THE PLACE OF THE BORDETELLE SPP. INFECTION IN THE RESPIRATORY SYNDROMS DOMINATED BY COUGH IN INFANTS AND CHILDREN, A 5 YEARS SURVEY

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Abstract

Introduction: Cough is a common indication of respiratory illness and is one of the more common symptoms of children seeking medical attention.

Material and Method: We conducted a clinic-based retrospective surveillance which analyzed the cases managed at “The National Institute for Infectious Diseases "Prof. Dr Matei Bals" – Pediatric Department, Bucharest during the period of January 2010 up to December 2014 who presented accusing cough episodes from over a week and who associated one of the following symptoms: paroxysms of coughing, inspiratory "whoop," posttussive vomiting or apnea. We selected 790 suitable cases for whom we analyzed: age, sex, vaccinal status, severity of the disease and the complications. The etiological diagnosis was made by serologic testing for Bordetella, Mycoplasma, Chlamydia, Adenovirus and by rapid testing for Sincitial Respiratory Virus (RSV).

Results and findings. Based on the etiological stratification 108 patients (13,8 %) were diagnosed with Bordetella Spp infections, 62,4% of them being completely unvaccinated against Pertusis, representing 11% of the national reported cases of Whooping Cough during the 5 years of survey. With decreasing frequencies the rest of the cases (682) were caused by: RSV (39,7%), Adenovirus (21,5%), Mycoplasma (18,3%), Chlamydia (6,7%). The majority of the cases evolved favorable, no fatal cases were registered but 279 presented with initial altered status and required, on average, 3 days of Intensive Care Unit management. The average hospitalization period registered is 6,9 days. All the severe complications were registered in the < 6 months age group. Conclusion: Whooping cough remains endemic in Romania and Bordetells Spp. infection is associated with substantial morbidity and mortality rates among children.

Key words: whooping cough, Bordetella, coqueluchoid syndrome

Introduction

The primary role of Bordetella Spp infection is causing lower respiratory tract disease among children and adults. The substantial morbidity and mortality rate associated with the whooping cough diagnosis has made its control a worldwide priority.

However, in Romania, the whooping cough is substantially under-diagnosed, especially due to the lack of awareness and the total burden of Bordetella Spp infection in the respiratory syndromes dominated by cough remains poorly defined, particularly in the rural settings and especially among our nomad minority.

Data reported by the Romanian Ministry of Health show that the vaccination rate against Bordetella Pertussis is substantially under the targeted 95% of immunized population with an important decrease (88.2) registered from the cohort of 2011.¹

The aim of our study is to characterize the Romanian whooping cough endemicity, from the point of view of one national infectious disease center and to determine the population based burden of Bordetella Spp. associated infection among hospitalized children and primary care settings (our day clinic). We further sought to describe the effect and potential risks associated with the constant decrease of European and national immunization coverage.

Material and method:

We conducted a clinic-based retrospective surveillance which analyzed the cases of pediatric respiratory syndromes dominated by cough and associated with infectious agents managed at “The National Institute for Infectious Diseases "Prof. Dr Matei Bals" Bucharest – Pediatric Department and Pediatric Intensive Care Unit, during the period of January 2010 up to December 2014.

Eligible children were under 18 years of age, presented with a history of cough episodes from over a week and who had received a diagnosis of acute respiratory infection, which was defined as an illness presenting with one or more of the
following symptoms: fever, nasal congestion, rhinorrhea, sore throat, vomiting after coughing, wheezing and labored, rapid or shallow breathing.

Excluded from our study were children who had respiratory symptoms dominated by cough but no infectious context or children with medical history of chronic cough. We obtained children’s demographic (age, sex, home environment), medical features (severity of the disease and the complications) and social histories (especially previous immunizations status) by questioning our hospital general database and by analyzing the standardized interviews of parents and legal guardians that were associated within the submission form and treatment sheets of all selected cases. For the risk factors stratification we recorded associated medical conditions which included prematurity history and chronic pulmonary, cardiac, renal, or immunodeficiency disease. Discharge diagnoses were based on clinical and laboratory information.

For the ethiological diagnosis we obtained nasal and throat swabs for viral detection (inpatient specimens were tested by reverse-transcriptase polymerase chain reaction (RT-PCR) or by using the MariPOC point of care multivariate analyzer for influenza A, influenza B and Parainfluenza viruses 1, 2, and 3, Respiratory sincitial virus and Adenovirus). Serological testing was used for the diagnosis of Mycoplasma Pneumoniae and Chlamydia Pneumoniae (using Elisa immunosorbent assays) and of Bordetella Spp. associated infections (testing in dynamic and using the serological agglutination tests for Bordetella. pertussis or determining the IgM, IgG and IgA titers of Bordetella Pertussis. using Elisa immunosorbent assay).

The choice of clinical management, including antibiotic regimens – if needed, hospitalization periods and intensive care stays – if needed, were determined by the child’s affiliated team of physicians, who also monitored the evolution and introduced the patient data in the central database.

Results.

During the studied period we identified 790 cases of acute respiratory infections with intense cough episodes as the main clinical aspect (suggestive presentation for “coqueluchoid” syndrome), which stand for 13.5% of the total respiratory infection cases addressed to our department.

Regarding the initial clinical form 279 patients presented with initial altered status and required, on average, 3 days of Intensive Care Unit management (see Fig. 1 repartition of cases on age groups).

