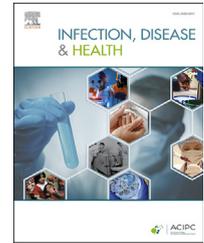




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Research paper

Rapid testing for respiratory viruses: Impact on antibiotic use and time to patient discharge

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KEYWORDS

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Abstract *Background:* Influenza-like illness is often caused by respiratory viral infections, and is a frequent cause of presentation to hospital. Rapid diagnostics for respiratory viruses, with turnaround times of less than sixty minutes, are increasingly available. Early physician knowledge of positive respiratory virus tests has previously been shown to impact patient care in a paediatric population but hasn’t been evaluated in adults.

Methods: Rapid testing for the respiratory viruses Influenza A, Influenza B and respiratory syncytial virus (RSV) was introduced in our institution in 2018. This reduced turnaround time for tests from more than 24 h, to 1–10 h depending on time of day. A retrospective cohort study was performed on patients presenting with influenza-like illness, in whom a nasopharyngeal swab for respiratory viruses was requested. Data was collected before and after the introduction of the rapid assay. Outcomes included antibiotic use (less or more than 24 h) and length of hospital stay (less or more than 24 h).

Results: In all patients who tested positive for a respiratory virus, there was an association between rapid testing and less antibiotic use. This was largely driven by paediatric cases; there was no change in prescribing for adult patients. There was no impact on timing of patient discharge.

Conclusions: Rapid testing for respiratory viruses has a potentially useful role in antimicrobial stewardship. It is unclear why earlier knowledge of positive viral test didn’t lead to less antibiotics in adults. This study showed no impact of rapid testing on time to patient discharge.

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Highlights

- Rapid testing for respiratory viruses is an increasingly used diagnostic modality in Australia.
- In this study, patients positive for Influenza A, Influenza B or RSV had reduced use of antibiotics for more than 24 hours.

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- This finding was driven by paediatric cases; there was no impact on antibiotic prescribing in adults.
- There was no impact on timing of patient discharge.

Introduction

Influenza-like illness is a common cause of presentation to hospitals. The syndrome is characterized by fever, cough and dyspnoea, and is usually caused by a respiratory virus. Respiratory viral infections are generally treated supportively with rehydration, analgesia and potentially an antiviral agent [1]. A common differential diagnosis for patients with influenza-like illness is bacterial pneumonia. Treatment for bacterial pneumonia includes empiric antibiotic therapy; antibiotics prescribed for this indication include penicillins, cephalosporins, macrolides and tetracyclines [2]. Exposure to these antibiotics puts patients at risk of adverse drug reactions, as well as cultivation of microorganisms resistant to conventional antibiotics [3–5].

The standard diagnostic specimen for respiratory virus detection is a nasopharyngeal swab (NPS). Reverse transcriptase polymerase chain reaction (RT-PCR) testing is performed to detect viral ribonucleic acid (RNA) within the specimen [6]. RT-PCR testing is highly sensitive and specific, and multiplex panels can identify multiple respiratory viruses [7]. Disadvantages of multiplex RT-PCR testing include prolonged turnaround time, and lack of timely widespread availability. Rapid assays for RT-PCR detection of viral RNA have recently been developed, with turnaround times of 15–30 min and sensitivity of 90.1% with specificity of 98.9% [8].

Early physician knowledge of tests positive for respiratory viruses have previously been shown to impact on length of patient stay and antibiotic prescribing in a paediatric population [9,10]. However, little has been reported on the clinical impact of rapid testing in adults. The potential clinical benefits of rapid testing and earlier diagnosis include earlier patient discharge, optimized antibiotic and antiviral use, and earlier implementation of appropriate infection control precautions.

This study aims to assess the impact of on-site rapid respiratory virus testing on patient care at Gold Coast University Hospital (GCUH), with regards to impact on antibiotic use and time to patient discharge. The hypotheses of the study are that rapid testing for respiratory viruses is associated with.

- Reduced use of antibiotics
- Earlier patient discharge from hospital.

Methods

Study design

This is a single centre retrospective cohort study. GCUH is 750 bed tertiary referral hospital with approximately

9000 emergency department (ED) presentations per month.

Intervention

Prior to 2018, NPS samples taken at GCUH were transported to a centralized laboratory in Brisbane (75 km away) for processing. Turnaround times between sample collection and result ranged from 24 to 36 h.

In 2018, on site rapid respiratory virus testing at GCUH was introduced. The testing platform was the Cepheid "Xpert Xpress Flu/RSV Assay". This assay tests for three respiratory viruses: Influenza A, Influenza B and Respiratory Syncytial Virus (RSV). Turnaround times for test results were reduced to less than 1 h on tests sent between 0700 and 2100, and a maximum of 11 h on swabs sent outside of those hours.

