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ORIGINAL ARTICLE

Infective triggers for asthma exacerbations in Malta

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Background

Several asthma exacerbations can be triggered by respiratory infections. Asthma guidelines do not provide detailed guidance on management of infective asthma exacerbations. The aims of this study were to identify whether asthmatics were investigated for infective triggers during an exacerbation, to identify micro-organisms responsible, and if these infective exacerbations were treated appropriately.

Method

The clinical notes and investigation results of patients discharged with a diagnosis of asthma between November 2018 and March 2019 from Mater Dei Hospital, Malta, were reviewed.

Results

Our cohort included 245 patients of which 66.5% were female. Chest X-ray was performed in 98.8%, of which 7.4% revealed consolidation. Results from respiratory screens via throat swab and sputum cultures were analysed and overall, 46.1% of the total number of patients had asthma exacerbations with an on-going infectious process. 63.7% of these were confirmed to be viral, commonly human rhinovirus and influenza A, while 22.1% had an on-going bacterial infection. Antibiotics were prescribed in 64.5% of the total, and antivirals in 3.7% of all patients including those with no on-going infectious process. When comparing bacterial versus viral triggers, there was no statistical significant difference in age, white cell count and C-reactive protein levels.

Conclusion

Most patients in our hospital with an exacerbation of asthma were investigated for infective sources. However, most were prescribed antibiotics, albeit there having been no evidence of a bacterial process. The use of procalcitonin could guide antibiotic prescription needs. This highlights the importance of formal guidelines to ensure judicial antibiotic use while reducing the burden of antibiotic resistance and any potential adverse effects.

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Background

Asthma is a serious and common respiratory condition affecting all age groups in which there is reversible airflow obstruction mediated by smooth muscle bronchoconstriction of the airways.[1] It is a chronic inflammatory airway disorder that is characterized by airway hyper-responsiveness. This leads to the typical symptoms of asthma which include chest tightness, shortness of breath, wheezing and coughing.[2]

Asthma can be managed and controlled in several ways including through environmental and lifestyle modifications, inhaled corticosteroids, short-acting and long-acting inhalers as well as oral or intravenous medications. In some instances, however, asthma control may be lost and asthmatics may experience an exacerbation of their condition. These episodes are usually provoked by specific stimuli such as irritant environmental triggers including infective processes, pollution, dust (PM2.5 and PM10), pollen, animal dander, cold temperatures and mould; stress, extreme emotional states and exercise; certain medications as well as lack of compliance to the prescribed asthma treatment. Exacerbations can have a significant negative impact on the quality of life of asthmatics, and in some cases may lead to death.[3-5]

Several guidelines on management of asthma are available, particularly the guidelines suggested by British Thoracic Society (BTS) and Global Initiative for Asthma (GINA) which are regularly updated and offer detailed information on the ideal, evidence-based management of asthma.[6-7]

Infective triggers, including bacterial and viral respiratory infections, are an important cause for exacerbations of asthma. Viral respiratory infections, particularly human rhinovirus (RV), are reported to be the commonest causes of infective asthma exacerbations.[8] Bacterial infections are less likely to be a direct cause of acute asthma exacerbations than viral stimuli; however, the increased production of mucus, impaired ciliary ability to clear mucus as well as viral-induced impairment of antibacterial defences can potentially increase the risk of a superimposed bacterial infection during a primarily viral-associated respiratory infection. This can therefore contribute to a bacterial exacerbation of asthma.[8-9]

Asthmatic patients are at high risk of asthma exacerbations despite ideal guideline-based management to control their asthma on a long-term basis. This highlights the importance of studying triggers for asthma exacerbations and the management of such events in order to decrease healthcare burden, as well as morbidity and mortality.[8]

This study focuses on these infective triggers for asthma exacerbations in adult patients prior to the global pandemic with Coronavirus Disease (COVID-19) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The primary aim was to identify whether patients admitted with a diagnosis of asthma were adequately investigated for possible infective triggers during their exacerbation. The secondary aim was to identify any micro-organism responsible and whether these infections were treated appropriately.

Methods and Materials

This retrospective study included analysing the data of 245 adult consecutive admissions to Mater Dei Hospital, Malta, who were discharged with a diagnosis of asthma between November 2018 and March 2019.

