UNIVERSITI TEKNOLOGI MARA

CLINICAL PERFORMANCE OF NANOSYSTEM FOR COVID-19 DNA/ANTIBODIES ON-THE-SPOT-TEST (NACOTS)

MUNIRAH BINTI ZULHAIREE

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ABSTRACT

In December 2019, the world has been shaken by a recent pandemic of highly contagious viral diseases coronavirus diseases 2019 (COVID-19). This illness has caused a global health crisis as it can transmit the virus from one person to another through droplets by symptomatic and asymptomatic patients. The diagnostic tools in COVID-19 detection play a crucial role in curbing the spread despite the presence of vaccines and ongoing development of therapeutic drugs. The real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR), a gold standard in detecting COVID-19 infections known as molecular diagnostic based on nucleic acid amplification test (NAAT). Even though it is high in specificity and sensitivity, RT-PCR involves a series of steps, temperature and condition, longer turnaround time (TAT) and analysis, requires skilled personnel and is high in cost. In this study, the clinical performance of Nanosystem for COVID-19 DNA/Antibodies On-The-Spot-test (NACOTS) was compared to RT-PCR to overcome the limitation of RT-PCR with shorter TAT and analysis time, portable, low cost, involves only isothermal temperature NACOTS system and high in sensitivity and specificity. The clinical performance includes the determination of clinical sensitivity, specificity, and the association between the threshold value (C_t) value of the RNA-dependent RNA polymerase (RdRp) gene by RT-PCR and positive samples of delta current I *(*ΔI*)* (µA) by NACOTS. This study was conducted under the approval of the Medical Research Ethics Committee, Institute for Medical Research (IMR), Setia Alam, Selangor with 148 nasopharyngeal swab samples (N=148). The samples were subjected to both real-time RT-PCR and NACOTS. The result of the clinical sensitivity, clinical specificity and the association between both methods were validated by Student's *t*-test using GraphPad Prism version 9 (GraphPad Softwares Inc). According to the result, a 95 % confidence interval (CI) was significant when the two-sided p-value was less than or equal to 0.05 ($p \leq 0.05$). The *p*-value of the mean difference between positive ($\Delta I = 1.283 \pm 0.05$) and negative ($\Delta I = 0.6285 \pm 0.05$) clinical samples is less than 0.0001 ($p < 0.0001$). Whilst, the *p*-value of the mean difference between the clinical performance of NACOTS and RT-PCR is 0.7729 ($p > 0.05$). The cut-off value obtained is 0.94 for NACOTS with clinical sensitivity and specificity for this study were 79 % and 85 % respectively. There was a negligible correlation between the threshold value (C_t) value of the RdRp gene and positive samples of delta current I *(*ΔI*)* (µA) as the r value is 0.08. Hence, the NACOTS prototype is suitable for COVID-19 detection in limited settings like immigration detaining centres, and clinics in rural areas and applicable among tourists at the airport.

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TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 Research Background

The deadly virus caused a global pandemic that has drawn worldwide attention known as Coronavirus disease 2019 also known as COVID-19 has caused a major threat to human health. The outbreak began in Wuhan, the capital of China's Hubei province on December 29, 2019. The novel coronavirus has now been called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) potentially induces severe respiratory syndrome. As reported by the World Health Organization (WHO) up until early December 2022, China had a total case of over 9 million cases with a total death report of 30, 388. Meanwhile, in Malaysia, over 4 million cases of COVID-19 have been reported by WHO and about 36, 695 deaths occurred (WHO, 2020).

COVID-19 can be transmitted during close contact among human to humans at a distance of 1 to 2 meters, by respiratory droplets created when an infected person coughs or sneezes within a distance of approximately 2 meters. On the other hand, exposure to contaminated objects or surfaces can lead to this detrimental viral infection (Doremalen et al., 2020; Huang et al., 2020; Zhu et al., 2020). The symptoms of SARS-CoV-2 range from common symptoms composed of fever, fatigue and dry cough to severe cases such as pneumonia, shortness of breath and breathing difficulties. However, some COVID-19 patients may experience asymptomatic symptoms. Hence, without proper treatment and rapid diagnosis, the symptomatic and asymptomatic patients may progress quickly to severe conditions which are acute distress syndrome (ARDS), septic shock, metabolic acidosis, coagulation dysfunction and even lead to fatal (Chen et al., 2020).

Nevertheless, an appropriate sampling method for suspected individuals with the symptoms mentioned is one of the precautionary steps to contain the outbreak. Even so, there are a definite number of sampling methods for COVID-19 that have been implemented during the pandemic, nasopharyngeal swabs contributed to high sensitivity and specificity in COVID-19 detection with RT-PCR (Clerici et al., 2021;