Chiang et al. conducted a study in Taipei, Taiwan, were they evaluated a sample of 410 patients from which 39 had a positive diagnosis of MP measured with IgM-ELISA. The mean age was 6.4 years which is comparable with the literature. The most common clinical manifestations were cough and fever. Radiographic studies revealed that interstitial infiltrates were present in 49% of the cases but concisely, the chest radiographs were variable and non-specific. Like Gong (2016), Shu-Chiang and colleagues emphasized clinical

symptoms and radiographic evidence as diagnosis methods for MP. Nonetheless, unlike Gong, who focused on CT scans as a radiographic tool, Shu-Chiang at al. used chest X-rays as a tool for diagnosis. Sondergaard et al. (2018) showed lobar infiltrations in over 80% of the patients which is in accordance with Chiang (2007).

Season:

An increase in the incidence of respiratory diseases may be related to natural disasters. According to Mirsaeidi and colleagues (2016), whose study was conducted with efforts from the University of Miami and Chicago, climate change may have an impact in respiratory infections. There is evidence of a seasonal component on the incidence of cases of influenza and streptococcal pneumonia, being higher during winter months. Also, there have been reports of infection outbreaks related to climate change. Moreover, Shultz et al. (2018), developed a study regarding the 2017 hurricane season in the Caribbean and the effect in certain aspects of public health. As part of it, they emphasized the power outages in Puerto Rico due to hurricane Maria. The authors mentioned that one of the public health consequences of hurricanes impact is the temperature spikes that is one of the factors that provoke an increase in heat-related mortality such as respiratory and cardiovascular mortality.

MP is a respiratory condition that might be expected to behave in a certain way. In Medjo et al. study (2014), the diagnosis was dispersed across the year with a peak in fall (33.3%). Likewise, Sondergaard and colleagues (2018), in their study conducted in Denmark, they described the peak of MP diagnosis for two consecutive years. The peaks were October 2010 and fall 2011, which is in accordance with Medjo (2014).

On the other hand, Duenas Meza et al., (2016) in their study conducted in Colombia, described a seasonal behavior of MP in the population studied. An 85.7% of the MP cases were between the months of December and February which corresponds to winter months. Nevertheless, 39% of the cases presented in the study of Merida-Vieyra et al. (2019), conducted in Mexico, occurred in the spring.

Age:

MP is known to affect all ages. However, most authors agree that school-aged children are at greater risk, like Chaudhry et al. (2016). Similarly, 81.2% of patients from Amin and colleagues' (2018) study developed in Iran were 5 years and older. Kumar and colleagues (2018), in a study conducted in New Delhi, India, concluded that MP is more common in children 5 years of age and above as well. Medjo et al. (2014), in their study developed in Serbia with a sample of 166 children, found that 24 were diagnosed with MP. From those diagnosed patients, 75% were 5 years old and over which supports the previously mentioned authors. According to Sondergaard et al. (2018), the age range with higher prevalence was school-aged children (65%) but the prevalence in pre-school children was also significant (30%). These authors from around the world agree in a higher prevalence of MP in patients 5 years of age and above. Nonetheless, in a study conducted in México by Merida-Vieyra and colleagues (2019) 57% of the study subjects were younger than 5 years old. Similarly, Duenas Meza et al (2016), in their study conducted in Colombia, found a tendency to a higher prevalence of MP in children under 5 years old, but the difference was not significant. These contradictions are relevant given that it provides information concerning Hispanic children such as the ones evaluated in Puerto Rico.

Co-infections:

Zhang and co-authors (2018) conducted a study in China, where they found that from 396 patients with a diagnosis of MP evaluated, 107 were co-infected with another pathogen in addition to MP. The more common co-infection was MP and *Streptococcus pneumoniae* (S. pneumoniae). The co-infected children were younger and had a longer length of stay. Likewise, Sun et al. (2015) conducted another study in China, where they developed a cohort study involving 2174 patients under the age range of 1 month to 12 months, from which 80 were diagnosed with MP. They found that, the older the infant, the greater the possibility of contracting MP since 36 out of the 80 infants were between 9 and 12 months of age. Co-infections were also more common in this age group with 27.59% out of all the co-infected patients (17 in total). The most common co-infection was MP with RSV with a total of 5 patients. It was concluded that the older the infant the more severe the disease was, characterized with a longer hospital stay. This study stressed the importance of MP as an etiologic agent for infants. From the 1322 neonates, aged less than 29 days, 89 were diagnosed with MP. From those 89 patients, 17.8% were co-infected with RSV and 1.1% with influenza A (Huang et al., 2016).

Duenas Meza and colleagues (2016) described coinfections with a virus in 100% of the patients with MP in their study which is why they suggested that a viral infection may predispose an MP infection. Additionally, they stated that this coinfection may trigger acute asthma exacerbations.

Moreover, Dotres Martinez et al (2017), developed a study that related MP and other respiratory diagnosis. They (2017) developed a descriptive study with patients under the age group between 1 month to 15 years, where they divided patients into groups depending on a diagnosis of

pertussis-like syndrome, interstitial pneumonia or asthma. From 120 patients diagnosed with pertussis-like syndrome, 25.8% had MP and 71.6% of them were younger than 6 years of age. From 74 patients with interstitial pneumonia, 17 had MP and 47.1% of them were between 1 and 5 years old. Finally, from 30 patients with asthma, 9 were also diagnosed with MP. These results are interesting because most of the patients were younger than what the literature reports. This study was conducted in Cuba and since we conducted our study in Puerto Rico, patients of both studies have in common the Hispanic ethnicity and might share similar conclusions.

Correspondingly, Duenas Meza and colleagues (2016) conducted a cross-sectional study to determine the prevalence of viral and MP infections in children with asthma exacerbation. They included 169 children between the ages of 2-15 with an asthma diagnosis in a minimum of 6 months prior the ER admission in three hospitals in Colombia. The prevalence of MP in their study was 12.4%.

On a similar note, Dr. Kassisse and his colleagues (2018) conducted a study in Venezuela with patients 2-12 years old to determine the prevalence of MP in patients with acute asthma exacerbation. They found a close relation between the two illnesses since MP was present in 46% of the patients studied in their prospective, observational study, which is greater than the findings of Duenas Meza et al. (2016). The average age was 4.9 ± 1.2 years old and 53% were females. They also found a significant association between the severity of asthma and MP infection.

Similarly, Giavina-Bianchi and Kalil (2016), from Sao Paulo, Brazil reported a relationship between MP and asthma. These authors' work is significant for the researcher because of the possible relation between asthma and MP. This article explained that one condition may predispose the other. Asthma is an inflammatory disease of the airway, making it easier for MP to infect the

subject. Alternatively, MP, causes bronchial inflammation impairing pulmonary function. The authors refer to another study where the patients with MP and a higher incidence of asthma, were males, which is the opposite of what was found in Kassisse et al. (2018), were the majority were females. The researcher is aware of the high incidence of asthma in pediatric patients in Puerto Rico, specifically in the community hospital she choose to evaluate patients.

Diagnosis:

Regarding diagnosis of MP, authors differ on the best approach. Mansour Amin and his colleagues compare PCR, IgM ELISA and bacterial growth cultures as diagnostic methods. Since IgM antibodies arise before IgG antibodies, around a week after the disease onset, it is a common marker for serologic diagnosis. He concluded that combining PCR with the IgM ELISA as a method of diagnosis was a reliable approach. This study, concords with literature in terms of age range at risk and the diagnosis deficiency of bacterial growth culture (2018). Kumar et al. (2018) made emphasis in the necessity of serology to diagnose MP but clarified that the combination of ELISA and particle agglutination (PA) test is better than PCR, which has a low or variable sensitivity. This contrasts with Amin (2018) who suggested the combination of PCR with IgM ELISA. Moreover, Medjo et al. (2014) suggested that the detection of IgM antibodies combined with RT-PCR results is a precise diagnosis of acute MP. This supported Amin (2018) and contradicted Kumar's (2018) study, in which PCR was not as reliable as PA when diagnosing MP.

Huang et al. (2016) stated that PCR is a useful technique for diagnosing MP in patients who were unable to mount an immune response to MP because of their age or immunocompromised state. Dash et al. (2018) conducted a prospective study in New Delhi, India, that included 130 patients of all ages admitted with radiological evidence of pneumonia and 30 volunteers who

served as a control group. Only 18 patients tested positive to MP, 50% via culture, 44.4% serology, 27.7% PCR and 33.3% real-time PCR. The authors concluded that there is no single test which can efficiently detect an infection due to MP. Dash et al. suggested the combination of two or three tests to detect pneumonia caused by MP. The researcher was interested in the diagnosis methods of MP, and Dash et al. provided four methods used in India to diagnose this infection. The most prevalent method on this study was culture. This is an interesting fact, since other authors have stated that culture is not as reliable as other methods to diagnose MP on its own.

MP can lead to different infections of the respiratory tract and nervous system complications. Chen et al. (2015) conducted a study in China, where they evaluated 152 children under the age group between 1 month to 12 years and who were diagnosed with pneumonia. A PA assay was performed with the serum samples and a 90.8% tested positive (titer > 1:320). The length of stay was, in average, 10 days. The study found that 44.7% of children had MP and 55.3% were males. Moreover, 40% of the diagnosed patients presented wheezing. Chen et al. concluded that a treatment with antibiotics should start even before obtaining the serological result to decrease the morbidity rate and the duration of the symptoms.

As part of laboratory tests, the percentages of neutrophils and lymphocytes can be determined. Abnormal levels of these immune cells have been associated with viral or bacterial infections. In a study performed by Guo et al (2014) in China with patients with CAP caused by virus or MP, it was determined that the percentage of lymphocytes was an independent factor that could differentiate between viral and MP CAP. They emphasized that an increase in the lymphocyte percentage was related to viral pneumonia. In another study conducted in China, Wang et al. (2014) related an increase in the percentage of neutrophils to MP. They explained that there was a positive correlation between neutrophils and MP load.

Table 1. Age-specific Neutrophils and Lymphocytes values

Age	Neutrophils Mean (range)	%	Lymphocytes Mean (range)	%
1mo	3.8/ 1-8.5	35	6.0 (2.5–16.5)	56
6mo	3.8 (1–8.5)	32	7.3 (4–13.5)	61
1yr	3.5 (1.5–8.5)	31	7.0 (4–10.5)	61
2yr	3.5 (1.5–8.5)	33	6.3 (3–9.5)	59
4yr	3.8 (1.5–8.5)	4	4.5 (2–8)	50
6yr	4.3 (1.5–8)	5	3.5 (1.5–7)	42
8yr	4.4 (1.5–8)	53	3.3 (1.5–6.8)	39
10yr	4.4 (1.5–8.5)	54	3.1 (1.5–6.5)	38
16yr	4.4 (1.8–8)	57	2.8 (1.2–5.2)	35

Table 1. was adapted from table 14-6 titled Age-specific Leukocyte Differential from The Harriet Lane Handbook (2015).