Patients were identified through the hospital's electronic discharge summary records from which the details of their demographic data, admission, treatment and management were obtained. Results of investigations were obtained through iSoft Clinical Manager. Data protection approval was obtained from data protection manager at Mater Dei Hospital. Ethical approval was obtained from the University Research Ethics Committee.

Patients' clinical examination findings were recorded, particularly temperature and chest findings.

When taken, serological, microbiological and radiological investigations were sought and the results were recorded. Admission blood investigations included a Full Blood Count (FBC), C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR). Microbiological investigations included nasopharyngeal/throat swab (Respiratory Screen) which included Polymerase Chain Reaction (PCR), Sputum for Microscopy, Culture and Sensitivity (MCS) as well as Blood Cultures for MCS. Radiological investigations included Chest X-Rays (CXR) and thoracic Computerized Tomography (CT) scans.

Analysis of Variance (ANOVA) test was used to compare variables. A *p*-value of less than 0.05 was taken to be statistically significant.

Results

Demographics

245 cases met the inclusion criteria between November 2018 and March 2019. December 2018 had the least frequent admission rate (mean 1.39 cases per day) and January 2019 had the most frequent admission rate (mean 1.84 cases per day). The shortest admission duration was 2 days, whilst the longest hospital stay was 43 days, with an average of 6.42 days.

The majority of admissions (*n*=163, 66.5%) were female. The age ranged between 18 to 93 years, with a mean of 58.3 years.

Respiratory co-morbidity was present in 33 (13.4%) of 245 patients, 2 of which had multiple respiratory co-morbidities. The commonest co-morbidities were obstructive sleep apnoea (OSA) (*n*=11), and asthma - chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS) (*n*=9). 169 (68.9%) of the patients had other, non-respiratory co-morbidities, of which 113 patients (46.1%) had multiple co-morbidities. The commonest were hypertension (*n*=86), diabetes mellitus type 2 (*n*=44), and heart failure (*n*=39).

Treatment on admission

The vast majority of patients (98.9%) were on regular 'reliever' inhaled treatment on admission. 44% of patients were on inhaled short-acting beta$_2$-agonist (SABA) only, 42.4% on a combination of SABA and long-acting beta$_2$-agonist (LABA) and 4.9% on a combination of SABA and short-acting muscarinic antagonist (SAMA). On admission, 88.1% of patients were on inhaled 'preventer' treatment. The commonest was fluticasone propionate (32.7%), followed by beclomethasone (30.6%). 10.2% of patients were on immunomodulatory treatment on admission, most of whom were on leukotriene receptor antagonists (9%). 3.8% were on immunosuppressive treatment, 2.9% were receiving regular systemic corticosteroids and 1.6% (4 patients) were on Omalizumab.

Clinical examination

10.6% of patients were febrile on admission. The maximum temperature recorded was 38.3˚C. 213 patients (86.9%) had documented clinical respiratory signs on examination. The commonest

findings were wheeze (85.9%) and decreased air entry (31.9%).

Investigations

All 245 patients had blood tests taken on admission. With regards to inflammatory markers, FBC and CRP levels were taken from all patients. An ESR level was taken from 26 patients (10.6%). Blood results are shown in Table 1.

Table 1 Blood Investigation Results

Blood Indices Measured	Range (Lowest – Highest)	Mean (± SD)
White cell count (x10^9 cells/L)	3.42 - 24.54	10.37 (± 3.75)
Neutrophils (x10^9 cells/L)	2.58 - 20.23	7.38 (± 3.37)
Lymphocytes (x10^9 cells/L)	0.32 - 7.71	1.8 (± 1.17)
Eosinophils (x10^9 cells/L)	0 - 2.69	0.3 (± 0.42)
ESR (mm in 1st hour)	2 - 133	43.42 (± 32.73)
CRP (mg/L)	0.17 - 405	27.74 (± 51.87)

Table 2 Radiology Investigations Results

Chest X-Ray (*n*=242)		CT scan (*n*=19)	
Result	**n (%)**	**Result**	**n (%)**
Normal	176 (72.7%)	Normal	7 (36.8%)
Atelectasis	5 (2.1%)	Atelectasis	1 (5.3%)
Consolidation	18 (7.4%)	Consolidation	6 (31.58%)
Pleural effusion	4 (1.7%)	Pleural effusion	3 (15.8%)
Other (Congestive Heart Failure, Elevated Hemidiaphragm, Emphysema, Fibrosis, Hiatus Hernia)	39 (16.1%)	Other (Fibrosis, Metastasis)	2 (10.5%)

