Pharmacogn J. 2024; 16(3): 691-697
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Research Article

The Effectiveness of Armpit Sweat Odor with COVID-19 Detection Device for Detecting COVID-19

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a disease caused by the SARS-CoV-2 virus. Diagnosis and screening for COVID-19 are crucial in controlling the disease. RT-PCR is used for diagnosis. However, this test is high-risk, time-consuming, and expensive. There is a need for specific non-invasive biomarkers to detect COVID-19 rapidly. Volatile organic compounds (VOCs) produced by the human body can be used to depict metabolic conditions. A COVID-19 detection device is an electronic device designed to differentiate and detect odors. This study aims to assess the effectiveness of armpit sweat odor with a COVID-19 detection device to detect COVID-19. This study was an observational analytic study with a cross-sectional design conducted on COVID-19 and non-COVID-19 patients in the special isolation ward of Dr. Soetomo Hospital and the outpatient clinic of the Indonesian Navy Hospital during April 2021-December 2021. COVID-19 examination using armpit sweat odor with a COVID-19 detection device. The results of the COVID-19 detection device and RT-PCR were then compared using the McNemar test. The general characteristics of the 168 subjects (81 COVID-19 patients, 87 non-COVID-19 patients) showed that the most common gender was male with the most common comorbidities being hypertension and diabetes mellitus. The results of the diagnostic test showed sensitivity and specificity of 88.9% and 97.7%, respectively with accuracy of 93.45%. The McNemar test showed no significant difference with the RT-PCR results. The results of RT-PCR were not different from the results of armpit sweat odor using COVID-19 detection device.

Keywords: Armpit sweat odor, COVID-19, COVID-19 detection device, RT-PCR, VOC.

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History

- Submission Date: 18-05-2024;
- Review completed: 12-06-2024;
- Accepted Date: 14-06-2024.

DOI : 10.5530/pj.2024.16.116

Article Available online

http://www.phcogj.com/v16/i3

INTRODUCTION

In March 2020, the WHO proclaimed COVID-19 to be a pandemic.[1-4] This pandemic resulted in a considerable death toll, social turmoil, and economic stagnation. In order to maintain this pandemic, screening and diagnosis as the healthcare methods are crucial.[5] Currently, reverse transcription-polymerase chain reaction (RT-PCR) is used to diagnose COVID-19. This test is expensive, time-consuming, and presents a considerable risk because it makes direct contact with the patient's mouth.[6] Thus, a low-cost, low-risk transmission system with fast signal detection is needed. Economies are presently starting to reopen globally while acknowledging the risk of COVID-19 spreading.[6] Reducing transmission and mortality of COVID-19 depends on the discovery of distinct biomarkers that can be used to swiftly and non-invasively diagnose the virus, even in the absence of symptoms.[5, 7, 8]

Grandjean and his team conducted research on sniffer dogs in 2 places (Paris, France and Beirut, Lebanon) to detect COVID-19 from sweat odor. The outcomes of earlier research on the olfactory identification of dogs in COVID-19 patients support this hypothesis. The ability of dogs to smell the unique odor of COVID-19 patient sweat is related to their ability to detect volatile organic compounds (VOCs) that are released. When introduced to sweat samples, most dogs can detect positive and negative cases from the samples with an accuracy rate of 76% to 100%.[9] Hundreds of VOCs are produced by the human body, where the VOC components reflect the metabolic condition of each individual. Pathological processes, such as infections and metabolic disorders, can affect our body odor by producing new VOCs or by changing the ratio of VOCs that are normally produced. Therefore, contracting infectious diseases or metabolic diseases often causes changes in body odor.[10]

The electronic gadget known as E-nose is made up of hardware and software parts that work together to distinguish and identify different smells. Computer scientists and sensor technology researchers have been interested in e-nos since 1928. The "sensor array," "interface circuit," "signal preprocessing unit," "odor handling and delivery system," and "pattern recognition unit" are the primary hardware and software parts of an e-nose. The odor is supplied to the sensor array via the odor management unit.[11] This study is to assess how well axillary sweat odor detects COVID-19 when used in conjunction with a COVID-19 detection equipment.