Having presented the different diagnosis techniques that can be used to detect MP and the difference in reliability, it is necessary to explain what test to diagnose MP is used in the hospital where the study was conducted. Like one of the techniques utilize to analyze the serum by Ma, YJ. et al. (2015), the hospital where the study took place, used a test called "Immuno Card Mycoplasma". It is described as an Enzyme Immunoassay (EIA) for the detection of IgM to MP in human serum. It consists of a card with ports, one section for a control and another for the testing sample. When the test is reactive there is a change in color from colorless to blue in both ports. When it is nonreactive, only the control port will turn blue. Its performance has a relative sensitivity of 88% ± 6% while its relative specificity is of 90% ± 3%. The limitations of this test method relay on the fact that IgM for MP can remain in the body from 2-12 months in some cases. To compensate the limitations, it is suggested to also consider the clinical evaluation of the patient and any other available information obtained from diagnostic procedures.

Intensive Care Unit admissions:

Khoury et al. (2016) developed a retrospective study focused on the patients admitted to the ICU in a hospital in Jerusalem, Israel for a period of five years. From a sample of 416 patients, 16.3% were admitted to the ICU and 72.1% were transferred from the Emergency Room directly to the ICU. In addition, 48% of the sample were pediatric patients of which 4.6% received critical care. The authors found that the number of patients admitted to the ICU was substantial with a higher frequency in the adult and elderly population and hence MP is a pathogen that should be considered in patients with pneumonia admitted to the ICU.

Kutty and colleagues (2019) developed a study in which from 2254 patients (younger than

18 years of age) with CAP and tested for MP, 182 (8%) of the patients were diagnosed with MP. Their study indicated that 12% of the hospitalized children with MP required admission to the ICU. Moreover, MP was the bacteria most detected among the hospitalized children with CAP. In addition, is the study of Merida-Vieyra et al. (2019), 26.8% of the children studied had complications and 4.6% of them died.

Treatment:

Kumar et al. (2018) postulated that because MP does not have a cell wall, the most efficient way to treat it is with macrolide antibiotics. Furthermore, Kashyap and Sarkar (2010) described azithromycin as the most active macrolide antibiotic for the treatment of MP. However, there is a macrolide-resistant MP (MRMP) and have been rising to 90-100% in Asia. Chaudry et al. (2016) supports the severity of the rise in MRMP, particularly in China and Japan, but that has been emerging in the USA and European countries as well. Also, from Diaz et al. study (2015), conducted in the United States, 7 patients tested positive for MRMP and 6 were under the age group of 18 years old. The proportions of MRMP in the United States are like the ones reported in northern Europe (3%-10%). Diaz et al. emphasizes the importance to reduce inappropriate and unnecessary antibiotic prescription to prevent the increase of MRMP prevalence in the region.

Ishiguro and co-authors (2017) developed an observational study made in 9 hospitals in Japan where they compared 4 antibiotics in patients with MP. There were 109 patients with MP from which 59 had MRMP and 50 had macrolide- sensitive MP (MSMP). The mean age in both groups was 9 years. The effect of azithromycin and clarithromycin, which are the macrolides being investigated, on patients with MRMP was characterized by longer duration of fever when compared to patients with MSMP. Regarding the antibiotic minocycline, the fever lasted less days than in patients treated with macrolides. Concerning treatment of patients with MRMP with

tosufloxacin, the duration of fever was like the fever's duration of the patients treated with macrolides. In patients with MSMP, the duration of fever was shorter when treated with macrolides and minocycline as opposed to treatment with tosufloxacin. This study is useful because it considers how different hospitals treat the same bacteria and can provide significant results of the efficiency of certain antibiotics over other without conducting an experimental study.

Besides antibiotics, studies, have shown that steroids such as methylprednisolone can be beneficial in the treatment against MP. Shan, LS. and his colleagues conducted a study in China in 2017 to analyze the effectiveness a treatment combining azithromycin with intravenous immunoglobulin or methylprednisolone in children with refractory MP pneumonia. The study comprised 168 children aged 2-14 years hospitalized between 2013-2015. They demonstrated that the patients treated with the combination of azithromycin and the steroid improved faster than those patients who only received the antibiotic. The authors further stated that there were no adverse events.

In addition, many patients treated with steroids also receive histamine-2 blockers such as ranitidine and famotidine. This is because corticosteroids, if prescribed for more than one month for doses that exceeds 1000mg can become ulcerogenic. According to a recent study developed by Sochet and his colleagues (2019) in which 217 children ages 5-18 years with status asthmaticus were included, there was no incidence of clinically important bleeding. Nonetheless, experimental studies and studies in animals have established that corticosteroids impair gastric functions that can result in ulcers. However, in clinical studies, the incidence of ulcers due to steroids is not as expected (Guslandi, 2013). For this reason, some authors suggest a target assessment of the presence of ulcers and other risk factors prior the administration of stress ulcer prophylaxis.

To summarize, MP is a pathogen that manifests in various ways affecting the respiratory tract and provoking extrapulmonary manifestations in many cases. Its prevalence is higher in patients over five years old, but cases of MP on patients under 5 years are also significant. Because of the diverse symptoms and lack of a specific test that could detect MP in its early stages, the condition might worsen or go underdiagnosed. Co-infections are also common, particularly in pediatric patients. Macrolides, like azithromycin, are the most frequently used treatment. Nonetheless, cases of a MRMP have been on the rise, especially in Asia. Studies regarding MP in Puerto Rico were not found, but a local newspaper has published two articles referring the rise of MP cases in pediatric patients and the increase of admissions with this condition in PICU. Because MP is a recurrent diagnosis in pediatric patients, we designed this study to evaluate the prevalence and clinical course of patients admitted to the PICU with MP in a community hospital in Puerto Rico.

Chapter 3: Methods

Study design:

The present study followed a quantitative methodology and a descriptive, cross sectional, non-experimental design. It is a cross-sectional retrospective study that evaluated patients' medical records from a community hospital in Puerto Rico. The medical records that the researcher evaluated were from patients diagnosed with MP between July 2015 and June 2018 and who were admitted to the Pediatric Intensive Care Unit (PICU) during their hospital stay. The study period was chosen to begin on July 2015 because it was when the electronic medical record at the institution where the study took place was introduced. Moreover, it was decided to include patients until June 2018 because that way three years-worth of data were collected, which was good to evaluate a representative sample within the time available to conduct the study. Furthermore, the

study period was divided into respiratory illnesses seasons which run from June to July. This way, three seasons were evaluated: 2015-2016, 2016-2017 and 2017-2018.

This is a correlational study because it compared variables looking for an association. The data were cross sectional since the researcher collected it from a define moment in time. Also, since a descriptive approach was followed, the study can be described as non-experimental because no experiment was conducted, and no variables were manipulated. Data was collected to look for similarities and differences between groups of patients. Given that the expected sample size was small, the sample was divided into two groups to be able to make more reliable comparisons by having similar number of patients in each group. The age cut-off was chosen to be 5 years of age since it was an age cut-off commonly found during the literature review.

Study subjects:

The current study included patients that were admitted to PICU at San Jorge Children and Women's Hospital in San Juan, Puerto Rico from July 2015 to June 2018 with a diagnosis of MP. The inclusion criteria for the study was patients under the age group of 0 to 21 years of both sexes with a confirmed diagnosis of MP and who received care in PICU. A list of patients fitting these criteria was obtained based on the ICD10 from the Medical Record Office of the hospital. There was an estimated number of 70 patients, but the sample was not restricted to this number because the exact number of patients that met the inclusion criteria was uncertain. Patients were excluded from the study if they had incomplete clinical or laboratory data or if their length of stay at the hospital was shorter than 24 hours.

Data collection:

To conduct this study, it was submitted for approval by the San Jorge Children and Women's Hospital Institutional Review Board and by the "Comité Institucional para la Protección de los Seres Humanos en la Investigación" (CIPSHI) from the University of Puerto Rico, Rio Piedras Campus. After obtaining the list of patients with the required diagnosis from the Medical Record Office, a master list was created to assign a subject ID for each patient. Patient's identity was not linked to their information while analyzing the data. Clinical, demographics, laboratory and radiological information was collected retrospectively from the patient's medical record, along with the health insurance (please refer to Patients Extraction Sheet: MP Study). Chest radiographs were read by a pediatric radiologist. Blood cultures were evaluated to analyze white blood cells (WBC), neutrophils (N%), lymphocytes (%L), IgM, IgG. Microbiological tests were considered to identify the presence of a MP infection and other respiratory tract infections, particularly, Influenza virus A, Influenza virus B and Respiratory syncytial virus (RSV). Moreover, the patient's municipality of origin were classified by the same seven health regions the Health Department of Puerto Rico categorizes the 78 municipalities of Puerto Rico. These are Mayaguez, Arecibo, Bayamon, Metro, Fajardo, Caguas and Ponce. Table 2 showed the distribution of the municipalities by the health regions.

Table 2. Health Regions of the Health Department of the Government of Puerto Rico

Health Regions						
Mayaguez	Arecibo	Bayamón	Metro	Fajardo	Caguas	Ponce
Aguadilla	Quebradillas	Vega Alta	Guaynabo	Río	Aibonito	Guánica
Isabela	Camuy	Dorado	San Juan	Grande	Cidra	Yauco
Moca	Hatillo	Toa Baja	Trujillo	Luquillo	Cayey	Adjuntas
Aguada	Arecibo	Cataño	Alto	Fajardo	Aguas	Guayanilla
Rincón	Barceloneta	Bayamón	Carolina	Ceiba	Buenas	Peñuelas
Añasco	Manatí	Toa Alta	Loíza	Culebra	Caguas	Jayuya
San Sebastián	Vega Baja	Corozal	Canóvanas	Vieques	Gurabo	Ponce
Las Marías	Florida	Naranjito			San Lorenzo	Juana Díaz
Mayaguez	Morovis	Comerío			Juncos	Villalba
Maricao	Ciales	Barranquitas			Las Piedras	Coamo
Hormigueros	Utuado	Orocovis			Yabucoa	Santa Isabel
San Germán	Lares				Maunabo	Salinas
Sabana					Humacao	Guayama
Grande					Naguabo	Arroyo
Cabo Rojo						Patillas
Lajas						

Table 2. was created with the information provided by the figure tittled "Mapa de Regiones y Facilidades de Salud" of the website of the Health Department of the Government of Puerto Rico (Departamento de Salud, gobierno de Puerto Rico, 2019).