Table 3 Respiratory Screen Results

Respiratory Screen (PCR) (*n*=170)	
Pathogen Identified	***n* (%)**
Human rhinovirus	29 (17.1%)
Influenza A	19 (11.2%)
Human coronavirus	8 (4.7%)
Influenza H1N1	7 (4.1%)
Enterovirus	6 (3.5%)
Moraxella catarrhalis	6 (3.5%)
Haemophilus influenzae	5 (2.9%)
Human parainfluenzae	4 (2.4%)
Klebsiella pneumoniae	4 (2.4%)
Human metapneumovirus	3 (1.8%)
Staphylococcus aureus	2 (1.2%)
Adenovirus	1 (0.6%)
Streptococcus pneumoniae	1 (0.6%)

A CXR was taken in 242 patients (98.8%). In one instance, it was omitted in view of pregnancy. They were reported as normal in 176 patients (72.7%). In the rest, the commonest abnormalities noted were changes suggestive of heart failure (*n*=25, 10.3%) and consolidation (*n*=18, 7.4%). A CT scan was performed in 19 patients (6.5%). 11 of these were thoracic scans, 7 were pulmonary artery scans, and 1 was a thoracic-abdomino-pelvic scan. Of these, 7 were normal (36.8%), and of the rest, the commonest abnormality detected was consolidation in 6 scans (31.6%). Radiology results are shown in Table 2.

A nasopharyngeal/throat swab (Respiratory Screen) and PCR was performed on 170 patients (69.4%). The commonest pathogens detected by PCR were human rhinovirus (29 swabs, 17.1%) and influenza A (19 swabs, 11.8%) as can be seen in Table 3.

A sputum sample for MCS was taken in 53 patients (21.6%). The commonest pathogen grown was *Haemophilus influenzae* in 6 sputum samples (11.3%). Five of the sputum samples (9.4%) were unsuitable for investigation. Table 4 highlights results from sputum samples.

Table 4 Sputum Culture Results

Sputum for microscopy, culture and sensitivity (*n*=53)	
Pathogen Identified	***n* (%)**
Haemophilus influenzae	6 (11.3%)
Unsuitable sample	5 (9.4%)
Candida albicans	2 (3.8%)
Eschericia coli	1 (1.9%)
Group C haemolytic Streptococcus	1 (1.9%)
Streptococcus canis	1 (1.9%)
Pasteurella multicoda	1 (1.9%)
Klebsiella pneumonia	1 (1.9%)
Pseudomonas aeuruginosa	1 (1.9%)
Streptococcus pneumoniae	1 (1.9%)

Blood samples for MCS were taken in 35 patients (14.3%). Of these, 18 patients had fever (51.4%). Only 2 of the blood MCS samples cultivated a pathogen: one revealed coagulase negative staphylococcus, and the other revealed *Propionibacterium acnes*.

Overall, there were 113 cases (46.1%) of asthma exacerbation with infectious aetiologies.

Of these, 25 (22.1%) had a bacterial cause, 72 (63.7%) were viral, and 16 (14.2%) had a co-infection.

Antibiotic treatment was started in 158 cases (64.5%) as shown in Table 5. The commonest antibiotic regimes were intravenous co-amoxiclav (*n*=74, 46.8%), or a combination of co-amoxiclav and clarithromycin (*n*=25, 15.8%).

Oseltamivir was prescribed to 9 patients (3.7%). 8 of these patients had influenza A virus detected on the respiratory screen. It is not known whether Oseltamivir was started prior to result of Respiratory Screen being confirmed.

Complications during admission were noted in 24 cases (9.8%). The commonest complication was type 2 respiratory failure (*n*=15, 62.5%), of which 10 patients then required transfer to Intensive Care Unit (ITU) as seen in Table 6.