MATERIALS AND METHODS

This study used an observational analytical study with a cross-sectional design. The study was conducted in the Special Isolation Inpatient Room of Dr. Soetomo Hospital and the Outpatient Clinic of the Naval Hospital Surabaya in the period between April and December 2021. The study sample was COVID-19 and non-COVID-19 patients who met the inclusion and exclusion criteria. 166 axillary sweat odor samples (81 from COVID-19 patients and 87 from non-COVID-19 patients) were examined. Inclusion Criteria: COVID-19 patients hospitalized at Dr. Soetomo Hospital, healthy individuals undergoing PCR swab screening at the Naval Hospital Surabaya

Cite this article: Parimba IS, Bakhtiar A, Soedarsono S, Sarno R. The Effectiveness of Armpit Sweat Odor with COVID-19 Detection Device for Detecting COVID-19. Pharmacogn J. 2024;16(3): 691-697.

outpatient clinic, and willing to sign informed consent to participate in the study. Exclusion Criteria: patients who were using perfume or deodorant at the time of axillary sweat odor sample collection. Sample collection procedure using the COVID-19 detection device:

1. Turn on the power button on the COVID-19 detection device
2. Enter patient data
3. Select the sampling process
4. Prepare a hose with a gauze-tied end
5. Connect the hose to the COVID-19 detection device and ensure the end of the hose is clamped in the middle of the armpit
6. Select start sampling on the COVID-19 detection device to start sampling and wait for 4 minutes until 100% sampling is complete
7. Select the sync button after data collection

Data are presented as frequency distributions. Differences in the results of axillary sweat odor analysis using the COVID-19 detection device and RT-PCR results were analyzed using the McNemar test ($p<0.05$).

RESULTS

Subject Characteristics

The COVID-19 patient patients in this study ranged in age from 12 to 76 years old, with a mean age of 50.38 years. With a minimum age of one year and a maximum age of 76 years, the mean age of the healthy subjects in this study was 41.93 years. The majority of the COVID-19 patient subjects were male, with 48 (59.3%) and 33 (40.7%) females. In this study, 60.5% had comorbidities and 39.5% did not. The documented comorbidity data of the study subjects were hypertension (28.4%), diabetes mellitus (22.2%), obesity (3.7%), tuberculosis (8.6%), and cancer (14.8%) (Table 1).

Positive and negative PCR findings differed significantly in age group, according to the Mann Whitney test ($p < 0.05$). Gender-based PCR swab findings did not differ significantly ($p > 0.05$), but the presence or absence of comorbidities did ($p < 0.05$) according to the Chi-square test with continuity correction. Additionally, the number of comorbidities between positive and negative PCR findings differed significantly, as indicated by the Mann Whitney test. Between positive and negative PCR results, there was a substantial difference in other comorbidities, however obesity was the only one that did not (Table 2).

The Mann Whitney test revealed a significant difference in age group between positive and negative COVID-19 detection device results ($p < 0.05$). The Chi-square test showed that there were no significant difference based on gender of the patients ($p > 0.05$). But, there was a significant difference in the presence or absence of comorbidities ($p < 0.05$). A significant difference was also shown in the number of comorbidities between positive and negative COVID-19 detection device results based on the Mann Whitney test. Other comorbidities did demonstrate a significant difference between positive and negative COVID-19 detection device results; obesity was the only condition that did not (Table 3).

48.2% of the PCR results in this investigation were positive. Meanwhile, the 44% of the COVID-19 detecting device's results were positive (Table 4). COVID-19 detection device showed 97.3% positive results with positive PCR, while 90.4% of COVID-19 detection device showed negative results with negative PCR. The McNemar test results show a p value > 0.05, which means there is no significant difference in the results of the COVID-19 detection device againts the PCR (Table 5).

Diagnostic test above showed that the COVID-19 detection device's sensitivity and specificity on PCR were, respectively, 88.9% and 97.7%, with corresponding 95% confidence intervals of 79.95%-94.79%) and 91.94%-99.72%). In terms of level accuracy, the results showed a 93.59%-96.69% 95% confidence interval for the positive predictive value and a 90.58%-95.53% 95% confidence range for the negative predictive value (Table 6).

DISCUSSION

Subject Characteristics and Comorbidities

In this study, the majority of the subjects were male (59.3%) just like previous research from Huang et al. The subjects' average age was 50.38 ± 14.562 years.[12] This is similar to the age range of COVID-19 patients in West Tehran, Iran (50-59 years) and the median age of 57 years reported in a study from Wuhan, China (70% of cases were in individuals over 50 years old).[13] Other studies have also shown that older age (>55 years) is a risk factor for SARS-CoV-2 infection.[14-17]

A record of the study patients' comorbid history was kept. Obesity (3.7%), diabetes mellitus (22.2%), cancer (14.8%), TB (8.6%), and hypertension (28.4%) were the most prevalent comorbidities. These results are in line with research from Wuhan, China, where the most prevalent comorbidities were diabetes mellitus and hypertension.[14]

Table 1: Subject Characteristics.