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Statistical analysis:

Statistical analysis was performed using GraphPad® Prism 8 and Stata® 13 software. Data was expressed as percentiles or medians ± 95% CI as appropriate. For continuous data, a D'Agostino & Pearson normality test was conducted to determine if data had a normal distribution. Because data was not normally distributed, a Mann-Whitney test was used to compare two groups. Finally, a two-sample t-test for percentages will be used to compare percentages. Patients were divided into two groups, <5 years, and ≥5 years, to perform comparisons. The level of significance was established as be $P< 0.05$.

Work Calendar

The firsts months were dedicated to collect data from the patients. The process consisted in accessing the electronic medical record of patients. The lists of patients that follow the inclusion criteria was provided by the Medical Record Office director of the Hospital. The data was collected in the document titled: **Patient's extraction sheet: Mycoplasma pneumoniae study**, which is enclosed in Appendix 1. Afterwards, a digital data base was created in excel to organize data for analysis. The statistical analysis was conducted using GraphPad Prism® 8 and Stata® 13 software. After results were analyzed, and then conclusions were formulated.

Limitations:

Because the present study is retrospective and the data was extracted from electronic medical records, the researcher depended on documentation form the hospital personnel during patient's admission. The researcher extracted data form notes from: emergency department physicians, PICU physicians, radiologists, nurses, and other specialists that were involved in the patient's care while hospitalized at the studied institution.

Another limitation of this study is related to the fact that MP has a long incubation period and affects people differently. For this reason, not every person infected with MP seeks medical attention and others do not require hospitalization. In addition, some diagnosis procedures may result in false positives, which mean that the inclusion of a patient who do not have the condition being included in the study. To minimize this risk, this study was retrospective to review the diagnosis of the patient along their stay and select those who have a confirmed diagnosis of MP.

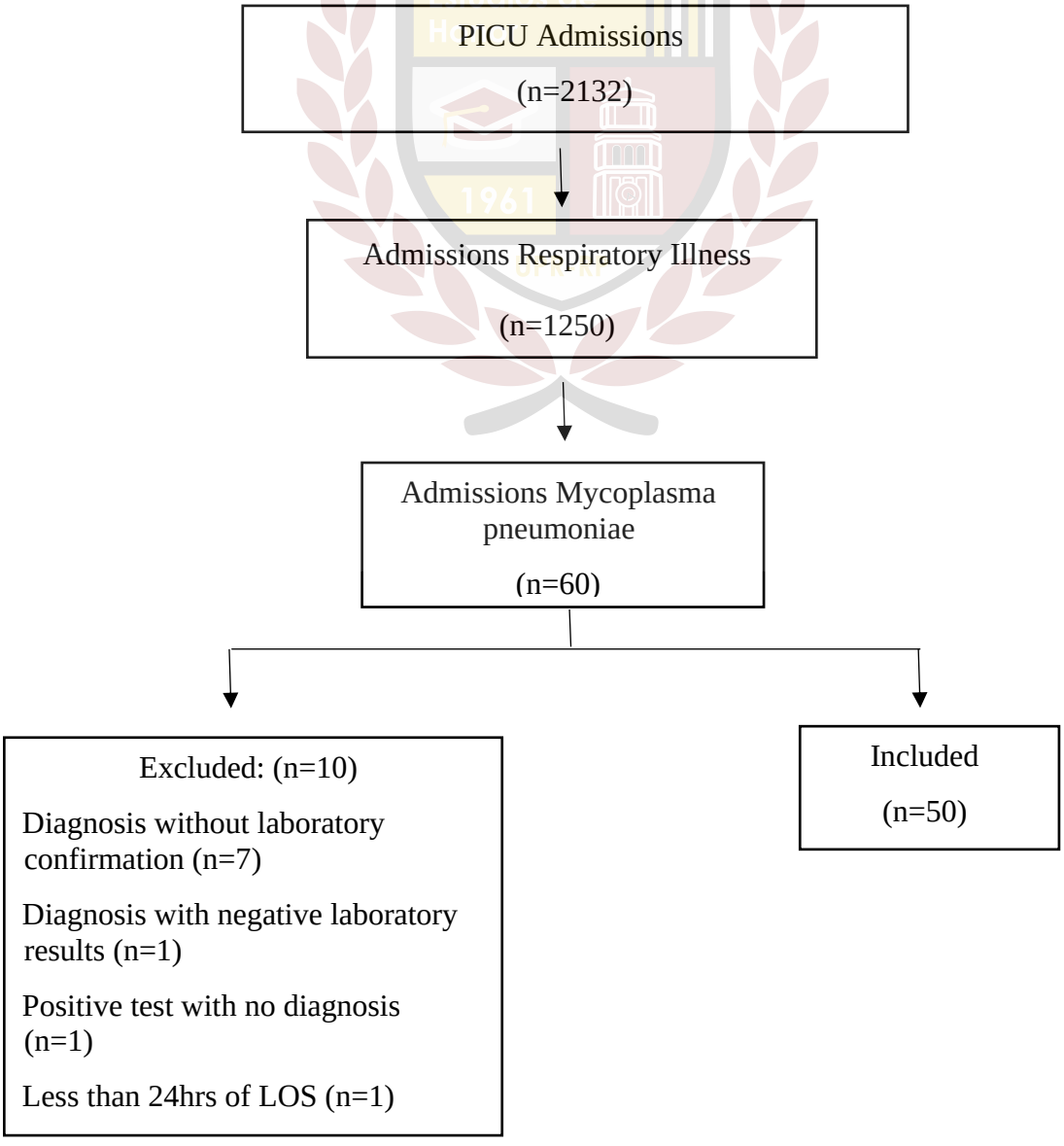
It is important to acknowledge that due to the MP diagnosis method of the hospital where the study was conducted, a certainty of a positive diagnosis cannot be given. Nonetheless, the study is conducted under the assumptions that the diagnosis was not made solely based on the laboratory test, but clinical symptoms and radiographic evidence was taken under consideration as well. To minimize the probability of false positives, patients with a positive laboratory test but no written diagnosis by the doctor taking care of the patient, was excluded from the study. In addition, patients without a positive laboratory test were also excluded. This is because the diagnosis was probably not made because the attending doctor, most likely, acted under the assumption that the test was a false positive due to the rest of his assessment of the patient. Nevertheless, patients without a positive laboratory test were also excluded because laboratory results are still valuable information worth looking into.

Chapter 3: Results

Study sample: Demographics and description

In the present section, the study sample is primarily described from the eligibility for inclusion process to clinical data. Comparisons were made concerning the admission date and by dividing the sample into age groups. The health regions were based on the divisions made by the Health Department of the government of Puerto Rico which were described on Table 2.

Figure 1. Patients eligibility process



The PICU Admissions number and the Admissions with Respiratory illness were extracted from the admission record books of the PICU. The admissions due to MP were provided by the Medical Record Office of the hospital. Since the list included all the admissions due to MP the present study focused on those patients who required admission to PICU, the researcher reviewed each patient provided and out of 430 patients, 60 were admitted to PICU, which was close to the 70 patients that were estimated when the study proposal was developed. Out of those 60 patients, 10 were excluded due to the above specifications, which is why the study was conducted with 50 patients.

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Table 3. Demographics

Variable	Mean value ±SD. or percentage (n)
Sex	
Male	70% (35)
Female	30% (15)
Age (in months)	77.1
Health Region	
Metro	68% (34)
Bayamón	12% (6)
Caguas	6% (3)
Arecibo	4% (2)
Mayaguez	4% (2)
Ponce	2% (1)
Fajardo	0
Other	4% (2)
Insurance	
Government	60% (30)
Private	40% (20)
PICU LOS	5.22 days
<5 years old	4.250 ± 2.511
≥5 years old	5.867 ± 5.309
Hospital LOS	11.66 days
<5 years old	11.25 ± 4.229
≥5 years old	11.93 ± 6.741

The "Other" category in the Health Region section included patients who did not live in Puerto Rico in the study period. Both patients designated to this category where from the United States, specifically Philadelphia and New Jersey. LOS stands for length of stay.

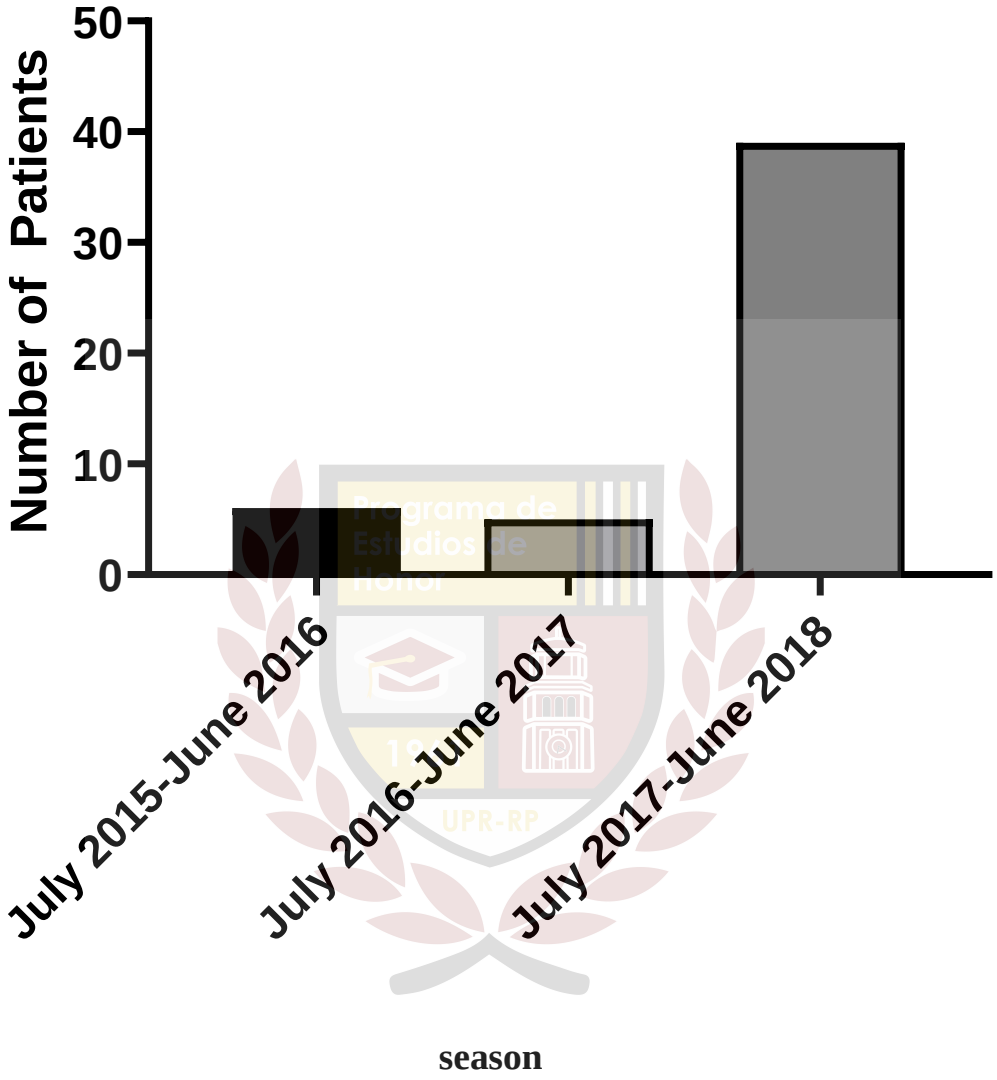

Figure 2. Number of Patients Confirmed with *Mycoplama Pneumoniae* Admitted to the Pediatric Intensive Care Unit. It displays the number of patients enrolled in the study categorized per season of admission (July-June). There is a marked difference between the MP admissions of the first two seasons compared to the July 2017- June 2018 season. These are interesting findings because during that third season Hurricane Maria hit Puerto Rico as a category 5 hurricane.