Table 5 Antibiotic Treatment

Antibiotic treatment (*n*=158)	
Antibiotic	***n* (%)**
Co-amoxiclav	74 (46.8%)
Co-amoxiclav + Clarithromycin	25 (15.8%)
Clarithromycin	5 (3.2%)
Doxycycline	10 (6.3%)
Levofloxacin	15 (9.5%)
Other (Amoxicillin, Ciprofloxacin, Azithromycin, Doxycycline, Metronidazole, Ceftazidime, Co-trimoxazole, Ceftriaxone, Cefuroxime, Piperacillin and Tazobactam)	28 (17.7%)

Table 6 Complications

Complications (*n*=24)	
Complication	***n* (%)**
Type 2 respiratory failure, requiring intensive care	10 (41.6%)
Type 2 respiratory failure, not requiring intensive care	5 (20.8%)
Phlebitis	2 (8.3%)
Persistent shortness of breath	2 (8.3%)
Allergic reaction to antibiotic therapy	1 (4.2%)
Delirium (Benzodiazepine withdrawal)	1 (4.2%)
Antibiotic-induced diarrhoea	1 (4.2%)
Lung collapse	1 (4.2%)
Sepsis	1 (4.2%)

Table 7 Data Comparison in Patients with Viral, Bacterial, or Co-Infections in Asthma Exacerbations

Parameter	Viral infection (PCR) n (%)	Bacterial infection (PCR and sputum MCS, blood MCS) n (%)	Co-infection (PCR and sputum MCS, blood MCS) n (%)	*p*-value
Total number of patients (% of total patient population)	72 (29.4%)	25 (10.2%)	16 (6.5%)	/
Age Range (years) Mean age (±SD)	19 – 92 55.9 (±21.7)	20 – 89 55.2 (±22.1)	22 – 87 67.75(±16.89)	0.113653
Number of Females n (% of group)	55 (76.4%)	17 (68%)	11 (69%)	/
Duration of admission range (days) Mean duration (±SD)	2 - 43 6.9 (± 5.7)	2 – 18 7.2 (±4.2)	3 – 32 12(±8.23)	0.007098
Abnormal chest radiograph (% of group) ➔ Consolidation ➔ Effusion ➔ Other findings	17 (23.6%) 6 (8.3%) 1 (1.4%) 10 (13.9%)	10 (41.7%*) 2 (8.3%) 0 8 (33.3%)	9 (56%) 2 (12.5%) 2 (12.5%) 5 (31.3%)	/
CRP Range (mg/L) Mean CRP (±SD)	0.6 - 204 25.8 (±36.1)	1.9 – 304 39.2 (±68.9)	0.17 – 308.4 36.62(±76.14)	0.470959
Neutrophils Range (x10^9 cells/L) Mean Neutrophils (±SD)	2.58 – 19.23 7.2 (± 4.0)	3.13 – 20.23 7.9 (±3.9)	5.15 – 16.49 8.71(±2.74)	0.334918
Lymphocytes Range (x10^9 cells/L) Mean Lymphocytes (±SD)	0.35 – 7.71 1.56 (± 1.0)	0.64 – 7.08 2.07 (±1.39)	0.37 – 7.47 1.42(±1.69)	0.143404
Treated with antibiotics (% of group)	55 (76.4%)	18 (72%)	12 (75%)	/
Complications (% of group) ➔ Respiratory Failure needing ITU ➔ Respiratory Failure not needing ITU ➔ Other	9 (12.5%) 6 (8.3%) 2 (2.8%) 1 (1.4%)	1 (4%) 0 1 (4%) 0	3 (18.8%) 2 (12.5%) 0 1 (6.3%)	/

** Values for abnormal chest radiographs in the bacterial infection group take into consideration 24 total cases not 25, as in one particular case a Chest X-Ray was not taken*

Twenty-four patients were admitted more than once to hospital for an asthmatic exacerbation within the period of data collection. 22 patients were admitted twice, and 2 patients were admitted thrice (both females), thus a total of 26 repeat admissions. Of these, 7 were male (mean age 61.6, range 31 - 92), whilst 17 were female (mean age 66.6 years, range 19 - 92).

Of these re-admissions, 4 were repeatedly infective asthma exacerbations and 3 of these confirmed to be viral-induced throughout. For 8 of these patients, their first admission was a non-infective exacerbation of asthma but their repeat admission was considered infective, of which 6 were confirmed to be viral-induced. For 3 patients who were re-admitted, their first visit was considered viral-induced but their re-admission did not reveal any infective source for their asthma exacerbation. Out of the re-admissions, 9 patients repeatedly had non-infective asthma exacerbations. Table 7 compares patients diagnosed with viral and bacterial infections.