Characteristics	PCR		COVID-19 detection device	
	Positive (n = 81)	Negative (n = 87)	Positive (n = 74)	Negative (n = 94)
Age (year)				
Mean Standard deviation	50,38 14,562	41,93 17,289	49,77 14,652	43,04 17,389
Median (min - max)	51 (12 – 76)	45 (1 – 76)	51 (12 – 76)	45,5 (1 – 76)
Gender				
Male	48 (59,3%)	44 (50,6%)	42 (56,8%)	50 (53,2%)
Female	33 (40,7%)	43 (49,4%)	32 (43,2%)	44 (46,8%)
Comorbid				
No	32 (39,5%)	87 (100%)	32 (43,2%)	87 (92,6%)
Yes	49 (60,5%)	0 (0%)	42 (56,8%)	7 (7,4%)
Comorbid type:				
Hypertension	23 (28,4%)	0 (0%)	19 (25,7%)	4 (4,3%)
Diabetes Mellitus	18 (22,2%)	0 (0%)	14 (18,9%)	4 (4,3%)
Obesity	3 (3,7%)	0 (0%)	3 (4,1%)	0 (0%)
Tuberculosis	7 (8,6%)	0 (0%)	6 (8,1%)	1 (1,1%)
Malignancy	12 (14,8%)	0 (0%)	10 (13,5%)	2 (2,1%)

Table 2: Differences in respondent characteristics based on PCR results.

Characteristics	PCR		p-value
	Positive (n = 81)	Negative (n = 87)	
Age (year)			
0 – 18 y	1 (1,2%)	9 (10,3%)	< 0,001[a]
19 – 59 y	52 (64,2%)	66 (75,9%)	
≥ 60 y	28 (34,6%)	12 (13,8%)	
Gender			
Male	48 (59,3%)	44 (50,6%)	0,330[b]
Female	33 (40,7%)	43 (49,4%)	
Comorbid			
Yes	49 (60,5%)	0 (0%)	< 0,001[b]
No	32 (39,5%)	87 (100%)	
Number of Comorbidities			
Median (min – max)	1 (0 – 3)	0 (0 – 0)	< 0,001[a]
Comorbid type			
Hypertension	23 (28,4%)	0 (0%)	< 0,001[b]
Diabetes mellitus	18 (22,2%)	0 (0%)	< 0,001[b]
Obesity	3 (3,7%)	0 (0%)	0,110[c]
Tuberculosis	7 (8,6%)	0 (0%)	0,005[c]
Malignancy	12 (14,8%)	0 (0%)	< 0,001[b]

Information: a = Mann Whitney test; b = Chi Square test with Continuity Correction; c = Fisher's Exact test

Table 3: Differences in respondent characteristics based on the results of the COVID-19 detection device.

Characteristics	COVID-19 detection device		p-value
	Positive (n = 74)	Negative (n = 94)	
Age (year)			
0 – 18 y	1 (1,4%)	9 (9,6%)	0,001[a]
19 – 59 y	48 (64,9%)	70 (74,5%)	
≥ 60 y	25 (33,8%)	15 (16%)	
Gender			
Male	42 (56,8%)	50 (53,2%)	0,761[b]
Female	32 (43,2%)	44 (46,8%)	
Comorbid			
Yes	42 (56,8%)	7 (7,4%)	< 0,001[b]
No	32 (43,2%)	87 (92,6%)	
Number of Comorbidities			
Median (min – max)	1 (0 – 3)	0 (0 – 2)	< 0,001[a]
Comorbid type			
Hypertension	19 (25,7%)	4 (4,3%)	< 0,001[b]
Diabetes mellitus	14 (18,9%)	4 (4,3%)	0,005[b]
Obesity	3 (4,1%)	0 (0%)	0,084[c]
Tuberculosis	6 (8,1%)	1 (1,1%)	0,045[c]
Malignancy	10 (13,5%)	2 (2,1%)	0,011[b]

Information: a = Mann Whitney test; b = Chi Square test with Continuity Correction; c = Fisher's Exact test

Table 4: Results of PCR and COVID-19 detection device.

