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Letter to the Editor

Comment to the article by Pedro Brotons: Validation and implementation of a direct RT-qPCR method for rapid screening of SARS-CoV-2 infection by using non-invasive saliva samples, IJID 110 (2021) 363–370


Dear Editor,

We read with interest the article entitled “Validation and implementation of a direct RT-qPCR method for rapid screening of SARS-CoV-2 infection by using non-invasive saliva samples” (Brotons *et al.*, 2021). This study validates and implements an optimized screening method for the detection of SARS-CoV-2 ribonucleic acid, integrating the use of self-collected raw saliva samples, single-step heat-treated virus inactivation and ribonucleic acid extraction, and direct reverse transcription-quantitative polymerase chain reaction (RT-qPCR). Although this article provides valuable information, we believe that when the authors evaluated the diagnostic accuracy of saliva-based direct reverse transcription-polymerase chain reaction (RT-PCR) versus standard RT-PCR on nasopharyngeal swabs, some results are worth discussing. We noticed that the agreement of the two assays was not assessed.

Generally, the question of agreement, or consistency among samples collecting data immediately arises due to the variability in different diagnosis methods. Thus, well-designed research studies must consequently incorporate procedures that measure agreement among the various data collectors (McHugh, 2012). There are a number of statistics that have been used to measure inter-rater reliability. A partial list includes overall accuracy (Asai *et al.*, 2022), Cohen's kappa (McHugh, 2012), Pearson's R (Salvagno *et al.*, 2021), Spearman Rho (Geisler *et al.*, 2020), intraclass correlation coefficient (Rezaeipandari *et al.*, 2022), concordance correlation coefficient (Campana *et al.*, 2022), Krippen-dorff's alpha (Dupuis *et al.*, 2021), and Matthews correlation coefficient (Qorri *et al.*, 2022). Here, we will only consider the most common measures, Cohen's kappa and overall accuracy (Table 1).

Generally, Cohen's kappa statistic is suitable for evaluating two raters (McHugh, 2012). In Cohen's kappa statistic, weighted kappa

statistic should be used to calculate the inter-rater reliability in the presence of more than two categories (Li *et al.*, 2022).

Weighted kappa is calculated as follows:

$$k_w = 1 - \frac{\sum_{i=1}^n \sum_{j=1}^n w_{ij} p_{ij}}{\sum_{i=1}^n \sum_{j=1}^n w_{ij} p_i q_j} \quad (1)$$

The value of $u_{jj}(ii')$ is the proportion of objects put in the same category j by both raters i and i' . The value of p_{ij} is the proportion of objects that rater i assigned to category j . According to McHugh (2012), the kappa result should be interpreted as follows: 0–0.20 indicating no agreement, 0.21–0.39 as minimal agreement, 0.40–0.59 as weak agreement, 0.60–0.79 as moderate agreement, 0.80–0.90 as strong agreement, and 0.91–1.00 as almost perfect agreement.

Therefore, according to the authors' data, the weighted kappa value between saliva-based direct RT-qPCR and standard RT-PCR on nasopharyngeal swab evaluated by us was 0.802 (95% confidence interval = 0.669–0.935), indicating a strong agreement. The overall accuracy between the two assays was 97.36%.

CRedit authorship contribution statement

Tianfei Yu: Writing – original draft. **Fangfang Liu:** Data curation. **Haichang Yin:** Data curation. **Nana Yi:** Data curation. **Ming Li:** Writing – review & editing.

Declarations of competing interests

The authors have no competing interests to declare.

Funding source

This research was supported by a grant (LH2020C110) from the Joint Guidance Project of Natural Science Foundation of Heilongjiang Province of China, a grant (HLJ2019017) Chinese Ministry

Table 1

Weighted kappa value and overall accuracy for calculating agreement between saliva-based direct RT-qPCR and standard RT-PCR on nasopharyngeal swab

Standard RT-qPCR	Saliva-based direct RT-qPCR					Overall accuracy
		Positive	Negative	Inconclusive	Total	
$k = 0.802$ (strong agreement)	Positive	22	0	1	23	97.36%, (22+273+0)/303
	Negative	0	273	0	273	
	Inconclusive	1	6	0	7	
	Total	23	279	1	303	

Note: The data has been cited from the article published by Brotons *et al.* (2021) and undergone modification. k is the weighted kappa value calculated by us. RT-qPCR, reverse transcription-quantitative polymerase chain reaction.

of Education “Chunhui Plan” International Scientific Research Co-operation Project, a grant (145109136) from the Fundamental Research Funds in Heilongjiang Provincial Universities and a grant from Heilongjiang Province Leading Talent Echelon Reserve Leader Funding Project.

Ethical approval

Not applicable.

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