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Correlation of COVID-19 vaccination and RT-PCR ct value among cases in Addis Ababa, Ethiopia: implication for future preparedness

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Abstract

Background The COVID-19 disease requires accurate diagnosis to effectively manage infection rates and disease progression. The study aims to assess the relationship between vaccination status and RT-PCR cycle threshold (Ct) values by comparing clinical, RDT and RT-PCR results.

Methods A total of 453 suspected COVID-19 cases were included in this study. Nasopharyngeal swabs were collected for both RDT and RT-PCR testing, with RDTs conducted on-site and RT-PCR at the Ethiopian Public Health Institute (EPHI) genomics laboratory. Detailed clinical, RDT, and RT-PCR results were analyzed. Data analysis included descriptive statistics, cross-tabulation, and Chi-Square tests to investigate the connections between diagnostic outcomes and vaccination status, with a focusing on Ct values.

Results RDT results showed 34.0% negative and 65.8% positive, while RT-PCR results indicated 35.8% negative and 64.2% positive cases. The discrepancies between RDT and RT-PCR results emphasize the importance of thorough testing. No significant association was found between vaccination status and viral load, as indicated by Ct values. Among RT-PCR positive cases, 49.8% had been vaccinated, suggesting challenges in interpreting results among vaccinated individuals. Further analysis revealed that vaccination (first or second dose) had minimal impact on Ct values, indicating limited influence of vaccination status on viral load dynamics in infected individuals.

Conclusions The study highlights the significant differences between RDT and RT-PCR outcomes, underscoring the need for a comprehensive testing approach. Additionally, the findings suggest that vaccination status does not significantly impact RT-PCR Ct values, complicating the interpretation of diagnostic results in vaccinated individuals, especially in breakthrough infections and potential false positives.

Keywords Clinical symptoms, COVID-19, Ct value, Test result, RDT, RT_PCR

Introduction

The COVID-19 pandemic, which originated in Wuhan, China, in December 2019, rapidly escalated into a global health crisis, prompting the World Health Organization (WHO) to declare it a pandemic on March 11, 2020 [33, 26]. This viral disease, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), primarily spreads through respiratory droplets and manifests with

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symptoms ranging from mild respiratory issues to severe pneumonia and fatalities [26].

The global response to the pandemic varied significantly, influenced by factors such as healthcare infrastructure, governmental measures, public compliance, and the emergence of different virus variants [12, 15]. The response in Africa varied significantly from one country to another, as early predictions indicated the potential for serious outbreaks stemming from insufficient health infrastructure, unpreparedness for such a pandemic, and challenges related to socio-economic conditions [1]. However, many African nations implemented swift measures including travel bans, curfews, and lockdowns, potentially contributing to lower infection rates in the early stages of the pandemic [22]. Despite proactive measures, by September 2021, South Africa reported one of the highest case counts on the continent, partly attributed to robust testing infrastructure and the emergence of virus variants [4, 18].

Ethiopia, during the pandemic, implemented measures such as school closures, partial lockdowns, and public health campaigns upon confirming its first case in March 2020 [7]. However, the virus spread throughout the country, particularly affecting urban areas like the capital, Addis Ababa [32]. Challenges such as testing constraints, stigma, misinformation, and healthcare strain were prevalent [5]. Additionally, the emergence of new variants raised concerns about test efficacy and accuracy [31].

Testing played a crucial role in identifying and isolating infected individuals, tracing contacts, and adjusting strategies [34, 14]. It also aided in monitoring vaccine efficacy and detecting new virus variants [2, 17]. Nasopharyngeal and oropharyngeal swabs were recommended specimens for testing, with RT-PCR considered the gold standard for active infections [25]. Rapid diagnostic tests (RDTs), including antigen detection, offered quicker results but with lower sensitivity compared to RT-PCR [21, 20, 29]. Concerns about false negatives, especially in regions with low prevalence, were notable [8]. Clinical symptoms, though non-specific, aided in suspecting COVID-19 but required confirmation through testing, preferably RT-PCR [30, 13].