Examination	n	%
PCR		
Positive	81	48,2
Negative	87	51,8
COVID-19 detection device		
Positive	74	44
Negative	94	56

Table 5: Cross tabulation data of the COVID-19 detection device against PCR.

COVID-19 detection device	PCR		Total	p-value
	Positive	Negative		
Positive	72 (97,3%)	2 (2,7%)	74 (100%)	0,065
Negative	9 (9,6%)	85 (90,4%)	94 (100%)	
Total	81 (48,2%)	87 (51,8%)	168 (100%)	

Table 6: Diagnostic test for the COVID-19 detection device on the PCR.

	value	Confidence Interval 95%
Sensitivity	88,9%	79,95% – 94,79%
Specificity	97,7%	91,94% – 99,72%
PPV	97,3%	90,58% – 99,67%
NPV	90,4%	82,60% – 95,53%
Accuracy	93,45%	88,59% – 96,69%

Diabetes mellitus, hypertension, and cardiovascular disease were the most prevalent comorbidities, according to a study done at the Petrokimia Gresik Hospital by Soedarsono et al.[16] This was especially true for patients with severe COVID-19.

The most prevalent comorbidity among COVID-19 patients is hypertension.[18, 19] Numerous investigations have revealed that among hypertensive individuals hospitalized with COVID-19, there is a high prevalence of hypertension and a much higher mortality rate. Acute lung infection is brought on by SARS-CoV-2 binding to ACE2 on alveolar epithelial cells in the lungs.[20] Renin-angiotensin-aldosterone system (RAAS) inhibitors, which include angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors, are among the most significant antihypertensive medications. However, they may worsen patient outcomes during the ongoing COVID-19 pandemic by increasing ACE2 expression.[21] When treating acute lung injury caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, several clinical trials and meta-analyses focused on antihypertensive therapies have shown the efficacy of RAAS inhibitors. Hypertension makes an individual's SARS-CoV-2 infection more severe. According to recent research, hypertension may be a major factor in the control of RAAS, inflammation, immunological response, and the gastrointestinal tract, which helps to explain why COVID-19 patients have worse results. Uncertainty persists on the risk variables linked to COVID-19 patients who have hypertension.[19, 22]

Diabetes mellitus is a widespread metabolic disease with a variety of causes, most commonly associated with insufficient or dysfunctional insulin secretion. People with diabetes are more prone to infections in addition to the disease's clinical consequences. Moreover, it has been determined that diabetes and its side effects, including poor blood glucose regulation and ketoacidosis, may increase the chance of dying from the 2009 influenza A (H1N1) pandemic, SARS-CoV infection, and MERS coronavirus.[23] High death rates among COVID-19 patients with diabetes have been found in a number of studies.[23, 24] Patients with COVID-19 have less lung elasticity because to non-enzymatic glycosylation of collagen and elastin in the lungs caused by hyperglycemia in diabetes mellitus. This causes the pulmonary capillary vessels' microvascular alterations and the alveolar epithelial basement membrane to thicken. This lowers the pulmonary capillary blood volume and diffusion capacity, which has an impact on the overall survival of the patient.[23]

Statistical Analysis

Tables 2 and 3 show the results of the Mann-Whitney test, which revealed a significant difference in age groups between positive and negative PCR and COVID-19 detection device results ($p < 0.05$). This indicates that age influences COVID-19 test results, both with PCR and the COVID-19 detection device. Chi-square test showed that there is no significant difference in PCR and COVID-19 detection device results based on gender ($p > 0.05$). This indicates that gender does not influence COVID-19 test results. There was a significant difference in the presence or absence of comorbidities between positive and negative PCR and COVID-19 detection device results ($p < 0.05$). This indicates that comorbidities influence COVID-19 test results. There was also a significant difference ($p < 0.05$) between the positive and negative PCR and COVID-19 detection device results, according to the Mann-Whitney test. This indicates that the more comorbidities an individual has, the higher the likelihood of a positive COVID-19 test result. Analysis based on the type of comorbidity revealed no significant difference in obesity between positive and negative PCR and COVID-19 detection device results. However, other types of comorbidities, such as diabetes, hypertension, and heart disease, showed significant differences. This suggests that specific comorbidities can increase the risk of people that have a positive COVID-19 result. In conclusion, age, comorbidities, and the number of comorbidities have an impact on COVID-19 test results, both with PCR and the COVID-19 detection device. Gender does not influence COVID-19 test results. Specific comorbidities, such as diabetes, hypertension, and heart disease, can increase an individual's risk of receiving a positive COVID-19 test result.

