Association between Household Exposure and Cycle Threshold in COVID-19 Infected Health Care Workers

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Abstract

Objective. Household COVID-19 contact constitutes a high-risk exposure for health care workers (HCWs). Cycle threshold (Ct) of reverse transcriptase–polymerase chain reaction testing provides an estimate of COVID-19 viral load, which can inform clinical and workplace management. We assessed whether Ct values differed between HCWs with and without household exposure.

Methods. We analyzed HCW cases whose Ct data could be compared. We defined low Ct at a cut-point approximating a viral load of 4.6x106 copies per ml. Logistic regression tested the association of household exposure and symptoms at diagnosis with a low Ct value.

Results. Of 77 HCWs, 20 were household exposures cases and 34 were symptomatic at testing (7 fell were both). Among household exposures, 9 (45%) manifested lower Ct values compared to 14 (25%) of all others. Both household exposure (Odds Ratio [OR] 1.3; 95 % Confidence Interval [CI] 1.03–1.6) and symptoms at diagnosis (OR 1.4; 95% CI 1.15–1.7) were associated a low Ct value.

Discussion. Household exposure in HCWs was associated with lower Ct values, consistent with a higher viral load, supporting the hypothesis that contracting COVID-19 in that manner leads to a greater viral inoculum.

Introduction

Cycle threshold (Ct) of reverse transcriptase–polymerase chain reaction, the number of amplification cycles for the target gene to exceed threshold detection, provides an estimate of COVID-19 viral load and is related to infectivity and disease severity.[1] Among health care workers (HCWs), Ct can inform return-to-work decisions.[2] Residing in the same household as a COVID-19 case constitutes a high-risk exposure.[3] This presumably reflects a greater viral inoculum, but whether this is linked to a higher viral load has not been established. In a cohort of HCWs with COVID-19 infection and well-characterized contact tracing, we assessed whether the Ct differed between those with illness likely contracted from a household member compared to all others.

Methods

As part of clinical quality improvement activities at the San Francisco Veterans Affairs Healthcare System, we analyzed positive COVID-19 RT-PCR testing (nasopharyngeal or oropharyngeal swab). These included both symptomatic and asymptomatic employees (the latter tested due to exposure or in routine surveillance monitoring). We limited analysis to cases March 2020 through January 2021 whose initial positive testing was performed at the San Francisco Veterans Affairs Healthcare System laboratory using the same Abbott RealTime SARS-COV-2 assay providing directly comparable Ct values. The Abbot assay is United States Food and Drug Administration Emergency Use Authorization-approved as a qualitative test and was calibrated in-house using standard reference materials.[2] We excluded cases initially diagnosed with other assays at our site or elsewhere. We reviewed our employee health unit's COVID-19

database, using narrative information to identify whether infection was attributable to residing with someone whose COVID-19 preceded that of the employee. We also determined if the employee was symptomatic at initial testing. We tested the cross-tabulation of household vs. symptomatic using the Chi square. We defined low Ct (indicative of higher viral load) as a value below the lowest quartile cutoff among the non-household contact cases: a Ct of 9.32 (estimated viral load approximating $4.6x10^6$ copies per ml). Logistic regression tested the association of household exposure alone or adjusted for symptomatic case status with low Ct (RStudio 2021; PBC, Boston, MA).

Results

Of 141 COVID-19 positive employees, 64 did not have their initial diagnostic test performed on the Abbott RealTime at the SFVAHCS laboratory. Of 77 analyzed, 20 (26%) were household exposures and 34 (44%) were symptomatic at testing. Being household exposed vs. symptomatic at testing was not statistically associated ($p > 0.3$; seven employees classified as both). Of 20 household exposure cases, 9 (45%) manifested lower Ct values; 14 (25%) non-household exposure cases had lower Ct values. The odds of lower Ct value associated with household exposure alone and adjusted for symptomatic at testing are shown in Table 1.

Table 1
Odds of Low Cycle Threshold (Ct) Among 77 COVID-19 Positive Health Care Workers

Logistic Regression Model	Risk Factor (no. with risk factor)	Odds Ratio	95% CI
Model 1	Household Exposure (20)	1.2	0.97–1.5
Model 2	Household Exposure (20)	1.3	1.03–1.6
	Symptomatic at Time of Test (34)	1.4	1.15–1.7
CI = Confidence Interval			

Discussion

Household exposure was associated with lower Ct, consistent with a higher viral load. This supports the hypothesis that contracting illness through household exposure represents a greater viral inoculum, through multiple potential factors (prolonged frequency and duration of exposure, no mask wearing at home, lack of physical distancing, inadequate ventilation). The association of household source to lower Ct was stronger taking into account being symptomatic. The latter has been shown to be related to lower Ct.[4] Limiting analysis to HCWs has the advantage of studying a cohort with consistent access to testing and with thorough, standardized contact tracing to ascertain that the household was the likely source of exposure. Nonetheless, this does limit generalizability. The relatively small study size accounts for wide confidence intervals, although this does not explain statistically significant associations that we did observe. The association of household exposure with lower COVID-19 Ct suggests that greater viral

inoculum leads to a higher viral load in infection, providing useful insights into this disease among HCWs that could inform case management.[2]

Abbreviations

HCW
Health care work
Ct
Cycle threshold
OR
Odds Ratio
CI
Confidence Interval

Declarations

Ethics approval: This report is an outgrowth of quality improvement efforts and was designated as exempt from further institutional review for research involving human subjects

Consent for publication: No personal identifying data were included.

Availability of data and materials: Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: AC and PDB carried out the data extraction and data analysis. SD, PDB, and HL originally conceived of the analysis. All authors collaborated in drafting and reviewing the manuscript.

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