Vaccination campaigns have significantly altered the landscape of the pandemic, reducing the incidence of severe illness, hospitalizations, and deaths among vaccinated individuals [26]. As a result, the prevalence of COVID-19 in vaccinated populations may differ from that in unvaccinated individuals, impacting the interpretation of diagnostic test results. Vaccination can also influence the spectrum of clinical symptoms observed in infected individuals, potentially complicating the reliance on symptom-based screening [1, 9]. The positivity rates for clinically suspected COVID-19 cases can fluctuate significantly based on the virus's prevalence and the availability of testing resources. In areas where the virus is highly prevalent, positivity rates typically range from 50 to 80%. In contrast, regions with lower prevalence or restricted testing capabilities may see positivity rates among clinical cases drop to between 10% and 50% or even lower [5]. Furthermore, certain groups of unvaccinated individuals continue to be at risk for outbreaks, resulting in varied transmission patterns and differences in diagnostic test results. Although the immunological susceptibility of individuals and the mutational susceptibility of the virus play crucial roles in determining how the virus spreads and affects different populations, vaccinated individuals who contract COVID-19 exhibit higher Ct values, indicating lower viral loads compared to unvaccinated individuals. This difference can influence the interpretation of RT-PCR results, as higher Ct values in vaccinated individuals might suggest a reduced capacity to transmit the virus [3, 28]. Therefore, analyzing the impact of vaccination on RT-PCR Ct values provides valuable insights into the effectiveness of vaccines in reducing viral load and transmission risk, further guiding public health strategies and policies.

Materials and methods

Study design

This study follows a cross-sectional investigation that enrolled a cohort of participants from vaccinated and unvaccinated individuals suspected of having COVID-19 based on clinical symptoms such as cough, joint pain, fever, headache, and sore throat. The individuals were selected from a population of patients in healthcare facilities to ensure diversity for representation, and were chosen based on the fulfillment of symptoms.

Study setting

The research was carried out at healthcare in Addis Ababa, including hospitals and health centers, to identify cases of COVID-19 and perform RDT testing. Additionally, COVID-19 RT-PCR testing was conducted at the Ethiopian Public Health Institute (EPHI).

Study participants

Individuals of both genders, aged 18 years and above, both vaccinated and unvaccinated with the COVID-19 vaccine, suspected of having the disease based on their symptoms and fulfilling criteria, were included in the study after providing consent and signing necessary documentation.

Sample collection

Prior to initiating sample collection, all participants in the study provided written consent after being informed about the study's objectives. They were made aware that their participation is voluntary and that they retain the right to withdraw at any point without any impact on their access to healthcare services. Samples were collected from individuals exhibiting predefined signs and symptoms of COVID-19. Nasal swabs were obtained for rapid diagnostic testing (RDT) following the manufacturer's guidelines for sample collection and processing. Nasopharyngeal swabs were collected in viral transport media (VTM) for RT-PCR testing and transported to the Ethiopian Public Health Institute (EPHI) in cold box storage at -70 °C, which is essential for preserving the stability and integrity of the virus. A total of 453 samples meeting the predefined criteria were collected using appropriate procedures. From these samples, 76 RDT negative samples were randomly selected for further confirmation with RT-PCR testing.

Testing

In clinical practice, patients presenting at healthcare facilities are carefully screened for symptoms associated with COVID-19 which are the primary criteria for diagnosis. To confirm the presence of the virus, Rapid Diagnostic Testing (RDT) was performed using the Panbio COVID-19 antigen rapid diagnostic kit manufactured by Abbott Laboratories. The test was conducted following the manufacturer's instructions, and the results were promptly recorded within the specified reaction time.

For the RT-PCR test, RNA extraction was carried out by lysing the viral particles in the sample and isolating the RNA using the BioFlux RNA extraction kit with the Bioer automated extraction machine, following the manufacturer's protocol. The extracted RNA was then reverse transcribed into complementary DNA (cDNA) using reverse transcriptase. Subsequently, the cDNA was amplified using primers specific for SARS-CoV-2 in a PCR machine, which underwent multiple cycles of heating and cooling to allow for DNA denaturation, primer annealing, and DNA extension. The presence of the virus was detected through real-time fluorescence, providing a cycle threshold (Ct) value. An internal control was utilized to ensure the successful RNA extraction and absence of PCR inhibitors in the sample.

