Burden of nosocomial COVID-19 in Wales: results from a multicentre retrospective observational study of 2508 hospitalised adults

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ABSTRACT

The burden of nosocomial SARS-CoV-2 infection remains poorly defined. We report on the outcomes of 2508 adults with molecularly-confirmed SARS-CoV-2 admitted across 18 major hospitals, representing over 60% of those hospitalised across Wales between 1 March and 1 July 2020. Inpatient mortality for nosocomial infection ranged from 38% to 42%, consistently higher than with participants with community-acquired infection (31%–35%) across a range of case definitions. Those with hospital-acquired infection were older and fatter than those infected within the community. Nosocomial diagnosis occurred a median of 30 days following admission (IQR 21–63), suggesting a window for prophylactic or postexposure interventions, alongside enhanced infection control measures.

Little is known regarding the prevalence and outcomes of in-hospital transmission of SARS-CoV-2 among medical patients. The largest and only multicentre cohort study to date reported outcomes in 1564 patients admitted with confirmed SARS-CoV-2 infection across 11 hospitals. Mortality in the nosocomial group appeared comparable to those with likely community-acquired infection (27.0% and 27.2%, respectively). This study was conducted early in the pandemic course, meaning reliable estimates of the true impact of hospital-acquired COVID-19 infection remain hampered by a paucity of publicly available data at national and regional levels.

Here, we update assessment of the relative burden of community-acquired and nosocomially-acquired SARS-CoV-2 infection, using anonymised patient-level hospital-level data collected via the National Pathway for Managing COVID-19 Infections in Secondary Care in Wales initiative (www.covid19hospitalguideline.wales.nhs.uk).

The methods and data sources relating to this work are described in detail elsewhere. Briefly, positive SARS-CoV-2 PCR results recorded between 1 March 2020 and 1 July 2020 in adults with a recorded hospital admission were identified for retrospective notes review. Local clinical teams across 18 centres (online supplemental file S1) performed data entry using a standardised online tool. Mandatory fields included dates of PCR sampling, admission and discharge, age, sex, comorbidity count and outcome (death or discharge). Supplementary fields included Welsh Index of Multiple of Deprivation (WIMD) and preadmission Clinical Frailty Scale (CFS).

The primary outcome was all-cause mortality, grouped by probable origin of SARS-CoV-2 infection based on (1) clinician-recorded source and (2) standardised case definitions (online supplemental file S2). Time-to-event analysis used time in hospital following a positive PCR test, to avoid introducing survivorship bias. All analyses were performed using R and GraphPad Prism.

We identified 6005 SARS-CoV-2-positive cases in a hospital location, in patients between 1 March 2020 and 1 July 2020 inclusive, of which 4112 were individual cases. Clinical information was obtained from 2384/4112 individuals (63%). A total of 76 individuals were excluded due to missing core data fields or initial PCR sampling date exceeding admission period by 31 days (online supplemental file S3). This left 2508 case records, representing approximately 61% of the total adult population hospitalised with COVID-19 within Wales. Admission features are summarised in table 1. The cohort had a median age of 74 years (IQR 62.5–85.5), of whom 54.3% were men and 45.7% were women. Individuals from the most-deprived WIMD quartile were over-represented relative to those in the least deprived quartile (31.2% vs 18.7%, χ² test: p<0.0001).

Clinician-defined admission source was available in 2354 cases (93.9%). Hospital-acquired COVID-19 was documented in 433 cases (17.3% of cohort, 37.8% mortality), comparable to mortality in cases presenting by ambulance (553/1359, 40.7%). Walk-in and GP referrals together accounted for 20.4% of the cohort and had the lowest inpatient mortality rate (17.1%–23.6%). The small number of patients admitted from care or nursing homes showed the highest inpatient mortality rate (23/50, 46.0%).

We next applied a standardised definition for nosocomial COVID-19, based on the interval between admission and diagnostic testing exceeding 14 days, identifying 411 cases (16.4% of cohort, consistent with previous reports). Community-acquired cases constituted the majority (n=1604, 64.0%), defined by PCR sampling preceding or within 5 days of admission. Monthly prevalence estimates are shown in online supplemental file S4. Overall, 39.2% of patients with nosocomial-infection died, compared with 31.7% with community-acquired infection. This proved consistent across the
Our findings expose the hitherto underestimated vulnerability and impact of nosocomial infection with SARS-CoV-2. Many potential mechanisms may underlie these observations, including the advanced age and frailty of patients who remain admitted and the advanced age and frailty of patients who remain admitted. 