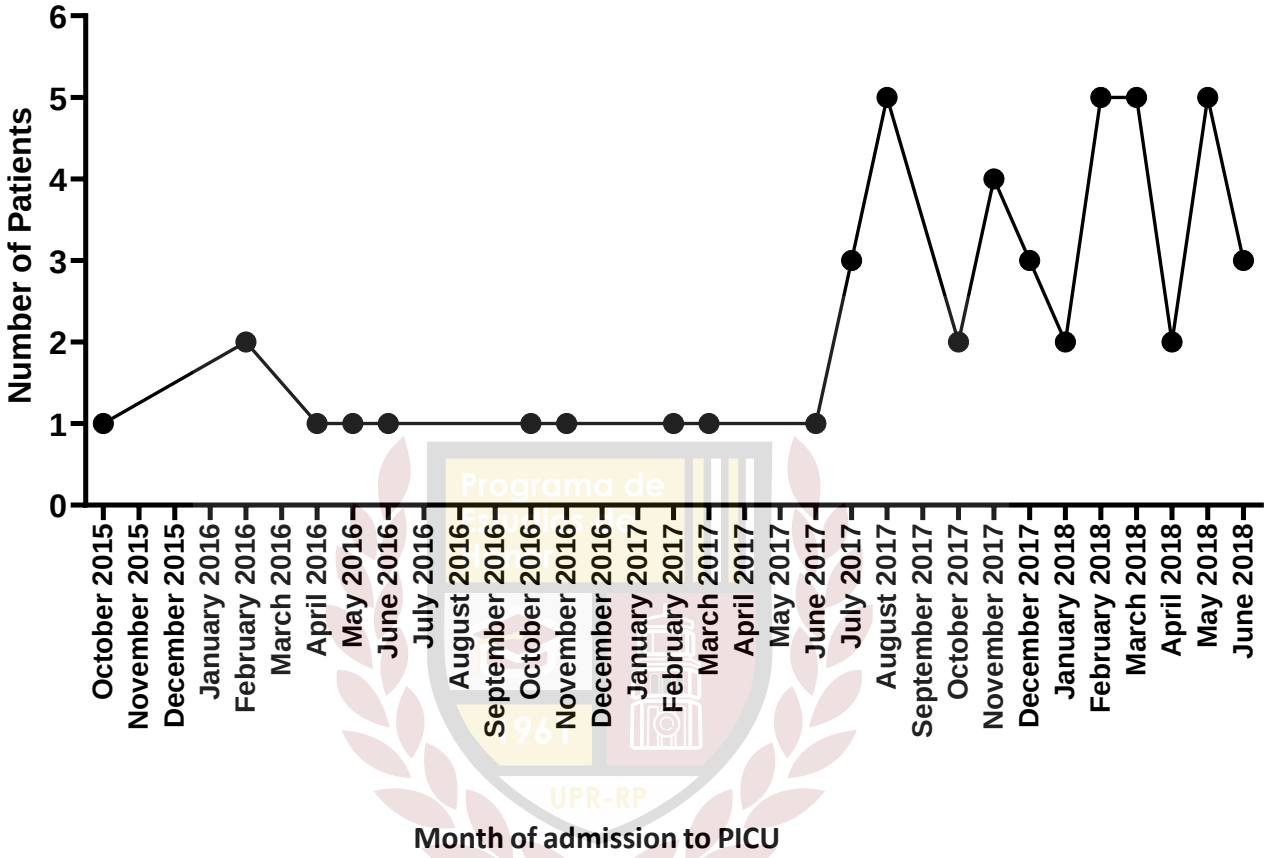

Figure 3. Number of patients admitted per month due to *Mycoplasma pneumoniae*. It showed the amount of admissions to the Pediatric Intensive Care Unit per month. Additionally, it confirms Figure 2 in showing how the PICU admissions distinctively increased in 2017 and 2018, especially after June 2017. The graph shows how MP admissions occur throughout the year on a similar basis with no marked differences among the seasons. Moreover, it can be seen how the admissions remained stable for about a year and afterward became inconsistent from month to month which is portrayed by the multiple peaks at the right corner of the graph.

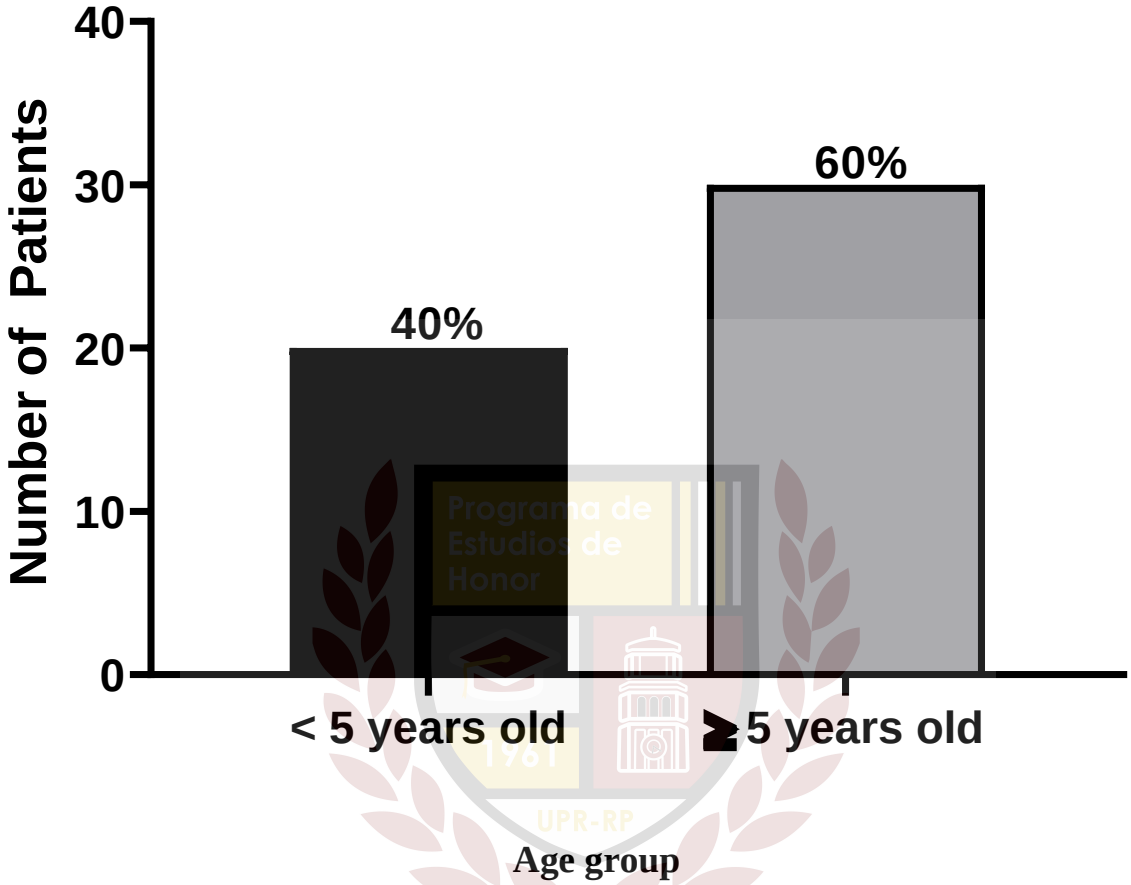

Figure 4. Number of patients with Mycoplasma pneumoniae categorized by age group.

It represents the number of study subjects categorized into two age groups: less than 5 years old and 5-21 years of age. Most patients were 5 years or older. Nonetheless, the difference between the groups is not significant (p = 0.17).

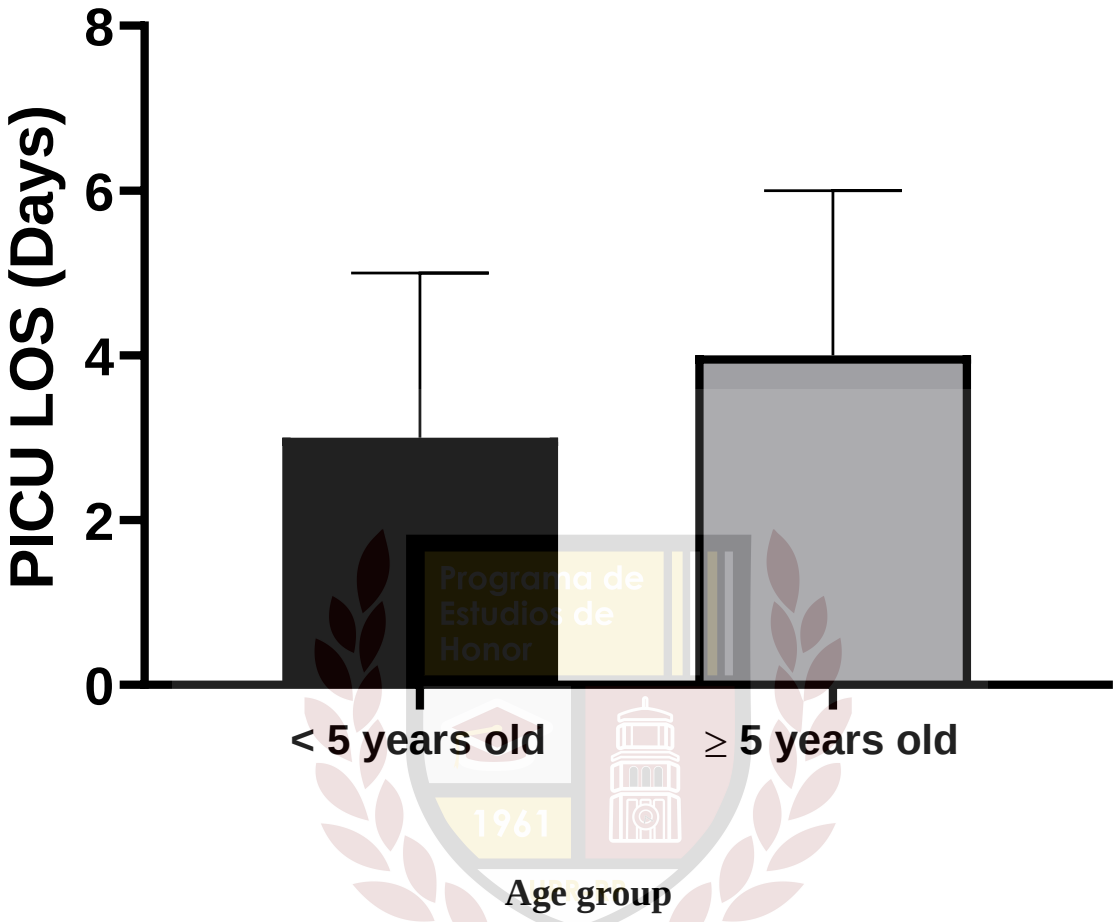

Figure 5. PICU Length of stay of patients. It depicts the relationship between how long the patients remain hospitalized and their age. There was no significant difference among the groups in their ICU stay (p= 0.43).