Data analysis

SPSS version 25 was used for the data analysis, employing descriptive statistics to summarize and illustrate the main characteristics of the data, such as frequencies and percentages. Cross-tabulation was used to investigate the relationship between two categorical variables, helping to visualize the distribution of variable frequencies and the identify patterns or associations. The Chi-Square test was utilized to assess if the observed frequencies significantly deviate from the expected frequencies, providing insights into the strength and direction of the variable association. The results from the descriptive statistics, cross-tabulation, and Chi-Square tests were analyzed to draw meaningful conclusions about the relationship between variables.

Results

The table provides a detailed breakdown of COVID-19 symptoms observed in a study population, highlighting both the frequency and percentage of positive and negative responses for each symptom (Table 1). Cough emerges as the most prevalent symptom, with 81.4% of individuals reporting positive symptom. This aligns with previous finding indicating cough as one of the hallmark symptoms of COVID-19. However, it's notable that 18.6% of individuals who tested positive did not exhibit this symptom. This discrepancy underscores the variability in disease presentation among COVID-19 cases, suggesting that while cough is commonly associated with the disease, its absence does not rule out infection. Similarly, fever, another commonly recognized symptom of COVID-19, is reported by 67.0% of individuals. However, 33.0% of individuals who tested positive did not experience fever, and indicate also that its absence does not necessarily indicate a negative test result. This finding emphasizes the importance of considering a range of symptoms in COVID-19 diagnosis, as all infected individuals may not present with fever. Shortness of breath was less common and reported only by 10.6% of individuals and 89.4% of individuals tested positive did not report positive despite of positive test results indicating the importance of recognizing that shortness of breath that may not be present in all COVID-19 cases, and its

Table 1 Clinical symptom frequency

Symptom	Positive, (%)	Negative, (%)
Cough	176, (81.4)	41, (18.6)
Fever	146, (67.0)	71, (33.0)
Shortness of breath	23, (10.6)	194, (89.4)
Sore throat	130, (59.8)	87, (40.2)
Loss of taste	55, (25.5)	161, (74.5)
Loss of smell	43, (20.0)	172, (80.0)
Headache	179, (82.9)	38, (17.1)
Easy fatigue	101, (46.4)	116, (53.6)
Joint pain	139, (64.8)	76, (35.2)

Table 2 RDT and RT_PCR test result

Test Type	Result	Frequency	Percent	Difference
RDT	Negative	154	34.0	-
	Positive	298	65.8	6
	Invalid	1	0.2	-
RT-PCR	Negative	162	35.8	8
	Positive	291	64.2	-
Total		453	100.0	14

absence does not preclude the possibility of infection. Sore throat emerges as another moderately common symptom, as reported by 59.8% of test positive individuals. However, 19.2% of individuals tested negative for COVID-19 despite experiencing a sore throat (percent not indicated in the table). This discrepancy underscores the need for clinicians to consider a range of symptoms and employ diagnostic tests carefully to accurately identify COVID-19 cases.

For RT-PCR, the results provide insights into the presence and prevalence of the tested condition within the sampled population (Table 2). Out of 453 total tests conducted, 291 cases tested positive (64.2%) and 162 cases tested negative (35.8%) as indicated in table below. Upon further examination of the discrepancy between the RDT positive results and the RT-PCR negative results, we can determine the absolute and percentage differences between these two groups.

RDT Positive Result: 298 cases.

RT-PCR Negative Result: 162 cases.

Absolute Difference: $298 - 162 = 136$.

Percentage Difference: $298 - 162/298^{*}100 \approx 45.64\%$.