Positive COVID-19 detection device and positive PCR results were found in a total of 72 participants (97.3%), whereas negative COVID-19 detection device and negative PCR results were found in 85 subjects (90.4%). With a p-value of 0.065 for the McNemar test, it was determined that there was no discernible difference between the COVID-19 detecting equipment and PCR results. In comparison to PCR, this study assessed the COVID-19 detection device's sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in identifying COVID-19 infection by axillary sweat odor. A sensitivity of 88.9% (95% confidence interval: 79.95%-94.79%) and a specificity of 97.7% (95% confidence interval: 91.94%-99.72%) were found in the diagnostic test results of the COVID-19 detection device against PCR. With an accuracy of 93.45% (95% confidence interval: 88.59%-96.69%), the positive predictive value was 97.3% (95% confidence interval: 90.58%-99.67%) and the negative predictive value was 90.4% (95% confidence interval: 82.60%-95.53%).

Previous research has looked into the use of body odor to identify disorders in humans.[25-27] In one study, endotoxin (lipopolysaccharide) injections were used to stimulate the innate immune system in healthy participants. It was discovered that these participants' body odor changed in a matter of hours as opposed to when they were given a placebo.[26] Sabilla et al. used Taguchi Gas Sensors (TGS) and SHT15 (Sensirion Humidity and Temperature Sensor 15) to detect variations in men's and women's axillary sweat odor at night with reference to the possible development of disease. With an accuracy rating of 92.3%, this study discovered that women were more likely than men to be ill.[28]

Tognetti et al. conducted a study to see if people could use axillary odor to identify acute respiratory illnesses that occur normally in other people. Axillary odor samples were gathered from donors, both while they were healthy and when they were sick. Assessors were given paired samples to identify the presence of ill body odor. Assessors were marginally but considerably better than chance in differentiating the body odor of ill patients from samples of healthy and sick axillary odor ($M \pm SD = 56.7 \pm 7.4\%$ vs. chance level 50%, $p < .001$, effect size, $r = 0.68$), according to the results of the Wilcoxon test with continuity correction.[27] An e-nose might identify respiratory illnesses with an accuracy rate of up to 93.4%, according to a different study by Malikhah et al.[29]

Research conducted by Kantele et al. at the University of Helsinki, Finland, found that trained dogs could recognize the body odor of people with COVID-19 with an accuracy of 92% (95% CI 90% to 93%), sensitivity of 92% (95% CI 89% to 94%) and specificity of 91% (95% CI 89% to 93%) compared to RT-PCR.[25] Malikhah et al. used an e-nose to detect viral respiratory infections by measuring the sensor response pattern to volatile organic compounds (VOCs) from axillary sweat, with results showing an accuracy rate of 94%, sensitivity of 96.7% and specificity of 91.5%.[30] Purbawa et al.'s subsequent study, which used an e-nose to identify the SARS-CoV-2 virus from axillary sweat odor, produced data with a 90.4% accuracy rate. The suggested e-nose

technology can be used to identify the SARS-CoV-2 virus in real time and can enhance the virus's detection capabilities.[31]

There have been prior studies investigating the use of the VOC technique in conjunction with electronic nose detection to identify COVID-19 patients.[32-36] Exhaled breath is typically used in these investigations to detect volatile compounds in the patients. Meanwhile, no studies on electronic nose technology that uses axillary sweat odor analysis to identify COVID-19 patients have been published.

According to one study, COVID-19 patients' exhaled breath smelled stronger than that of healthy individuals. The e-nose machine was also shown in this investigation to be capable of classifying breath samples into three groups: individuals who were not categorized, infected COVID-19 patients, and healthy participants. Individuals who had recovered recently from a COVID-19 infection or had many respiratory diseases were considered unclassifiable cases.[34] Using an electronic nose (e-nose), Li et al. measured the sensor response pattern to volatile organic compounds (VOCs) in human exhaled breath in order to identify COVID-19 infection. With an identification rate of 79%, the researchers created and evaluated multiple handheld e-nose sensor system prototypes that successfully differentiated between COVID-19 positive and negative subjects.[32] An electronic nose can identify COVID-19 patients with a 66.7% sensitivity, according to a different Israeli study.[35] In comparison to the non-COVID-19 group, breath air analysis using the Cyranose 320 device by Zamora et al. produced a sensitivity of 96.7% and specificity of 100% in identifying COVID-19 patients.[37] In one study, the BioVOC breath sampler was able to identify COVID-19 patients with an accuracy of 80–91%.[38] An electronic nose was used in a study by Winjent et al. to screen patients for COVID-19 prior to surgery. The results showed an 86% sensitivity and a 92% negative predictive value (NPV).[39]