Patients' profile

This study evaluated events of MP cases in a community hospital in San Juan. By comparing the medical record number of each of the cases available with a diagnosis of MP during the study period, it was determined that each subject is in fact a different patient. This means that there were no instances in which the same patient had more than one admission at the chosen institution during the study period. In addition, not all patients were diagnosed with MP at the time of admission. Some were diagnosed early in their stay at the hospital or had other problems that were in more eminent need of attention. For these cases, MP was regarded either as a final principal diagnosis or as a secondary diagnosis. The following section presents the profile of the patients which includes clinical symptoms and laboratory and radiographic findings among other clinical information.

Table 4. Patient's Profile

Variable	Percentage (n)
Admission Diagnosis	
Pneumonia due to MP	46% (23)
Asthma	38% (19)
Other respiratory conditions	12% (6)
Other	4% (2)
Secondary Diagnosis of MP	12% (6)
Final Principal Diagnosis	42% (21)
Origin	
Emergency Department	72% (36)
Ward	20% (10)
Other hospital	8% (4)
Comorbidities	
Premature birth	6% (3)
Asthma history	42% (21)
Neurologic condition	10% (5)
Genetic condition	6% (3)
None	44% (22)
Clinical Symptoms	
Fever	50% (25)
Cough	88% (44)
Wheezing	86% (43)
Shortness of breath	62% (31)
Fast breathing	62% (31)
Chest retractions	78% (39)
Dermatological manifestation	16% (8)
Vomit	18% (9)
Laboratory findings	
Neutrophils %	92% (46)
Lymphocytes %	94% (47)
MycopAB	80% (40)
MycopIgM	20% (10)
MycopIgG	8% (4)

Table 4. Patient's Profile (Continuation)

Variable	Percentage (n)
Radiographic findings	
Atelectasis	58% (29)
Infiltrates	58% (29)
Bronchitis/Bronchiolitis	10% (5)
Pleural effusion	8% (4)
Peribronchial cuffing/ wall thickening	16% (8)
Bronchial asthma	20% (10)
pneumonia	10% (5)

From the 27 patients who were not admitted because of a diagnosis of MP, at the end of their hospital stay, 8 had a diagnosis of MP as a secondary diagnosis and 22 had MP described as a final principal diagnosis. Neutrophils % and lymphocytes % represent the percentage and number of patients who had abnormal levels of each type of leukocyte. MycopAB is the name given to the test provided by the Immuno Card Mycoplasma, which detects IgM to MP. MycopIgM and MycopIgG are other tests that measure IgM and IgG to MP respectively.

Examining the admission and discharge physicians notes of the patients we noticed that the most common diagnosis at the time of admission to the hospital were pneumonia due to MP and asthma. MP was described as a secondary diagnosis in 12% of the cases and as final principal diagnosis in 42% of the cases. Furthermore, since only the patients admitted to PICU were included, three possible origin prior the admission to PICU were described. These were: admission from the emergency department, transfer from ward or transfer from other hospital. There was a notable majority of 72% of patients who after assessment at the emergency department, required intensive care. Only 10 study subjects, equivalent to a 20% were admitted to PICU after receiving treatment in ward with no improvement. The remaining 8% of patients were transferred from other hospitals and, upon arrival, were directly admitted to PICU. The PICU admission of the latter group of patients is expected because usually when patients are transferred to other institutions is

because their condition is, although stable, delicate and the other institution is better equipped to provide the care they need.

Comorbidities were categorized into four groups: premature birth, a history of asthma, neurologic condition or genetic condition. The most prevalent one was a history of asthma while a minority of patients had a neurologic or genetic condition or were born prematurely. It is important to clarify that some patients fit into more than one category by, for example, being born prematurely and having a history of asthma which is why, when adding the number of patients included into each category, the result is greater than the sample studied.

The most common clinical manifestation was cough including one case of cough with blood. Following cough, other respiratory symptoms such as wheezing, and chest retractions were mostly described. Fever was present in half of the patients enrolled in the study and dermatological manifestations and vomiting were present in a minority of the cases studied. The most prevalent dermatological manifestation in the study was dry skin, accounting for 50% of the patients with dermatological manifestations. Following dry skin, rash that was either localized or all over the patient's body was noted and one case presented with pallor and mottled skin.

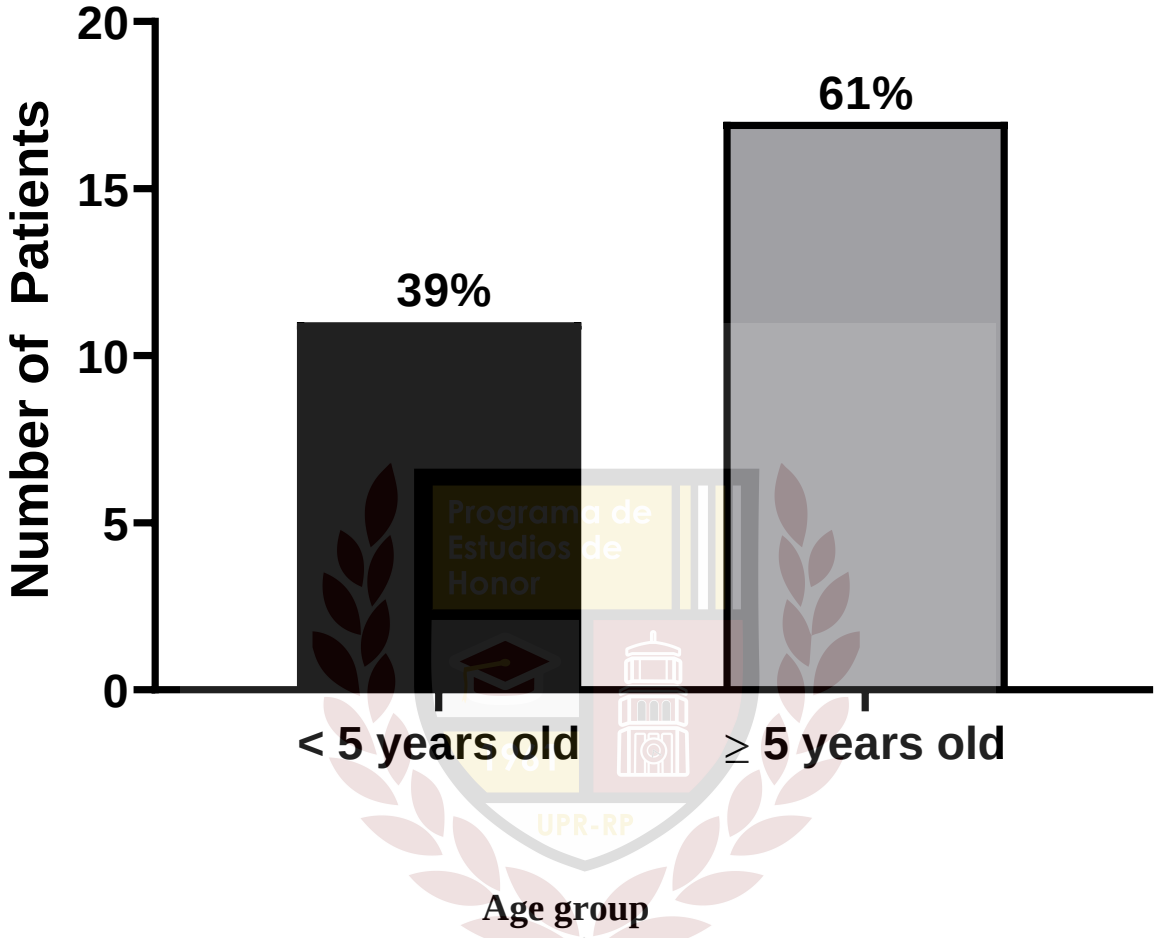

Figure 6. Patients with lung infiltrates. It depicts the presence of lung infiltrates detected by the chest x-rays according to the age groups. Even though the older patients presented many of the infiltrate cases, the difference was not significant (p = 0.28).

Every patient evaluated for this study had a chest X-ray performed to look for radiographic evidence. Atelectasis and infiltrates were the most common with a prevalence of 58%. Wall thickening and pleural effusions were also noted in some cases. In 20% of the cases, the radiologist suggested that the patient may be suffering from asthma while in 10% of the radiographs, indications of pneumonia or bronchitis and bronchiolitis were found.

Pharmacologic and Respiratory Treatment

Mycoplasma pneumoniae is commonly treated with macrolide antibiotics. Nonetheless, when the infection is complicated by other illnesses or vice versa, another condition is worsened by MP, more medicines are needed. Moreover, the medicines used to treat the illnesses cause side effects that in turn, require pharmacological treatment. Also, respiratory therapies are demanded to treat the pulmonary manifestations in addition to oxygen and mechanical ventilation support. This section presented the most common medicines and respiratory support received by the patients during their stay at the hospital, both in PICU and in ward.

Table 5. Clinical Management

Variable	Percentage (n)
Respiratory Support	
Oxygen Support	98% (49)
Mechanical Ventilation	28% (14)
Mechanical Ventilation type	
BPAP	32% (16)
CPAP	4% (2)
Endotracheal tube	4% (2)
Mechanical Ventilation Time	
<5 years old	3.429 ± 1.988
≥5 years old	6.857 ± 5.014
Medications	
Steroids	92% (46)
Albuterol/Levalbuterol	100% (50)
Ranitidine/ Famotidine	90% (45)
Ipratropium	46% (23)
Budesonide	84% (42)
Acetaminophen	36% (18)
Antibiotics	
Azithromycin	100% (50)
Ceftriaxone	56% (28)
Clyndamycin	12% (6)
Cefepime	10% (5)

BPAP is an acronym for Bilevel positive airway pressure
CPAP stands for Continuous positive airway pressure
To make the calculations concerning mechanical ventilation, 2 patients were excluded because due to a previous condition, they use BPAP for sleep at hospital and at home. They were both over five years old.