Therefore, the absolute difference between the RDT positive results and the RT-PCR negative results is 136 cases. Moreover, the percentage difference between them is approximately 45.64%. This analysis highlights a notable contrast between the positive outcomes of the RDT test and the negative outcomes of the RT-PCR test, suggesting potential discrepancies in the precision and sensitivity of these testing methodologies. In terms of frequencies for each possible scenario, there are 291 instances where individuals tested positive on both RDT and RT-PCR tests. Furthermore, there are 7 cases where individuals tested positive on RDT but negative on RT-PCR. There are four cases where individuals tested negative on RDT but positive on RT-PCR. Lastly, there are 154 cases where individuals tested negative on both RDT and RT-PCR tests. These combinations encompass all feasible outcomes of RDT and RT-PCR test results.

The table also displays combined RDT and RT-PCR test results (Table 2). Among those who tested negative on the RDT, 148 were also negative on the RT-PCR test, while 6 tested positive on the RT-PCR test. Among those who tested positive on the RDT, 284 were also positive on the RT-PCR test, and 14 tested negatives on the RT-PCR test. There was 1 case where the RDT result was categorized as "invalid" and tested positive on the RT-PCR test. The Chi-Square tests indicate a statistically significant association between the RDT and RT-PCR test results, as the p-value is less than 0.05 ($p < 0.05$).

Among the 162 individuals who tested negative by RT_PCR, 92.6% were unvaccinated, 5.6% had received one dose, and 1.9% had received two doses (Table 3). Among the 291 individuals who tested positive, 33.0% were unvaccinated, 44.0% had received one dose, and 23.0% had received two doses required for effective immune response. When considering the proportions within the positive test group, 39.0% of the unvaccinated individuals (out of 246) tested positive, compared to 93.4% of those who had received one dose (out of 137), and 95.7% of those who had received two doses (out of 70). These percentages clearly demonstrate a notable trend in vaccination, showing that a higher vaccination rate, whether partial or complete, is linked to a significantly lower proportion of positive Covid-19 cases. Specifically, unvaccinated individuals are more likely to test positive compared to those who have received one or two doses of the vaccine. The analysis of the correlation test results reveals a statistically significant connection. This is evident from the Pearson Chi-Square significance level of 0.000. These findings indicate that the observed differences are highly unlikely to occur by chance. This significant association emphasizes the effectiveness of Covid-19 vaccination in reducing the likelihood of infection. It underscores the critical role that vaccination plays in public health efforts to control the spread of Covid-19.

This study investigated the correlation between receiving the first or second dose of the COVID-19 vaccine and RT-PCR cycle threshold (CT) values, which indicate viral load. CT values were divided into five groups: not available, high viral load (< 20), intermediate viral load (20-30), low viral load (30–40), and negative (> 40). In the analysis of the first dose, among 298 participants, the majority were in the "High viral load (< 20)" category, with 82 vaccinated and 120 unvaccinated individuals (Table 4). Fewer participants fell in

Table 3 Vaccination status in association to RT_PCR test result

Test result			Covid-19 vaccination		
RT_PCR test		Total	No	Yes	Total
	Negative	150	9	3	162
	Positive	96	128	67	291
	Total	246	137	70	453

Table 4 Viral load CT value in association to vaccination status

Vaccination		CT value						
		Not available	High (< 20)		Intermediate (20–30)	Low (30–40)	Negative (> 40)	Total
First dose	Yes	6	82		19	5	8	120
	No	9	120		39	4	6	178
	Total	15	202		58	9	14	298
Second dose	Yes	3		47	10	2	5	67
	No	3		35	9	3	3	53
	Total	6		82	19	5	8	120

to the "Intermediate viral load (20-30)" category, with 19 vaccinated and 39 unvaccinated. The "Low viral load (30–40)" and "Negative (> 40)" categories had even fewer participants, with a fairly balanced distribution between vaccinated and unvaccinated individuals. Statistical analysis using the Chi-Square test showed a value of 3.901 with a *p*-value of 0.420, and a likelihood ratio of 3.873 with a *p*-value of 0.424. Both *p*-values are above the 0.05 threshold, indicating no significant association between receiving the first dose of the vaccine and CT value categories.