The average hospitalization period registered is 6,9 days, from a total of 2971 hospitalisation days/cohort. All the severe complications were registered in the < 6 months age group all the patients evolved favorable, no fatal cases were registered, and all the emerging complications were reversible, the patients being discharged without important sequelae.

Based on the etiological stratification 108 patients (13,8 %) were diagnosed with Bordetella Specie infections (106 patients diagnosed with Bordetella Pertussis infection and only 2 diagnosed with Bordetella Parapertussis infection) and representing 11% of the national reported cases of Whooping Cough during the 5 years of survey; the Romanian Ministry of Health’s listed in March 2015 the total number of 1010 confirmed cases of Whooping cough, with 2 picks of incidence in 2012 and 2014, years that registered a maximum of Bordetella Spp associate infections diagnosed in our clinic too (33 respectively 25 cases – see Fig. 2, Fig. 3 for correlation).

Within decreasing frequencies the rest of the cases (682 patients) were caused by: RSV (39,7%, which counts for 314 cases), Adenovirus (21,5% which counts for 170 cases), Mycoplasma (18,3% which counts for 139 cases), Chlamydia (6,7% which counts for 51 ).
The highest rate of complications was registered in infants, especially those under 6 months of age and accounted, in a decreasing frequency rate, of apnea or slowed breathing 65 cases (60.1%), associate/secondary pneumonia 43 cases (39.8%), dehydration and/or weight loss due to feeding difficulties 42 (38.7%), subconjunctiva hemorrhages 48 cases (44.4%), epistaxis 12 (11.1%) seizures 4 (3.7%), 
ribbon incomplete fracture 1 case (0.9%), and syncope and brain damage 2 cases (1.8%).

In our work cohort 62.4% of the patients diagnosed with Whooping cough were found to be completely unimmunized; in absolute value – 67 children were found to be completely unvaccinated against Pertussis, 9 of them being infants under the age of 2 months at the time of the diagnoses, so too young to be vaccinated, and 3 of them were documentary linked to a family cluster of Whooping cough.

Sub-classifying the unvaccinated children we registered a higher rate of unimmunized children among the rural population (with a ratio of rural: urban cases of 69:39).

Significantly more family clusters (from a total of 17) of linked cases with Bordetella Persussis infections were identified in the rural regions of Romania, at least one case from the considered clusters was clinically and serologically diagnosed with Whooping Cough in our clinic.

Only 19 unvaccinated children were the result of an imperative refusal of the national immunization programs – declared and assumed anti-vaxxers - the rest of the unimmunized children were either social cases, either too young to be vaccinated or the victims of unawareness regarding the national immunizations programs.

Based on the age distribution the most affected age group was the 0-1 year group, 71 patients being under the age of one at the time of the diagnosis, 51% of them being younger than 6 month and in consequence too young to be completely immunized against Pertussis (see table 1 for age details).

The smallest prevalence of the infection registered among pupils (age > 6) with only 12 cases affiliated to the last mentioned age group. Analyzing the cases on the sex distribution bases we observed a male predominance (60.7%) and a seasonal incidence of the cases, with higher rates of Whooping cough diagnosis during the Autumn-Winter months, seasonality that is known to be characteristic for the respiratory tract infections.

Table 1 – Complications rates.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea</td>
<td>65 (60.1%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>4 (3.7%)</td>
</tr>
<tr>
<td>Subconjunctival Hemorrhages</td>
<td>48 (44.4%)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>12 (11.1%)</td>
</tr>
<tr>
<td>Secondary/Associated Pneumonia</td>
<td>43 (39.8%)</td>
</tr>
<tr>
<td>Sincope</td>
<td>2 (1.8%)</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>84 (77.7%)</td>
</tr>
<tr>
<td>Incontinence (la children&gt;4 years)</td>
<td>6 (5.55%)</td>
</tr>
<tr>
<td>Leukocitosis &gt;100,000 elem/mmcc</td>
<td>12 (11.2%)</td>
</tr>
<tr>
<td>Rib incomplete fractures</td>
<td>1 (0.9%)</td>
</tr>
</tbody>
</table>

Discussions and conclusions

Our findings from one national center for infectious diseases, which addresses to diverse populations groups, highlights once again that the Bordetella Spp. associated infection remain endemic in Romania and that the diagnosis of Whooping cough is associated with important rates of morbidity and mortality with a general burden rate that is greater among children within the first 6 years of life; young age imposed a significantly greater risk of severe illness.
Characteristics that were most frequently associated with Bordetella Spp. associated illness requiring hospitalization include lower socioeconomic status, male sex, chronic coexisting medical conditions, contact with other children and also lack or incomplete vaccination, which in our group proved to be the consequence of poverty and unawareness, and only in a small amount of cases the direct result of the anti-vaccines movement.

Historically controlled infections like Whooping cough have the potential to make a real and aggressive comeback not only in Romania but in the whole world.

The facts and data that we are now facing represent only the “tip of the ice-berg” since every day, more and more children are missing their vaccine doses, the heard immunity is fading and the medical community fears become real life experiences.

There is a certain amount of complacence today toward diseases that are thought to be largely a thing of the past. However we are now experiencing a resurgence of some of these diseases like Whooping cough and while the causes are complex and need to be teased apart, they are worsened by vaccine refusal which in turn is spawned by an anti-vaccine movement that is spreading misinformation and unwarranted fears.

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