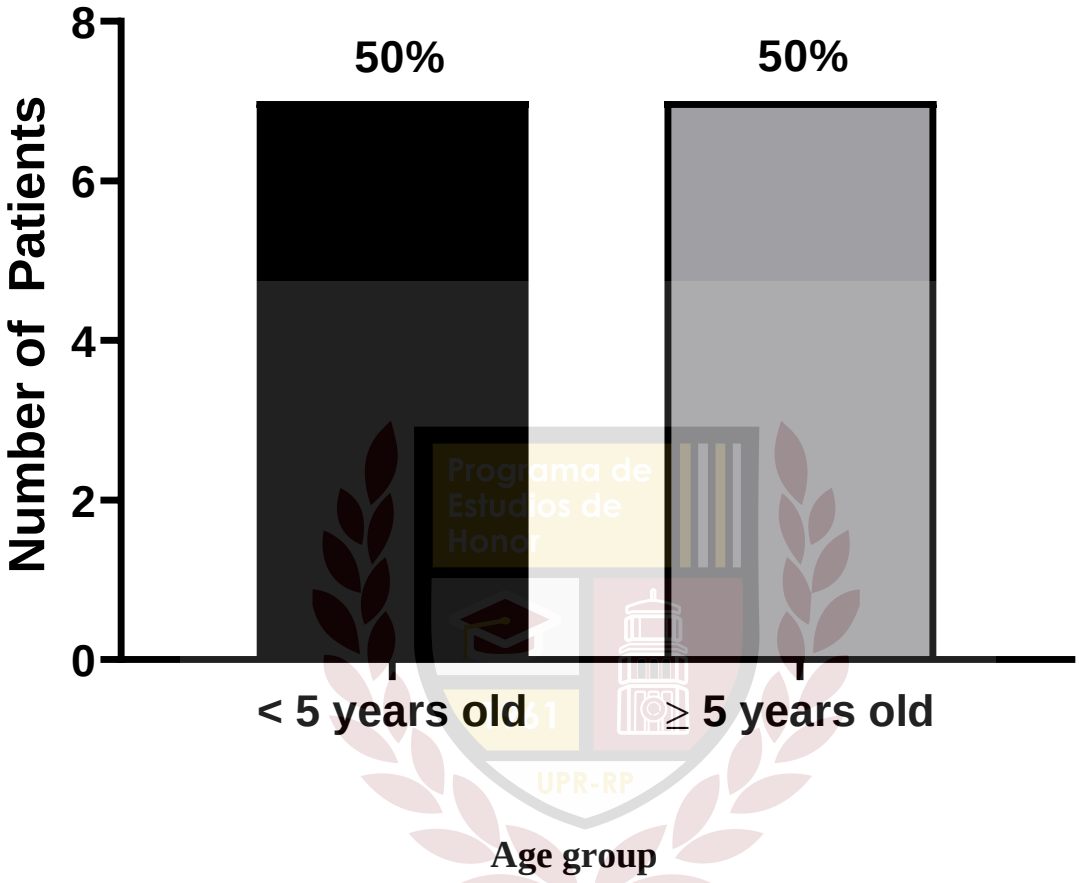

Figure 7. Patients on mechanical ventilation support. The figure above presents the number of patients who needed mechanical ventilation support during their PICU stay distributed by age groups. Although 32% of patients were treated with mechanical ventilation during their stay, only 28% was included in the graph above given that the patients excluded were on mechanical ventilation prior the hospitalization.

Chapter 5: Discussion

The patients included in the sample were mainly males. This supports the findings of Giavina-Bianchi and Kalil (2016) and Chen et al. (2015) who found that most patients in their studies where males. However, the difference is more marked in this study since 70% of the patients compared to a 55.3% of the patients in Chen et al. (2015) study were males. Furthermore, the mean age of the patients was 77.1 months which is equivalent to 6 years of age. These findings concords with the literature review. It is also worth mentioning, that although the study included patients from 0-21 years of age, the older patient was 14 years old.

Regarding the health region, most patients, 68%, were part of the Metro region, which includes San Juan. Given that the hospital where the study was conducted is in San Juan, it was expected that this region was the most common concerning the municipality of origin of the patients included in the study. Following, the Metro region, Bayamón and Caguas were the regions with more patients assigned to with a 12% and 6% of the patients respectively. These regions are bordering the metro region which could explain why they contain more patients than the remaining health regions. It is worth mentioning that the patient described as a member of the Ponce region and one of the patients categorized in the Arecibo region were transferred to the institution via ambulance to receive better care. This justifies why patients from further regions were hospitalized in the studied institution. Moreover, the 4% of the patients who reside in the United States rather than in Puerto Rico, were visiting family on the Island which explains why they were hospitalized in the medical institution chosen for this study.

The patients had mainly a government's insurance, although the hospital studied is a private institution. This could mean that many of the patients in the study come from low-income families. Low economic resources could influence their admission to PICU, not only because of difficulties

costing maintenance medications, but also for their poor access to primary health care. The average length of stay (LOS) of 11.66 days can be compared to the studies of Gong et al. (2016) in which a mean LOS of 8.9 ± 2.1 days was reported. Similarly, in Chen's et al. (2015), the average LOS was 10 days. The average LOS of the present study is longer than these two studies (11.66 days). This could be attributed to several factors, a poor response to the albuterol treatment in Puerto Rican patients, for example.

The findings shown on Figure 2 support Dr. Ramos statements with reference to a raise in PICU admissions due to MP when interviewed in Parés Arroyo's (2018) article. This is alarming because the cases of the July 2017- June 2018 season are approximately triple the cases of the first two seasons combined. The fact that Hurricane Maria hit Puerto Rico that same season should be mentioned. As stated by Mirsaeidi and colleagues (2016), respiratory infections may be affected by climate change. A natural disaster such as a category 5 hurricane devastating Puerto Rico on September 20, 2017 is a significant environmental event that might have contributed in the marked increase of PICU admissions of patients with MP. Moreover, Shultz et al. (2018) mentioned how public health is affected by heat-related mortality such as respiratory mortality and emphasized the problem of the power outages Puerto Rico suffered. The impact to the infrastructure of Puerto Rico and the measures taken to deal with the aftermath of Hurricane Maria could have been concerning as well. For instance, the inaccessibility to health care for some people and the gas emitted by power generators can be harmful for some people.

To exemplify how Hurricane Maria and its aftermath affected the health of the pediatric community, three cases are presented below. In all, Hurricane Maria can be cataloged as a contributing factor for the deterioration of the children's health. Although the cases are true, some details were changed to protect the identity of the children.

Case 1:

An obese 8 years old boy with a history of asthma. One day on December 2017, he presented respiratory distressed and collapsed at his house. His dad managed to resuscitate him giving him mouth to mouth. An ambulance took him to a nearby hospital where he arrived in respiratory failure. He was transferred to the studied hospital and admitted with a diagnosis of moderate persistent asthma with (acute) exacerbation. His parents explained that there were power generators near their home and that follow up with their son's pneumologist was hard.

Case 2:

A 10-year-old girl with a history of asthma. When she started with cough on October 2017, her mom tried to take her to her pediatrician but was unavailable due to emergency after Maria. Her conditioned worsened which is why a few days later she was taken to the emergency room. She was admitted straight to PICU with a diagnosis of pneumonia due to MP.

Case 3:

A 13 years old and had her asthma under control until September 2017. She had no electricity at her house which is why her mom was treating her with an albuterol pump. One day on December 2017, she was not feeling well at school and her mom picked her up and took her to her job. Since there was electricity at her mom's job, she was able to take albuterol with power nebulizer, but she did not improve and was taken to the hospital. Amanda was admitted straight to PICU with a diagnosis of pneumonia due to MP.

In the cases presented the patients had a medical history of asthma which might have made them more prone to be affected by the post-hurricane environment. Among the post-hurricane factors, the lack of electricity was a problem for people who required maintenance medicine or instruments such as electric nebulizers (case 3). Not everyone had the economic resources to own

a power generator and obtained gasoline, which was being rationed. Those who had them, were presented with a double edge sword. This is because power generators, on one hand provide electricity, but on the other emit smoke that could trigger respiratory problems just as suspected on case 1.

Lack of electricity also affects primary care because private medical offices could not open if there is no power, which might have been what happened in case 2. In addition, this case was about a month after the hurricane and at that time, many people were still working on personal issues since many lost their properties and some lost family members which could also justify why a doctor did not open his office.

Furthermore, the infrastructure of Puerto Rico was severely damaged, and lack of power, water and communication are some examples. After the hurricane many resources were being rationed such as gasoline, batteries and bottled water. The amount of money allowed to be extracted from the ATMs was also limited, which left many people with a reduce money to cover all their expenses since debit and credit cards were not being accepted in many places. Financial circumstances and access to a pharmacy with the required medicine could also mean that a previous condition was not being appropriately treated which will compromise a child's health.

Some of these mentioned factors might also explain why so many patients were admitted to PICU straight from the emergency department. The inaccessibility to primary care may explain why the children's health's declined enough to require PICU admissions since they did not receive appropriate primary care or were unable to reach a hospital sooner due to problems with roads and transportation. Similarly, follow up check ups became compromised which in turn, negatively impacts the health care of the children. Moreover, no electricity at home could compromise maintenance treatment which could cause a rapid progression of the disease.

To summarize, there might have not been a seasonal component on admissions to PICU due to MP. However, the impact of a hurricane might be an important factor to justify why the admissions increased the way they did.

Similarly, to Figure 2, Figure 3 depicted the increase in admissions, but it also specifies the month of admission. The findings agree with Medjo and colleagues' (2014) in that the diagnosis is dispersed across the year but are not in accordance with the same authors and Sondergaard et al. (2018) when they described a peak in the fall months. With the information provided, our hypothesis regarding the seasonality of MP with peaks in fall is rejected since the results showed no marked difference between seasons. Furthermore, it can be stated that admissions of patients with MP to PICU remained fairly similar throughout the year with the peculiarity that in the last year of the study they increased and became irregular having one patient admitted on one month and five PICU admissions two months later.

Regarding the findings on Figure 4, there were somewhat conflicting with what was found during the literature review. On one part, its concords with most authors cited regarding that school-aged children were at greater risk of contracting MP which is supported by Kumar and colleagues (2018), and both Medjo et al. (2014) and Amin et al. (2018). On the other hand, the difference was not significant, which is why, according to these findings, age shouldn't be a factor to diagnose MP and that patients under 5 years old should be given the same consideration when MP is suspected.