In order to detect COVID-19 patients using samples from breathed air, Nurputra et al. conducted a study at two hospitals in Indonesia, the COVID-19 special field hospital in Bantul and the Bayangkara Hospital in Sleman, using the GeNose C19 device.[33] Sixteen breath samples total—333 positive and 282 negative samples—were confirmed by RT-qPCR from forty-one COVID-19 positive patients and forty negative patients. Four distinct machine learning algorithms—stacked multilayer perceptrons, support vector machines, linear discriminant analysis, and deep neural networks—were used to identify the VOC patterns of COVID-19 patients. The detection system's accuracy (88-95%), sensitivity (86-94%), and specificity (88-95%) were assessed using the test dataset.

A component of VOC metabolism in healthy humans is exhaled from the breath at levels and concentrations within specific ranges and molar ratios that reflect a state of health. A potential disease is indicated when respiratory VOC levels depart from the usual range, which is dependent on age, race, and other factors. Numerous metabolic pathways are impacted by COVID-19, according to research on the metabolomics of the disease's etiology. These findings may provide an indirect explanation for the wide range of quantitative changes in VOC levels in COVID-19 patients' breath. COVID-19 patients' exhaled breath has greater quantities of aldehydes and ketones. An increase in the production of aldehydes is the result of tissue damage brought on by inflammation. Ketones from the metabolism of fatty acids and carbohydrates are additional metabolic VOC sources in patients. Patients with SARS-CoV-2 infection have higher blood alcohol concentrations because to acetaldehyde metabolism, which primarily occurs in the liver and increases ethanol.[36]

Aldehydes are the main compounds that represent VOC components that are higher in concentration in COVID-19 patients' volatile breath tests than in controls. Significantly higher levels of volatile organic compounds (VOCs) in the breath of COVID-19 patients include alcohols and alkanes. According to Berna et al., heptanal was found to be the most reliable and significant volatile organic compound (VOC) indicator in SARS-CoV-2-infected individuals.[36] Thousands of volatile organic compounds (VOCs), intermediate and final products of numerous bodily metabolic processes, are exhaled by humans. All of the volatile organic compounds (VOCs) in the breath sample are proportionately responded to by the e-nose device's sensor arrays, which are sensitive to different VOCs. Only a tiny portion of the VOCs in the breath sample are recognized as COVID-19 disease biomarkers by the e-nose device, which does not identify every single VOC in the sample.[36]

Ruszkiewicz et al. used GC-IMS instrument to investigate the VOC breath profile of COVID-19 patients. There were ten volatile organic compounds (VOCs) found that might be signs of the illness. COVID-19 patients had higher levels of these component volatile organic compounds (VOCs) in their breath than healthy controls because the SARS-CoV-2 virus promotes the overexpression of nine volatile metabolites and the downregulation of methanol. A few odd minor volatile metabolites have been found in some studies, but the breath of COVID-19 patients also contains a greater number of volatile compounds, such like 2,4-octadiene, camphene, benzaldehyde, isoprene, 2-pentyl furan, and isoprene and β-cubebene. In many COVID-19 patients, several of these minor metabolites are identified at low enough levels to be undetected due to their low level of overexpression, but they may also be qualitative indications of the virus.[36] Mendoza et al. recorded several volatile organic compounds (VOCs) in exhaled breath during the acute phase of COVID-19. These included aldehydes, 2,8-dimethyl-undecane, n-propyl acetate, ethanal, acetone, 2-butanone, methanol, isoprene, propanal, propane, methylpent-2-enal, and 2,3-butanedione. Decane, tridecane, butanoate, butyraldehyde, isopropanol, octanal, nonanal, heptanal, acetone, alcohol, carbon monoxide, and 1-chlorheptane.[37]