Study population

All patients presenting to GCUH emergently in whom an NPS was requested, within 24 h of hospital presentation, were eligible for inclusion in this study. This included adults, paediatric and obstetric patients, who presented to either the emergency department (ED), maternity assessment centre or the haematology/oncology day unit.

Exclusion criteria included patients already admitted to the hospital for longer than 24 h at the time the swab was requested, and patients in whom an NPS was taken during routine outpatient appointments and not admitted to hospital.

Data collection

Data was collected retrospectively using local electronic medical records. The pre-intervention period was 01/05/2017-31/08/2017, and the post-intervention period was 01/05/2018-31/08/2018, in line with the traditional Australian flu season.

In relation to antibiotics, each case was categorized as receiving antibiotics for either less than or more than 24 h. There was no distinction made between oral and intravenous antibiotics. Regarding patient discharge, each case was categorized based on time between initial presentation and discharge: either less than or more than 24 h.

Statistical analysis

Chi squared or Fisher's exact testing were performed as appropriate, to assess for an association between rapid respiratory virus testing and reduced antibiotic use as well as earlier patient discharge.

Results

Cases included in the study are shown in [Table 1](#). There was notably higher prevalence of all respiratory viruses in 2017 compared to 2018. This was in line with national prevalence data for the two years under study. Influenza A was the most prevalent virus in all age groups in 2017, RSV was more common in 2018. There were no cases of Influenza B in 2018 in this study.

[Table 2](#) shows the association between rapid respiratory virus testing and antibiotic usage. In patients who were positive for one of Influenza A, Influenza B or RSV, there was a statistically significant association between rapid testing and reduced antibiotic use (51.3% v 64%, $p = 0.03$). This association is predominantly attributable to paediatric cases; outcomes were essentially unchanged in adult patients. There was no impact on antibiotic prescribing in patients who tested negative for respiratory viruses.

[Table 3](#) shows the association between rapid respiratory virus testing, and patients discharging within 24 h. Within all cohorts of patient groups, and regardless of result of

respiratory virus test, no association was seen between rapid testing and earlier patient discharge.

Discussion

In this study, there was an association between a positive rapid NPS test for Influenza A, Influenza B and RSV, and reduced use of antibiotics. This association was primarily driven by paediatric cases; earlier physician knowledge of test positive for a virus had no impact on antibiotic prescribing in adult patients. There was no impact on time to patient discharge in any group. This study is limited by wide differences in virus prevalence in the two years under study.

Prevention of antimicrobial resistance is a global challenge of increasing urgency [11,12]. Antimicrobial stewardship programmes are part of the National Safety and Quality Health Service Standards for Hospitals in Australia [13]. Expedited diagnostic testing should be an important component of effective antimicrobial stewardship [14,15], and rapid testing for respiratory viruses is relatively new technology. The findings of this study suggest that rapid respiratory virus testing is useful as a diagnostic and an antimicrobial stewardship tool in paediatric cases. However, knowledge of positive rapid virus tests did not alter antibiotic prescribing habits in adult cases.

It is unclear why early knowledge of positive rapid viral NPS results did not lead to reduced antibiotic use. Possible explanations may include that physicians were unfamiliar with the new rapid test and were concerned about false positive results, and that clinicians had low thresholds for diagnosing secondary bacterial pneumonia. Data from the Australian National Antimicrobial Prescribing Survey (NAPS)

Table 1 Patient characteristics.

| Patient characteristics | 2017 | 2018 |
|----------------------------|------|------|
| Total patients | 903 | 793 |
| Adults | 515 | 539 |
| Paediatrics | 388 | 254 |
| Influenza A detected | 163 | 22 |
| Influenza B detected | 61 | 0 |
| RSV detected | 118 | 67 |
| No virus detected | 494 | 704 |
| Alternative virus detected | 90 | n/a |

Table 2 Impact of rapid testing on antibiotic prescribing.