Likewise, Figure 5 portrays no significant difference between the length of stay in PICU when comparing the younger children with the older ones. These findings contradict the study of Ma, YJ., and colleagues (2015) who found that the patients younger than 5 years of age had a longer hospitalization than the older patients.

Regarding reason for admission, in this study, 38% of the subjects received a diagnosis of asthma at the time of admission but were also treated for MP. This is supported by Kassisse et al. (2018) who relate asthma to MP after describing a prevalence of MP in 46% of their study subjects who also had a diagnosis of asthma. Both the present study and the one by Dr. Kassisse and his colleagues had a higher incidence of MP in patients with asthma than the study of Duenas Meza which was conducted in 2016 and in which the prevalence was of 12.4%. Considering what Giavina-Bianchi and Kalil (2016) stipulated concerning the probability that one condition, either MP or asthma, may predispose the other, it could be added that it could have also worsened the condition of the patient causing an admission to the PICU.

We found that 72% of the patients admitted to PICU were admitted straight from the emergency room. This can be compared with the 72.1% of the patients from Khoury et al. (2016)'s study who were admitted to the ICU that came directly from the emergency room. Nonetheless, it should be noted that this sample contains patients of all ages from which only, 48% of the sample were pediatric patients and 4.6% required intensive care. Having such a big percentage of patients admitted straight to the PICU after being assessed at the emergency department should be alarming because it suggests a problem at the primary care level. One explanation may be that parents do not fully understand the symptoms that signal a need for a hospital visit and wait to see if the minor gets better allowing time for their condition to worsen, requiring immediate PICU admission. Another reason could be that the primary care physician belittles the gravity of the situation. Finally, the high percentage of patients that require PICU admissions early in their hospital stay could mean that the condition is progressing at a faster rate than the necessary to realize that the minor is in distress and requires hospital intervention. Either way, education involving the

prevalence of MP and the risks associated with it for the pediatric population is necessary as a method to create awareness and reduce the need for an admission to PICU.

Kutty and colleagues (2019) included underlying conditions of the patients studied with MP. In comparison to the ones presented in the present study, 30% had asthma or a reactive airway disease, while 29% had a preterm birth. Concerning a history of asthma, the patients included in this study had a higher prevalence of this illness with 42%. However, just 6% were born prematurely which is about 1/5 of the percentage presented by Kutty at al. In terms of neurological and chromosomal disorders, Kutty and colleagues presented 6% and 9% of cases respectively while in this study the prevalence was of 10% and 6% respectively.

When discussing the clinical symptoms with was found during the literature review process, it can be can be said that in the study by Khoury et al. (2016), cough was present in 49.3% of the patients which accounts for 33 patients out of 67 who were admitted to the Intensive Care Unit. However, in the present study, cough was described in 88% of the sample. This percentage relates more to the findings of Kutty and colleagues (2019) who presented an incidence of 96% of cough and fever. A 67.8% of the subjects of Khoury et a. (2016) developed fever in comparison with 50% that was found in this study. Moreover, 44% presented wheezing while chest retractions were described in 25% of the patients in the study by Kutty et al. (2019). These findings are low when compared to the 86% and 78% of this study respectively.

Concerning laboratory findings, most patients presented abnormal levels of neutrophils and lymphocytes percentages. Specifically, the levels of neutrophils were abnormally high, while the levels of lymphocytes were abnormally low. This combination has been found to be associated with bacterial infections. Guo et al. (2015) found that MP load was particularly related with

neutrophils and this cell could even amplify the airways inflammation. Wang and colleagues (2014) described lymphocytes as a factor to differentiate between viral and MP CAP.

The most common radiological findings were atelectasis and infiltrates, which accounts for 58% of the patients each. According to De-Quan, S. et al (2019), MP complicated with atelectasis is common and can cause systemic damage which is why an early diagnosis is key. On the other hand, on the study by Sondergaard and colleagues (2018), 80% of the patients had evidence of lobar infiltrations. These percentages are also comparable to the 49% of the study subjects of Shu-Chiang et al. (2007) and similarly to this latter reference study, chest radiographs were variable. It is worth mentioning that in one of the cases were a pleural effusion was described, the radiographic technique used was a CT scan. This finding, not shown on the chest X-ray previously performed on the patients supports the emphasis of Gong et al. (2016) of using CT scan as a tool of diagnosis for pediatric pneumonia. Nonetheless, it is important to consider the higher levels of radiation that a patient will be exposed to if chosen CT scan as a diagnosis method over X-ray.

In terms of respiratory treatment, 4% of patients who were on CPAP as a mechanical ventilation support, also were on BPAP. According to the study of Ma, YJ. et al. (2015) more children younger than 5 years of age required ventilation use when compared to the older patients. This was not seen in the present study since, the percentages were the same between both study groups. Also, the 28% of patients who required it as part of their treatment, is like the 26.8% of the Mexican patients of the study of Merida-Vieyra et al (2019) who required mechanical ventilation as well.

Concerning pharmacological managements, all patients included in the study received Albuterol therapies and azithromycin. The efficacy of azithromycin as choice of antibiotic is backed up by Kashyap and Sarkar (2010) who described azithromycin as the most active macrolide

antibiotic for treatment for MP. Most subjects received steroids (92%), particularly methylprednisolone which, according to Shan, LS. (2017), in combination with azithromycin, is an effective approach for the treatment of MP. Also, nearly all patients received either ranitidine or famotidine (90%) which prevents heartburn and acid indigestion among others. The reason the percentages of steroids and ranitidine/famotidine are so similar is because these medicines are prescribed to prevent the bleeding risk caused by gastric and duodenal ulcers that the steroids may induce. Nonetheless, some studies have argue that the need for steroid-induced ulcer prophylaxis is a myth based on disputable clinical evidence and that an assessment for the presence of ulcers should be performed before administrating the pharmacological protection (Guslandi, 2013 and Sochet, et al., 2019).

Chapter 6: Conclusions and recommendations

Finalizing the study, the hypothesis assuming a seasonal description, particularly in fall of MP was rejected because the number of admissions by month compared along the years selected for the study were irregular. Nevertheless, an increase of admissions was seen in the season of 2017-2018, when Hurricane Maria hit Puerto Rico, which is why hurricanes may be a contributing factor in the admissions to PICU of pediatric patients with MP. In addition, the second hypothesis, although apparently correct given that most patients in the study were 5 years of age and above, the difference was not significant which is why it cannot be stated that children 5 years old and over are at greater risk of contracting MP. In a similar way, there was no clear difference among the factors described form the clinical course of the patients. However, some factors were present in many of the patients. Abnormally high levels of neutrophils and abnormally low levels of lymphocytes were present in the laboratory findings. Moreover, cough and wheezing were clinical symptoms commonly presented at the time of admission, while no radiographic findings were

detected in enough cases to be considered a reliable mark to suspect MP. No significant difference was found between the age groups and the length of stay, neither in the hospital, nor in PICU, the presence of infiltrates and the need for mechanical ventilation, to mention a few. These findings are interesting because they do not support several articles previously published with subjects of other nationalities and ethnic groups and in which significant difference between age groups of patients was found. This rouses the questions of whether Puerto Rican children respond differently to MP or if the primary care system is lacking in certain areas such as prevention and initial treatment, particularly because most patients in this study were admitted straight to PICU instead of first being admitted to ward. Also, it can be concluded that the prevalence of PICU admissions of patients with MP increased throughout the years studied. However, since the increase of cases were detected around the time of a natural disaster, a longer study period is needed to determine if the increase in cases was related to Hurricane Maria or any other factors. Even so, this is a matter of public health that should be further address by the corresponding authorities to educate the public to minimize the need for PICU admissions and protect the vulnerable pediatric population.

Recommendations for future research:

It is recommended that for future research, a longer study period is considered. By doing this, a bigger sample will be examined, and the results will be more representative. In addition, extending the time frame of the study will provide a broader understanding of how MP is behaving across the years. Also, since the hurricane season of 2018 and 2019 were less active when compared to the one from 2017, extending the study period could provide important information concerning a possible relationship between natural disasters such as hurricanes and a rise in MP cases with admissions to PICU. Moreover, since the results presented in this study demonstrated that the diagnosis of MP is on the rise, it is suggested a similar study to be conducted considering

more hospitals, not only on the metropolitan area, but in other parts of Puerto Rico. This will facilitate comparisons of the prevalence of MP throughout the Island. This will respond to uncertainties such as if the same increasing pattern of MP diagnosis are occurring on other hospitals or if it is localized on certain areas of Puerto Rico. Furthermore, a study that considers those patients that are admitted to the hospital with MP but do not require care at the PICU should be considered. By doing this, other variables will be considered and more information regarding the prevalence and clinical course of patients with MP will be collected. These suggestions for future research will provide a bigger impact on public health and might improve the approach taken to diagnose and treat MP.

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References

1. Amin, M., Abadi, M. S., Navidifar, T., Torabizadeh, M., & Alavi, S. M. (2018). Detection of mycoplasma pneumoniae among children with pneumonia using bacterial culture, polymerase chain reaction, and the enzyme-linked immunosorbent assay techniques in ahvaz, iran. *Jundishapur Journal of Microbiology*, *11*(2), 1-6. doi: http://dx.doi.org/10.5812/jjm.55554
2. Chaudhry, R., Ghosh, A., & Chandolia, A. (2016, January-March). Pathogenesis of Mycoplasma pneumoniae: An update. Indian Journal of Medical Microbiology, 34(1), 7. Retrievedfromhttp://link.galegroup.com/apps/doc/A441458270/AONE?u=uprpiedras&sid=AONE&xid=58 b640d8
3. Chen, F., Yang, Y., Yu, L., & Bi, C. (2015). Prevalence of Mycoplasma pneumoniae: A cause for community-acquired infection among pediatric population. Nigerian Journal of Clinical Practice, 18(3), 354. Retrieved from http://link.galegroup.com/apps/doc/A406784721/AONE?u=uprpiedras&sid=AONE&xid=1cf 09ab4
4. Dash, S., Chaudhry, R., Dhawan, B., Dey, A., Kabra, S., & Das, B. (2018). Clinical spectrum and diagnostic yields of mycoplasma pneumoniae as a causative agent of community-acquired pneumonia. *Journal of Laboratory Physicians, 10*(1) doi: http://dx.doi.org/10.4103/JLP.JLP_62_17
5. Diaz, M.H., Benitez, A.J., Cross, K. E., Hicks, L. A., Kutty, P., Bramley, A. M., … Winchell, J. M. (2015). Molecular Detection and Characterization of Mycoplasma pneumoniae Among Patients Hospitalized With Community-Acquired Pneumonia in the

United States. Open Forum Infectious Diseases, 2 (3). https://doi.org/10.1093/ofid/ofv106.