Discussion

Although evidence-based and guideline-based treatment of asthma is essential to reduce asthma attacks, asthma patients are still prone to experiencing exacerbations of asthma. Aside from significant impact on patient health and lung function, it also increases healthcare utilisation and expenses.[8]

This local retrospective study focuses on a common cause of asthma exacerbations, the infectious aetiologies including viral and bacterial respiratory infections. 46.1% of patients in this cohort had evidence of a respiratory infection, of which 63.7% were viral. 22.1% of the cohort seemed to have an on-going bacterial infection. The commonest viral aetiology in the cohort studied was human rhinovirus which concurs with global trends.[8] Other common viruses causing an asthma exacerbation were influenza A and human coronavirus (this does not include SARS-CoV-2). There is less evidence in the literature about bacterial infections directly causing an asthma attack, albeit the possibility of secondary bacterial infections following a primary viral respiratory infection, particularly due to lack of normal macrophage activity against bacteria in human alveoli during a viral respiratory infection.[8,10]

There is a lack of evidence as to the efficacy of antibiotics given as part of the treatment regime in an acute asthma exacerbation.[11] The BTS Asthma Guideline 2016 suggests that routine prescription of antibiotics is not indicated for patients with acute asthma, and deciding on the use of antibiotics in acute asthma should be guided by objective measures, including procalcitonin where available.[6] There are no other international evidence-based guidelines on antibiotic prescription and management of infective exacerbations of asthma apart from BTS 2016 and the updated GINA guidelines 2021.[6-7]

In spite of this, our results have shown that the majority of our cohort (64.5%), which included patients with no particular on-going respiratory infection, was initiated on antibiotic treatment when admitted to Mater Dei Hospital in view of an asthma attack. Of those who had an infectious agent which seemed to be causing their exacerbation, approximately 63.7% had a confirmed viral infection. Of these patients with viral-induced asthma exacerbations, 76.4% were treated with antibiotics as can be appreciated in Table 7. Antiviral treatment was initiated in only 3.7% of the cohort. The routine prescription of antibiotics for asthma exacerbations in Mater Dei Hospital could be multifactorial. Some possible reasons as to why this occurs include the lack of more specific, rapidly

available testing such as procalcitonin; no available local guidelines or lack of awareness of international guidelines. In addition, the lack of clinical pharmacists on acute medical wards, as well as having the more junior staff managing such patients, especially after hours, who may lack the necessary experience with such cases and therefore may choose to err on the side of caution.

In a randomised double blind study, Graham et al. revealed that, in patients with an asthma exacerbation, there was no significant difference in improvement of condition between a cohort of patients who were treated with an antibiotic such as amoxicillin and a cohort of patients who were given a placebo.[12] Similarly, in a retrospective study performed in Tunisia to determine the role of antibiotics in asthma exacerbations, and whether the outcome is impacted, it concluded that the outcome was similar for patients who were treated with antibiotics when compared to those who were not.[13] In another study of antibiotic prescription in acute asthma attacks in patients presenting to several Emergency Departments (EDs) in the United States of America in 1993-2004, it was noted that antibiotic prescription has maintained a steady rate, approximately 22%, despite antibiotic resistance campaigns and guidelines stating routine antibiotic prescription in asthma is not advised. This is in comparison to a general reduction in antibiotic prescription rate to all patients presenting to the same EDs.[14] In a randomized control trial of a cohort of patients with acute asthma exacerbation in Shangai, withholding antibiotic treatment for patients did not cause any obvious repercussions in the year following the exacerbation, which further highlights that antibiotics should not be prescribed routinely in such cases.[15]

Our cohort was considered to be thoroughly assessed through available investigations that included serological, microbiological and radiological studies, however, treatment of these patients was not considered concordant to the results of said investigations. The rising concerns with over-prescription of antibiotics in patients who may not require such treatment include potential side effects of said treatment, as well as antibiotic resistance, which is a worrying global healthcare issue.[11]

There could be numerous factors which drive antibiotic prescription in asthma exacerbations. These may include doubtful diagnosis and/or reason for exacerbation, lack of resources, lack of awareness of current guidelines, as well as lack of confidence in the use of guidelines, especially when facing difficult cases. Some may also consider the risk of potential worsening of patients' condition resulting in the routine use of antibiotics out of habit should this risk be considered likely to happen. In addition, the possibility of medico-legal action against the clinician may steer them towards a more proactive approach, even if treatment is not required at the time, as opposed to watchful waiting.[16]