| Category | Year | No antibiotics/antibiotics <24 h | % | Antibiotics >24 h | % | P value for independence |
|--|------|----------------------------------|------|-------------------|------|--------------------------|
| All Patients | 2017 | 432 | 47.8 | 471 | 52.2 | 0.20 |
| | 2018 | 404 | 51 | 389 | 49.1 | |
| Patients positive for Influenza A/Influenza B/RSV | 2017 | 176 | 51.3 | 167 | 48.7 | 0.03 |
| | 2018 | 57 | 64 | 32 | 36 | |
| Adults positive for Influenza A/Influenza B/RSV | 2017 | 61 | 32.5 | 127 | 67.6 | 0.97 |
| | 2018 | 9 | 32.1 | 19 | 67.9 | |
| Paediatric patients positive for Influenza A/Influenza B/RSV | 2017 | 115 | 73.7 | 41 | 26.3 | 0.45 |
| | 2018 | 48 | 78.7 | 13 | 21.3 | |
| Influenza A positive patients | 2017 | 70 | 42 | 93 | 57.1 | 0.53 |
| | 2018 | 11 | 50 | 11 | 50 | |
| Influenza B positive patients | 2017 | 30 | 48.4 | 32 | 51.6 | 1.00 |
| | 2018 | 0 | | 0 | | |
| RSV positive patients | 2017 | 76 | 64.4 | 42 | 35.6 | 0.56 |
| | 2018 | 46 | 68.7 | 21 | 31.3 | |

Table 3 Impact of rapid testing on timing of patient discharge.

| Category | Year | Discharged <24 h | % | Discharged >24 h | % | P value for independence |
|--|------|------------------|-------|------------------|-------|--------------------------|
| All Patients | 2017 | 225 | 24.92 | 678 | 75.08 | 0.17 |
| | 2018 | 175 | 22.07 | 618 | 77.93 | |
| Patients positive for Influenza A/Influenza B/RSV | 2017 | 76 | 22.16 | 267 | 77.84 | 0.46 |
| | 2018 | 23 | 25.84 | 66 | 74.16 | |
| Adults positive for Influenza A/Influenza B/RSV | 2017 | 32 | 17.11 | 155 | 82.89 | 0.92 |
| | 2018 | 5 | 17.86 | 23 | 82.14 | |
| Paediatric patients positive for Influenza A/Influenza B/RSV | 2017 | 44 | 28.21 | 112 | 71.79 | 0.85 |
| | 2018 | 18 | 29.51 | 43 | 70.49 | |
| Influenza A positive patients | 2017 | 36 | 22.09 | 127 | 77.91 | 0.59 |
| | 2018 | 6 | 27.27 | 16 | 72.73 | |
| Influenza B positive patients | 2017 | 7 | 11.29 | 55 | 88.71 | 1.00 |
| | 2018 | 0 | | 0 | | |
| RSV positive patients | 2017 | 33 | 27.97 | 85 | 72.03 | 0.70 |
| | 2018 | 17 | 25.37 | 50 | 74.63 | |

may shed further light on prescribing habits within the hospital, once 2018 data is released.

There are several possible reasons why rapid testing for respiratory viruses had no impact on time to patient discharge. The decision to discharge a patient is more likely to depend on their clinical status (haemodynamic parameters, work of breathing etc.) rather than the microbiological aetiology of their illness. Social history is also important: elderly patients living alone or patients with reduced mobility are less likely to be discharged early compared to otherwise healthy patients, regardless of microbiology results.

The main strength of this study is that it investigates a common clinical problem: there are multiple daily presentations to EDs throughout Australia each winter with influenza-like illness, and these findings are relevant to clinicians across multiple medical disciplines.

The primary weakness of the study is the difference in prevalence of respiratory viruses across the two years of the study. There was an influenza epidemic in Queensland in 2017, with relatively low prevalence of the virus in 2018 [16,17]. It would be useful to repeat the study across two years of similar virus epidemiology. Another weakness of this study is that we do not have data on patients who presented with influenza-like illness, in whom NPS was not performed. It is possible that, particularly during the 2017 influenza epidemic, patients were presenting with symptoms of influenza, were diagnosed clinically as influenza without diagnostic testing, and were managed with supportive therapies rather than with antibiotics. This group represents an unmeasured confounder in our study; this is a weakness of retrospective studies.

The potential role of rapid testing in infection control decision making (earlier de-isolation of patient from

droplet precaution rooms) was not assessed as the vast majority of patients in GCUH are managed in single rooms.

In summary, this study highlights the potential of rapid testing for respiratory viruses as an antimicrobial stewardship tool. Earlier clinician knowledge of a positive viral result had a statistically significant association with reduced antibiotic prescriptions. There was no impact on timing of patient discharge.

Ethics

Ethical approval for the study was granted by the Gold Coast Hospital and Health Service Human Research Ethics Committee (reference HREC/18/QGC/217).

Authorship statement

KO was responsible for data extraction and manuscript formulation. KJ was responsible for implementation of rapid respiratory virus testing at GCUH, and provided input on manuscript revision and editing.

Conflict of interest

No conflicts of interest to declare.

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Provenance and peer review

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