6. Departamento de Salud, gobierno de Puerto Rico (2019). Coaliciones de Servicios de Salud. Retrieved from http://www.salud.gov.pr/Profesionales-y-Proveedores/Pages/Proveedores/Coaliciones-de-Servicios-de-Salud.aspx
7. De-Quan, S., Jin- Fan, L., Zhi-Qiang, Z. (2019) Clinical Analysis of 122 Cases with Mycoplasma Pneumonia Complicated with Atelectasis: A Retrospective Study. *Advances in Therapy*. https://doi.org/10.6084/ m9.figshare.9980762.
8. Dotres Martínez, C. P., Álvarez Carmenate, M., Vega Mendoza, D., Mondeja, Rodríguez, B., Rodríguez Preval, N. M., Fernández Molina, C., … Rodríguez Cutting, J. M. (2017). Mycoplasma pneumoniae y enfermedad respiratoria en niños y adolescentes. *Revista Cubana de Pediatría*, 89(4), 1–12. Retrieved from http://search.ebscohost.com/login.aspx?direct=true&db=asn&AN=129268776&site=ehost-live
9. Duenas Meza, E., Jaramillo, C., Correa, E., Torres-Duque, C., García, C., González, M., … Del Pilar, M. (2016). Virus and Mycoplasma pneumoniae prevalence in a selected pediatric population with acute asthma exacerbation. *Journal of Asthma,* 10.3109/02770903.2015.1075548.
10. Giavina-Bianchi, P., Kalil, J. (2016). Mycoplasma pneumonia infection induces asthma onset. *Journal of Allergy and Clinical Immunology*. 137(4), 1024-1025.
11. Gong, L., Zhang, C.-L., Zhen, Q. (2016). Analysis of clinical value of CT in the diagnosis of pediatric pneumonia and mycoplasma pneumonia. *Experimental and Therapeutic Medicine, 11*(4), 1271–1274. http://doi.org/10.3892/etm.2016.3073

12. Guo, W. (2015). Differentiation between mycoplasma and viral community-acquired pneumonia in children with lobe or multi foci infiltration: a retrospective case study. *British Medical Journal*. 5. doi:10.1136/bmjopen-2014-006766.

13. Guslandi, M. (2013). Steroid ulcers: Any news?. World Journal of Gastrointestinal Pharmacology and Therapeutics, 4(3), 39-40. doi:10.4292/wjgpt.v4.i3.39

14. Harriet Lane Service (Johns Hopkins Hospital). (2015). *The Harriet Lane Handbook: A manual for pediatric house officers.* United States of America: Elsevier Sauders.

15. Huang, F., Lu, L., Jiang, W., Yan, Y., Ji, W., Yang, B., & Yu, S. (2016). The epidemiology and clinical features of mycoplasma pneumoniae infection in neonates. The Brazilian Journal of Infectious Diseases, 20(4), 374+. Retrieved from http://link.galegroup.com/apps/doc/A488820118/AONE?u=uprpiedras&sid=AONE&xid =f98 1cc2c

16. Ishiguro, N., Koseki, N., Kaiho, M., Ariga, T., Kikuta, H., Togashi, T., … Tabata, Y. . (2017). Therapeutic efficacy of azithromycin, clarithromycin, minocycline and tosufloxacin against macrolide-resistant and macrolide-sensitive Mycoplasma pneumoniae pneumonia in pediatric patients. PLoS ONE, 12(3), 1–13. https://doi.org/10.1371/journal.pone.0173635 10. Kashyap, S., & Sarkar, M. (2010). Mycoplasma pneumonia: Clinical features and management. Lung India, 27(2), 75-85. doi:http://dx.doi.org/10.4103/0970-2113.63611

17. Kassisse, E., García, H., Prada, L., Salazar, I., Kassisse, J. (2018). Prevalence of Mycoplasma pneumoniae infection in pediatric patients with acute asthma exacerbation. Arch Argent Pediatr 2018;116(3):179-185.

18. Khoury, T., Sviri, S., Rmeileh, A., Nubani, A., Abutbul, A., Hoss, S., …, Nir-Paz, R. (2016). Increased rates of intensive care unit admission in patients with Mycoplasma pneumoniae: a retrospective study. *Clinical Microbiology and Infection*. 711-714. http://dx.doi.org/10.1016/j.cmi.2016.05.028.

19. Kumar, S., Garg, I., Sethi, G., Kumar, S., & Saigal, S. (2018). Detection of immunoglobulin M and immunoglobulin G antibodies to Mycoplasma pneumoniae in children with community-acquired lower respiratory tract infections. Indian Journal of Pathology and Microbiology, 61(2), 214. Retrieved from http://link.galegroup.com/apps/doc/A536049157/AONE?u=uprpiedras&sid=AONE&xid=0e 74add3

20. Kutty, P., Jain, S., Taylor, T., Bramley, A., Diaz, M., Ampofo, K., …, Hicks, L. (2019). Mycoplasma pneumoniae among children hospitalized with community-acquired pneumonia. *Clinical Infectious Diseases*. 5-12 10.1093/cid/ciy419.

21. Ma, YJ., Wang, SM., Cho, YH., Shen, CF., Liu, CC., Chi, H., …. Mu, JJ. (2015) Clinical and epidemiological characteristics in children with community-acquired mycoplasma pneumonia in Taiwan: A nationwide surveillance. *Journal of Microbiology. Immunology and Infection*, 2015; 48: 632-638.

22. Medjo, B., Atanaskovic-Markovic, M., Radic, S., Nikolic, D., Lukac, M., & Djukic, S. (2014). Mycoplasma pneumoniae as a causative agent of community-acquired pneumonia in children: Clinical features and laboratory diagnosis. Italian Journal of Pediatrics, 40 doi:http://dx.doi.org/10.1186/s13052-014-0104-4

23. Merida-Vieyra, J., Aquino-Andrade, A., Palacios-Reyes, D., Murata, C., Ribas-Aparicio, R., De Colsa Ranero, A. (2019). Detection of Mycoplasma pneumoniae in Mexican

children with community-acquired pneumonia: experience in a tertiary care hospital. Infection and Drug Resistance, 12: 925-935.

24. Mirsaeidi, M., Motahari, H., Taghizadeh, M., Sharifi, A., Campos, M., Schraufnagel, D. (2016). Climate Change and Respiratory Infections. Ann Am Thorac Soc.13(8):1223-30. doi: 10.1513/AnnalsATS.201511-729PS.
25. Parés Arroyo, M. (2018, october 26). Una enfermedad respiratoria afecta a un colegio en Humacao. *El Nuevo Día*. Retrieved from https://www.elnuevodia.com/noticias/locales/nota/unaenfermedadrespiratoriaafectaaunco legi oenhumacao-2455411/
26. Parés Arroyo, M. (2019, February 26). Varios médicos advierten sobre aumento en casos de micoplasma. *El Nuevo Día*. Retrieved from https://www.elnuevodia.com/noticias/locales/nota/variosmedicosadviertensobreaumentoe ncasosdemicoplasma-2479143/
27. Shan, LS., Liu, X., Kang, XY., Wang, F., Han, XH., Shang, YX. (2017). Effects of methylprednisolone or immunoglobulin when added to standard treatment with intravenous azithromycin for refractory Mycoplasma pneumoniae pneumonia in children. *World J Pediatr* ,10.1007/s12519-017-0014-9.
28. Shultz, J., Kossin, J., Shepherd, M., Ransdell, J., Walshe,R., Kelman, I., Galea, S. (2018). Risks, Health Consequences, and Response Challenges for Small-Island-Based Populations:Observations From the 2017 Atlantic Hurrican Season. Disaster Med Public Health Prep, 13(1):5-17. doi: 10.1017/dmp.2018.28.
29. Sochet, A., Son, S., Ryan, K., Roddy, M., Barrie, E., Wilsey, M., … Nakagawa, T. (2019). Stress ulcer prophylaxis in children with status asthmaticus receiving systemic

corticosteroids: a descriptive study assessing frequency of clinically important bleeding. Journal of Asthma, doi: 10.1080/02770903.2019.1614617

30. Sondergaard, M. J., Friis, M. B., Dennis Schrøder Hansen, & Jørgensen, I. M. (2018). Clinical manifestations in infants and children with mycoplasma pneumoniae infection. *PLoS One, 13(4) doi:http://dx.doi.org/10.1371/journal.pone.0195288*
31. Sun, H., Chen, Z., Yan, Y., Huang, L., Wang, M., & Ji, W. (2015). Epidemiology and clinical profiles of mycoplasma pneumoniae infection in hospitalized infants younger than one year. *Respiratory Medicine, 109*(6), 751-757. doi:http://dx.doi.org/10.1016/j.rmed.2015.04.006
32. Wang, M. (2014). Clinical and laboratory profiles of refractory mycoplasma pneumoniae in children. International Journal of Infectious Diseases, 29, 18-23.
33. Zhang, X., Chen, Z., Gu, W., Ji, W., Wang, Y., Hao, C., . . . Yan, Y. (2018). Viral and bacterial co-infection in hospitalised children with refractory mycoplasma pneumoniae pneumonia. *Epidemiology and Infection, 146*(11), 1384-1388. doi:http://dx.doi.org/10.1017/S0950268818000778

Appendices:

A. Patient Extraction Sheet: Mycoplasma pneumoniae Study
ID # _____

Admission Diagnosis: _____

Secondary Diagnosis: _____

Hospital Admission Date: _____ (mm/dd/yy) Hospital Discharge Date: _____ (mm/dd/yy)

PICU Admission Date: _____ (mm/dd/yy) PICU Discharge Date: _____ (mm/dd/yy)

Age_____ Sex _____ Weight _____Kg Height_____ cm

Address:_____ Insurance: _____

Home medications:_____

How many times was admitted to the hospital/PICU in the last year _____ Mycoplasma Confirmation date_____

Variable	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
PICU or Ward														
Azithromycin Frequency														
Ceftriaxone Frequency														

Pulmicort Frequency														
Variable	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**	**Day 8**	**Day 9**	**Day 10**	**Day 11**	**Day 12**	**Day 13**	**Day 14**
Albuterol Frequency														
Steroids Frequency														
Oxygen Support (mL/min)														
Mechanical Ventilation Support Type														
Temperature (H:L)														
FiO_2 (H:L)														
Respiratory Rate (H:L)														

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Saturation (H:L)														
Other														

Laboratories (IgM, IgG, COLDAGGL, COLDAGGT, CBC [CRP, WBC, Neut, Lymph, Mono, MP], Influ A, Influ B, RSV)

_____

_____

_____

Official Radiology Lecture

_____

Other Hospital Medications

_____

_____

Discharge Medications

_____

Clinical Symptoms

_____

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