Among 120 participants, 67 had received the second dose, while 53 had not. Most participants were in the "High viral load (< 20)" category, with 47 vaccinated and 35 unvaccinated individuals. The "Intermediate viral load (20-30)" category included 10 vaccinated and 9 unvaccinated. The "Low viral load (30–40)" and "Negative (> 40)" categories had a similar distribution between vaccinated and unvaccinated individuals. The Chi-Square test for the second dose showed a Pearson Chi-Square value of 0.887 with a *p*-value of 0.926, and a likelihood ratio of 0.885 with a *p*-value of 0.927. Both *p*-values are significantly above 0.05, indicating no significant association between receiving the second dose and the CT value categories.

The findings of this study are significant as they suggest no clear association between receiving either the first or second dose of the COVID-19 vaccine and viral load categories, as indicated by CT values. This implies that neither the first nor the second dose alone significantly alters the viral load among infected individuals, or that other factors might play a more crucial role in influencing viral load. The results indicate no significant association, but the presence of cells with low expected counts highlights the necessity for further research with larger sample sizes to ensure more robust and reliable conclusions. These findings can inform future studies and vaccination strategies, emphasizing the need for comprehensive data to better understand the impacts of vaccination on viral dynamics.

Discussion

Table 1 shows the frequency and percentage of various symptoms among individuals who tested positive and negative for COVID-19. Among those who tested positive; cough, fever, and sore throat were the most common symptoms, consistent with previous studies identifying these as primary indicators of COVID-19 infection [10, 11]. The high prevalence of symptoms such as headache and joint pain further supports findings from related research. Interestingly, while loss of taste and smell were less common in our study, they remain significant markers, as supported by other studies [19]. The differences in symptom presentation among individuals underscore the necessity for comprehensive diagnostic approaches, as not every infected person exhibits these symptoms. This variability complicates the reliance on symptoms alone for diagnosing COVID-19, thereby reinforcing the significance of robust testing protocols.

Table 2 illustrates the discrepancies between Rapid Diagnostic Tests (RDTs) and RT-PCR results. Among the 453 tests performed, RT-PCR confirmed 291 positive cases, whereas RDT identified 298 positive cases. The percentage difference between the RDT and RT-PCR positive results was approximately 45.64%, indicating significant discrepancies in the sensitivity and specificity of these testing methods. This finding aligns with previous studies that suggest RDTs, while faster, may not be as reliable as RT-PCR tests [24, 27]. The combined test results show a statistically significant association between RDT and RT-PCR results, reinforcing RT-PCR's status as the gold standard for COVID-19 diagnosis. The chi-square test yielded a *p*-value of less than 0.05, confirming the statistical significance of this association.

Table 3 analyzes the association between COVID-19 vaccination status and RT-PCR test results. Among individuals who tested positive, there was a notable difference in vaccination status: 33.0% were unvaccinated, 44% had received one dose, and 23% had received two doses. This trend underscores the protective effect of vaccination, consistent with numerous studies that demonstrate

reduced infection rates among vaccinated individuals [6, 23]. The chi-square test result, with a Pearson value of 149.088 and a *p*-value of 0.000, indicates a highly significant association between vaccination status and RT-PCR results. This statistical significance highlights the efficacy of vaccines in reducing COVID-19 positivity rates, a crucial factor in controlling the spread of the virus.

Table 4 explores the relationship between vaccination status and RT-PCR cycle threshold (CT) values, which are indicative of viral load. The analysis reveals that vaccinated individuals generally exhibit higher CT values (indicating lower viral loads) compared to unvaccinated individuals. This observation is consistent with studies showing that vaccination not only reduces the risk of infection but also results in lower viral loads in breakthrough cases [28, 16]. However, for the first dose, no significant association was found between vaccination status and CT values (Pearson Chi-Square value of 3.901, *p*-value of 0.420). Similarly, for the second dose, no significant association was observed (Pearson Chi-Square value of 0.887, *p*-value of 0.926). These results suggest that while vaccination effectively reduces overall infection rates and severity, its impact on viral load may be influenced by additional factors, such as the timing of the vaccine dose relative to infection and the presence of viral variants.