Table 1 Demographics and clinical features at presentation

| Variable                  | Died (%) | Discharged (%) | Total (%) |
|---------------------------|----------|----------------|-----------|
| Admission hospital        |          |                |           |
| A                         | 174 (40.6)| 255 (59.4)     | 429 (17.1)|
| B                         | 165 (38.9)| 259 (61.1)     | 424 (16.9)|
| C                         | 96 (39.8) | 145 (60.2)     | 241 (9.6) |
| D                         | 78 (32.9) | 159 (67.1)     | 237 (9.4) |
| E                         | 97 (42.9) | 129 (57.1)     | 226 (9.0) |
| F                         | 46 (27.1) | 124 (72.9)     | 170 (6.8) |
| G                         | 35 (22.4) | 121 (77.6)     | 156 (6.2) |
| H                         | 48 (33.3) | 96 (66.7)      | 144 (5.7) |
| I                         | 19 (22.6) | 65 (77.4)      | 84 (3.3)  |
| J                         | 22 (27.2) | 59 (72.8)      | 81 (3.2)  |
| K                         | 35 (43.2) | 46 (56.8)      | 81 (3.2)  |
| L                         | 24 (32.0) | 51 (68.0)      | 75 (3.0)  |
| M                         | 14 (21.2) | 52 (78.8)      | 66 (2.6)  |
| N                         | 24 (38.7) | 38 (61.3)      | 62 (2.5)  |
| O                         | 6 (25.0)  | 18 (75.0)      | 24 (1.0)  |
| P*                        | 2 (25.0)  | 6 (75.0)       | 8 (0.3)   |
| Age group (years)         |          |                |           |
| <65                       | 115 (14.7)| 667 (85.3)     | 782 (31.2)|
| 65–75                     | 305 (44.4)| 382 (55.6)     | 687 (27.4)|
| 75–85                     | 273 (50.6)| 267 (49.4)     | 540 (21.5)|
| >85                       | 192 (38.5)| 307 (61.5)     | 499 (19.9)|
| Sex                       |          |                |           |
| Female                    | 377 (32.9)| 768 (67.1)     | 1145 (45.7)|
| Male                      | 508 (37.3)| 855 (62.7)     | 1363 (54.3)|
| Median comorbidity count  |          |                |           |
| Ceiling of care           |          |                |           |
| WIMD†                     |          |                |           |
| Q1—most deprived          | 265 (33.9)| 517 (66.2)     | 782 (31.2)|
| Q2                        | 251 (38.0)| 409 (62.0)     | 660 (26.3)|
| Q3                        | 163 (34.5)| 310 (65.5)     | 473 (18.9)|
| Q4—least deprived         | 168 (35.7)| 302 (64.3)     | 470 (18.7)|
| WIMD unrecorded           | 38 (30.9)| 85 (69.1)      | 123 (4.9)|
| CFS score                 |          |                |           |
| 1—very fit                | 21 (12.8) | 143 (87.2)     | 164 (6.5) |
| 2—fit                     | 32 (16.1) | 167 (83.9)     | 199 (7.9) |
| 3—managing well           | 47 (27.3) | 125 (72.7)     | 172 (6.9) |
| 4—vulnerable              | 63 (39.9) | 95 (60.1)      | 158 (6.3) |
| 5—mildly frail            | 70 (52.6) | 63 (47.4)      | 133 (5.3) |
| 6—frail                   | 117 (49.6)| 119 (50.4)     | 236 (9.4) |
| 7—severely frail          | 87 (50.0) | 87 (50.0)      | 174 (6.9) |
| 8—very severely frail     | 36 (62.1)| 22 (37.9)      | 58 (2.3)  |
| 9—terminally ill          | 7 (63.6)  | 4 (36.4)       | 11 (0.4)  |
| CFS score unrecorded      | 405 (33.7)| 798 (66.3)     | 1203 (48.0)|

*Represents three combined centres (<5 patients each). WIMD†=most deprived, 1909=least deprived. CFS, Clinical Frailty Scale; CPAP, continuous positive airway pressure; WIMD, Welsh Index of Multiple Deprivation.
methodology, acknowledging the competing risks of discharge and death and multiple case definitions. This is relevant to interpretation of publicly reported figures. For instance, defining nosocomial cases based on the median 5-day incubation period identified 14.2% additional cases and 13.7% more deaths than a commonly used 7-day threshold. This suggests the burden of nosocomial COVID-19 may be significantly under-reported, which has major public health implications for infection control policy globally, particularly given the rapid spread of more infectious and severe SARS-CoV-2 variants.

Our study also has limitations, including its retrospective nature. Although sites retrieved notes at random, we cannot fully exclude risk of ascertainment bias. As the total number of patients at risk of infection was unknown, we cannot infer the risk of acquiring SARS-CoV-2 within the hospital. Similarly, we did not collect data on recent hospitalisations, and it is possible that nosocomial COVID-19 cases have been classified as community. We also recognise our findings represent crude inpatient mortality rate estimates, based on all-cause mortality. Future studies using national linked datasets including genomic analysis and estimating excess mortality are suggested.

In conclusion, we performed a national service evaluation to document the burden of nosocomial SARS-CoV-2 infection during and following the first wave in Wales. We found many of those dying with probable hospital-acquired COVID-19 had been in the hospital for at least a month prior to exposure. We suggest this highlights an opportunity for pre-exposure and early postexposure prophylactic measures, including inpatient vaccination and clinical trial enrolment.11 12

This work was presented to the Welsh Technical Advisory Group and Directors of Nursing Group, contributing to a recommendation to ministers supporting vaccination of inpatients without a diagnosis of COVID-19 within priority groups and those being admitted for a planned procedure at increased risk.

Figure 1  Inpatient mortality rates by admission hospital sites scatter plot showing inpatient mortality rates for patients with community-acquired COVID-19 (circles) and nosocomial COVID-19 (triangles) by individual sites, with hospitals arranged by decreasing overall case load are plotted from the left. for 11/15 sites, inpatient mortality rates for nosocomial cases exceeds that of community acquired cases. Individual sites with fewer than five cases were excluded from analysis.

Figure 2  Competing risk analysis plot of nosocomial and community infection outcomes of patients with COVID-19. Time to event analysis cumulative incidence analysis for the competing risks of discharge and diagnosis, using the time from SARS-CoV-2 diagnosis. COVID-19 origin is assigned by the commonly used case definition, as outlined by Carter et al, nosocomial and community-acquired COVID-19 as labelled. Dotted lines: cumulative incidence of death, continuous lines: cumulative incidence of discharge on probability scale. To deal with potential survivorship bias introduced by including community-diagnoses tested prior to admission (who cannot reach discharge or death until admission), day 0 was defined as the more recent of day of admission or date of first positive diagnostic SARS-CoV-2 testing.
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