One way of reducing antibiotic over-prescription to patients who are only experiencing viral exacerbations of asthma is via the use of procalcitonin levels. This is a more specific and useful test for bacterial infective processes, and would not normally be elevated in patients with viral infections or inflammation.[15] In our study, procalcitonin level results were excluded as this is not a readily available investigation in our hospital. Although a more costly test than routine inflammatory markers, it may be worth considering as an investigation in acute asthma exacerbations if it is more readily available in order to guide

appropriate treatment. Its use has also been suggested by the BTS Asthma Guideline 2016 for the same reason.[6]

CRP and CBC can be useful low-cost investigations in suspected respiratory infections; however, they are non-specific and could be elevated in conditions other than bacterial infections. Table 7 reveals comparison of data between patients in our cohort having viral and bacterial asthma exacerbations. In our study, the mean CRP level in viral infections was 25.8mg/dL, albeit not significantly lower than that in bacterial infection (39.2mg/dL). A difference in abnormality of chest radiograph can be appreciated between viral and bacterial infections in our cohort, with 41.7% being abnormal in bacterial infections as opposed to 23.6% in viral infections, however, this is also non-specific. Therefore, use of procalcitonin can aid in reduction of unnecessary antibiotic prescription in asthma exacerbations which are mostly viral in aetiology.[15]

Concerning the global pandemic with COVID-19, GINA guidance suggests that asthmatics are not at an overall increased risk of COVID-19 as there was no obvious rise in asthma exacerbations during the pandemic. In fact, many countries experienced a reduction in cases, which may be due to use of facemasks, social distancing and overall improved hand hygiene. There was no mention of routine antibiotic prescription with regard to asthma exacerbations in the setting of COVID-19 infection, however, the guideline does suggest to avoid routine antibiotic prescription in primary care or acute care facilities unless there is strong evidence of a bacterial infection.[7]

Limitations of our study include that this cohort of patients included only those who were hospitalized at Mater Dei Hospital. This study therefore excludes patients who were treated exclusively at the Accident and Emergency (A&E) Department, patients who left hospital against medical advice, patients in other governmental or private hospitals or within the community such as governmental or private General Practitioners' (GP) Clinics. It is a retrospective study and so we were unable to conduct face-to-face interviews. Discharge summaries, prepared by different people, were used for data collection and so could lead to variable data. Another limitation is that we were unable to ascertain whether each patient was on inhaled vs. nebulized treatment on admission. In addition, the study was carried out during the cold winter months and may not be wholly representative of all asthma exacerbations.

Conclusion

Most patients with an exacerbation of asthma in our cohort were thoroughly investigated for potential infective triggers. However, most of these patients were prescribed antibiotic treatment, albeit there having been no evidence to a bacterial process in the majority of cases. The use of procalcitonin, where available, could be of guidance to antibiotic prescription. However, the results of this study highlight the importance of needing clear and evidence-based guidelines on infective exacerbations of asthma to be communicated across all health care levels globally. This can be done through further studies on the subject as well as discussion between bodies providing formal guidance on respiratory diseases. It would be ideal to include the management of an asthma exacerbation secondary to a viral or bacterial respiratory tract infection. This will ensure judicial and appropriate antibiotic use while reducing their potential adverse effects as well as the burden of antibiotic resistance.

Summary

Facts known about asthma exacerbations:

1. Infectious triggers are common causes of asthma exacerbations.
2. There is minimal guidance on management of infective asthma exacerbations.
3. Antibiotics are over-prescribed to patients who have exacerbations of asthma.

New findings from this study:

1. In our cohort, 63.7% of patients had viral triggers for their asthma exacerbation whilst 22.1% had a confirmed bacterial trigger.
2. Antibiotics were over-prescribed in our cohort: 64.5% of the total cohort were prescribed antibiotics; 76.4% of the patients who had a viral trigger were prescribed antibiotics whilst 72% of those with a bacterial infection were also prescribed antibiotics.
3. Our findings confirm the need for more detailed guidance in this regard.
4. We suggest the use of procalcitonin as guidance for antibiotic prescription in such cases.

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