Researchers in Beijing, China, found that the breath of COVID-19 patients included a number of putative volatile organic compounds (VOCs), including acetone (C3H6O), ethyl butyrate, butyraldehyde, and isopropanol. They discovered, in a discovery exclusive to COVID-19 patients, that metabolic alterations brought on by SARS-CoV-2 infection resulted in a drop in acetone (C3H6O) levels and an increase in ethyl butyrate levels. Furthermore, compared to lung cancer patients, non-COVID-19 respiratory infection patients, and the control group (healthy population), COVID-19 patients had lower levels of butyraldehyde and isopropanol.[5]

A partnership of French researchers also looked at the metabolomics of breath in critically ill COVID-19 patients. Four volatile organic chemicals (VOCs)—methylpent-2-enal, 2,4-octadiene, 1-chlorheptane, and nonanal—were found to be capable of distinguishing ARDS patients with and without COVID-19.[33] Although the technical classification is the same, the results are not the same as those of studies conducted in Janesville, Wisconsin, and Detroit, Michigan, two American cities. Liangou et al. discovered eight other substances in these investigations, including ethanol, propionic acid, butene, acetaldehyde, heptanal, nitrogen oxide, and methanol water cluster, which are significant indicators for COVID-19 detection in human breath.[40] In the meantime, a study conducted in Leicester, England, using GC-MS identified seven VOCs in exhaled breath that could be used to differentiate between PCR-positive COVID-19 patients and healthy patients, such like iodobenzene, betacubebene, camphene. 3,6-dimethylundecane, propanol, benzaldehyde, and another unidentified compound.[40] Chen et al. presented the results of two successive studies on breath biomarkers that used the same technique (GC-IMS) but produced radically different results. The first study, published in 2020, suggested that three compounds—ethyl butyrate, butyraldehyde, and isopropanol—could be used to distinguish between health and non-health persons because of Corona virus infection. The

second study from 2021 suggests that acetone is a biomarker among many VOC species to be considerable as COVID-19 patient breath marker.[40] Out of all the MS research that has been covered, there are still some COVID-19 biomarkers that are difficult to identify in breath and can produce a wide range of chemicals depending on location, measuring technique, filtering approach, and kind of breath sample. Therefore, additional in-depth research based on cases, race, and community is needed.[33, 40]

When compared to the previous studies above, the detection of COVID-19 patients from axillary sweat odor using a COVID-19 detection device has an accuracy, sensitivity, and specificity comparable to the detection of COVID-19 patients based on electronic nose analysis of exhaled air. When compared to RT-PCR results, there is also no statistically significant difference. This result shows that the COVID-19 detection device has great potential as a rapid screening tool for infected patients. The limitation of this study is that it cannot detect the type of VOCs from the armpits of infected patients.

CONCLUSIONS

The characteristics of the COVID-19 subjects in this study were predominantly male, with an average age of 50.38 years. The most common comorbidities were hypertension and diabetes mellitus. The analysis of axillary sweat odor using the COVID-19 detection device in COVID-19 patients yielded a positive result of 88.9%. The results of the axillary sweat odor analysis with the COVID-19 detection device did not differ from the RT-PCR results in COVID-19 patients. Gas chromatography studies to detect VOC content in the axillary sweat of COVID-19 patients in the future are necessary to improve the accuracy of axillary VOC analysis in COVID-19 patients.

ACKNOWLEDGEMENTS

The author thanks to assistance from various parties, all the involved patients, families, medical doctors, nurses, and microbiology laboratory for their support.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This research was funded by Special Program for Research Against COVID-19 (SPRAC) managed by AUN/SEED-Net and the Indonesian Ministry of Research and Technology or National Agency for Research and Innovation and the Indonesian Ministry of Education and Culture under Penelitian Terapan Unggulan Perguruan Tinggi (PTUPT) Program, and under PMDSU Program managed by Institut Teknologi Sepuluh Nopember (ITS).

ETHICAL CLEARANCE

Ethical committee approval for this study was obtained from Dr. Soetomo Hospital with ethical number 0173/KEPK/IV/2021 and Naval Hospital Surabaya with ethical number 26.a/EC/KERS/2021.

AUTHOR CONTRIBUTOR'S

All authors contributed toward data analysis, drafting, and revising the paper and have collectively assumed responsibility for all aspects of the work.

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Cite this article: Parimba IS, Bakhtiar A, Soedarsono S, Sarno R. The Effectiveness of Armpit Sweat Odor with COVID-19 Detection Device for Detecting COVID-19. Pharmacogn J. 2024;16(3): 691-697.