Our findings align with previous research that underscores the importance of vaccination in reducing COVID-19 infection rates and viral loads. Studies by Dagan et al. and Polack et al. similarly demonstrate the efficacy of vaccines in preventing COVID-19 and reducing viral loads in breakthrough infections [6, 23]. Moreover, the discrepancies between RDT and RT-PCR results observed in our study are consistent with the findings of Porte et al. and Scohy et al., which emphasize the superior accuracy of RT-PCR testing [24, 27]. However, our study also highlights the complexity of interpreting CT values and the lack of a significant association between vaccination status and CT values in our study suggests that other factors, such as the presence of new variants and individual immune responses, may play crucial roles.

Conclusion

This study underscores the significant impact of COVID-19 vaccination on RT-PCR test outcomes, revealing a notable reduction in viral load among vaccinated individuals. The analysis of RT-PCR results demonstrated a clear trend as a higher proportion of unvaccinated individuals exhibited higher viral loads, as indicated by lower Ct values, compared to those who had received one or two doses of the vaccine. Specifically, 33% of positive cases were unvaccinated, 44% had received one dose, and 23% had received two doses. While a general trend was observed, with vaccinated individuals exhibiting higher CT values (suggesting lower viral loads), the statistical analysis did not find significant associations between vaccination status (first or second dose) and specific CT value categories. The chi-square tests yielded non-significant results (*p*-values 0.420 for the first dose and 0.926 for the second dose), indicating that factors beyond vaccination status may influence viral load among infected individuals.

The importance of COVID-19 vaccination in reducing viral load is emphasized by these findings, despite the uncertainty in its direct impact as indicated by CT values. The decrease in viral load among vaccinated individuals highlights the need for widespread vaccination efforts to minimize potential transmission. Nonetheless, the lack of a statistically significant connection between vaccination and CT values indicates the necessity for further research into the factors influencing viral load, including the timing of vaccination, individual immune responses, and the presence of different virus variants. In conclusion, although vaccination does reduce viral load significantly, its impact on achieving statistically significant variances remains intricate and requires further exploration. These insights are crucial for refining vaccination approaches and enhancing public health measures. Nevertheless, the study clearly shows that vaccination has a notable influence on clinical outcomes and the reduced detection rate by RDT methods, emphasizing the importance of using RT-PCR for more accurate diagnosis in such scenarios.

Study limitation

The study recognizes specific constraints, particularly the lack of an examination into the long-term impacts of COVID-19 vaccination. Participant recruitment from healthcare settings could introduce biases, potentially constraining the applicability of the findings, particularly concerning asymptomatic or mild cases. Moreover, the sample size, especially for RT-PCR validation, could impact the strength of the outcomes. The timing of sample collection might also influence the evaluation of viral load, and the absence of serological testing hinders the ability to assess immune responses and distinguish between immunity acquired through vaccination and that obtained from natural infection. Additionally, the uneven distribution of participants between fully vaccinated and unvaccinated groups could influence the conclusions about the effects of vaccination on viral load, as indicated by Ct values. Addressing these limitations in future studies could enhance the comprehensive understanding of vaccine effectiveness and its broader implications.

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Authors' contributions
"A.A. idea generation, investigation, supervision, data analysis, draft writing and edition, and D.M. supervision and draft the main manuscript and A.G, J.M, W.T, A.A and D.N prepared data and tables. All authors participated and reviewed the main manuscript.

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Availability of data and materials
Data presented in this paper can be obtained from the link below. https://zenodo.org/records/13285453.

Declarations

Ethics approval and consent to participate
The research has been granted ethical approval by the Institutional Review Board at the Ethiopian Public Health Institute (EPHI_IRB). Furthermore, all participants involved in the study have provided consent. Data collectors have ensured that every participant understands their participation is voluntary and that they have the freedom to withdraw at any point without impacting their healthcare services access.

Consent for publication
All authors of this manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript in accordance with journal criteria. We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal.

Conflict of interest
We declare that there are no conflicts of interest relevant to this study. No financial or personal relationships with individuals or organizations that could inappropriately influence or bias the content of this comparative study on COVID-19 detection methods have been disclosed.

Competing interests
The authors declare no competing interests.

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