

Udayana COVID-19 Scoring System: a simple diagnosing aid for early detection of COVID-19

Udayana COVID-19 Scoring System: um auxílio de diagnóstico simples para a detecção precoce do COVID-19

Sistema de Puntuación Udayana COVID-19: una ayuda de diagnóstico simple para la detección temprana de COVID-19

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Abstract

Coronavirus Disease-19 (COVID-19) is a highly transmittable disease. While the most common symptoms of COVID-19 include fever, cough, and fatigue, severe symptoms could feature acute respiratory distress syndrome and severe pneumonia. Reverse-transcription polymerase chain reaction (RT-PCR) remains the gold standard for diagnosing COVID-19. Unfortunately, it has high cost, extensive waiting time, and low availability in remote areas. Therefore, we developed the Udayana COVID-19 Scoring System (UCSS) for quick detection of COVID-19. This study aims to determine the cutoff score and measure the sensitivity and specificity of the UCSS. We conducted an observational cross-sectional study from June 2020 to July 2020. A questionnaire consisting of 3 objective and subjective scores assesses COVID-19 symptoms and risk factors. Participants were patients suspected of COVID-19 awaiting RT-PCR test results. The UCSS total score then compared with the RT-PCR test result and analyzed to determine the cutoff score, sensitivity, and specificity. 150 participants were included in this study (74 male, 49.3%; mean age 42 ± 15.7). The UCSS total score was significantly correlated with RT-PCR test result (p -value = 0.000). The receiving operator characteristic analysis showed an optimal cutoff score of 7, with a sensitivity of 72% and specificity of 71%. Therefore, the UCSS' accuracy is at a moderate level. The UCSS showed acceptable sensitivity and specificity, and has the potential to be used as a diagnostic aid for COVID-19 early detection. Further study in diverse areas and larger sample size are needed.

Keyword: COVID-19; Diagnosis; Scoring system.

Resumo

A Doença do Coronavírus-19 (COVID-19) é uma doença altamente transmissível. Embora os sintomas mais comuns do COVID-19 incluam febre, tosse e fadiga, sintomas graves podem incluir síndrome do desconforto respiratório agudo e pneumonia grave. A reação em cadeia da polimerase com transcrição reversa (RT-PCR) continua sendo o padrão-ouro para o diagnóstico de COVID-19. Infelizmente, tem alto custo, tempo de espera extenso e baixa disponibilidade em áreas remotas. Portanto, desenvolvemos o Udayana COVID-19 Scoring System (UCSS) para detecção rápida do COVID-19. Este estudo tem como objetivo determinar a pontuação de corte e medir a sensibilidade e especificidade do UCSS. Realizamos um estudo transversal observacional de junho de 2020 a julho de 2020. Um questionário composto por 3 escores objetivos e subjetivos avalia os sintomas e fatores de risco da COVID-19. Os participantes eram pacientes com suspeita de COVID-19 que aguardavam os resultados do teste RT-PCR. A pontuação total UCSS então comparada com o resultado do teste RT-PCR e analisada para determinar a pontuação de corte, sensibilidade e especificidade. 150 participantes foram incluídos neste estudo (74 homens, 49,3%; idade média $42 \pm 15,7$). A pontuação total UCSS foi significativamente correlacionada com o resultado do teste RT-PCR (p-valor = 0,000). A análise característica do operador receptor mostrou uma pontuação de corte ideal de 7, com sensibilidade de 72% e especificidade de 71%. Portanto, a precisão do UCSS está em um nível moderado. O UCSS mostrou sensibilidade e especificidade aceitáveis e tem potencial para ser usado como auxílio diagnóstico para detecção precoce de COVID-19. Mais estudos em diversas áreas e tamanho amostral maior são necessários.

Palavras-chave: COVID-19; Diagnóstico; Sistema de pontuação.

Resumen

La enfermedad por coronavirus-19 (COVID-19) es una enfermedad altamente transmisible. Si bien los síntomas más comunes de COVID-19 incluyen fiebre, tos y fatiga, los síntomas graves pueden incluir síndrome de dificultad respiratoria aguda y neumonía grave. La reacción en cadena de la polimerasa de transcripción inversa (RT-PCR) sigue siendo el estándar de oro para diagnosticar COVID-19. Desafortunadamente, tiene un alto costo, mucho tiempo de espera y baja disponibilidad en áreas remotas. Por lo tanto, desarrollamos el Sistema de puntuación Udayana COVID-19 (UCSS) para la detección rápida de COVID-19. Este estudio tiene como objetivo determinar la puntuación de corte y medir la sensibilidad y especificidad de la UCSS. Realizamos un estudio transversal observacional desde junio de 2020 hasta julio de 2020. Un cuestionario que consta de 3 puntajes objetivos y subjetivos evalúa los síntomas y factores de riesgo de COVID-19. Los participantes eran pacientes sospechosos de COVID-19 que esperaban los resultados de la prueba RT-PCR. La puntuación total de UCSS luego se compara con el resultado de la prueba RT-PCR y se analiza para determinar la puntuación de corte, la sensibilidad y la especificidad. 150 participantes fueron incluidos en este estudio (74 hombres, 49,3%; edad media $42 \pm 15,7$). La puntuación total de UCSS se correlacionó significativamente con el resultado de la prueba RT-PCR (valor de $p = 0,000$). El análisis de características del operador receptor mostró una puntuación de corte óptima de 7, con una sensibilidad del 72 % y una especificidad del 71 %. Por lo tanto, la precisión del UCSS está en un nivel moderado. La UCSS mostró sensibilidad y especificidad aceptables, y tiene potencial para ser utilizada como ayuda diagnóstica para la detección temprana de COVID-19. Se necesitan más estudios en diversas áreas y un tamaño de muestra más grande.

Palabras clave: COVID-19; Diagnóstico; Sistema de puntuación.

1. Introduction

Novel Coronavirus Disease (COVID-19) caused by SARS-CoV2 virus was first discovered on December 2019, appearing as clusters of pneumonia cases in Hubei Province, China. Since then, the virus shows alarming transmission rate, spreading to 210 country. The WHO has declared it as a global pandemic by March 2020. By the end of 2020, number of infections reach 79 million globally with more than 1.5 million deaths.(Manski & Molinari, 2021; McIntosh K,Hirsh M, 2021; Park et al., 2020)

Most common symptoms of COVID-19 include fever, cough and fatigue, while severe symptoms include acute respiratory distress syndrome and severe pneumonia. Previous study has found that human to human transmission is present via droplet and airborne routes. The virus is easily transmitted through pre-symptomatic or even asymptomatic patients although having approximately 5 days incubation period. Several scholars predicted that transmission from presymptomatic and asymptomatic patients were responsible for more than 50% of COVID-19 case worldwide.(Lauer et al., 2020; Moghadas et al., 2020; Morawska & Milton, 2020; Rothan & Byrareddy, 2020) Limited therapeutic options to combat COVID-19 are limited, therefore early detection and containment is key to prevent outbreaks.

Currently, reverse transcription polymerase chain reaction (RT-PCR) test is the gold standard of COVID-19 detection.

RT-PCR test needs certain facilities and instruments to be performed. Meanwhile, said technologies are not easily present across the nation, generally only possessed by hospitals in central cities. This condition creates accessibility difficulties for patients in need of COVID-19 screening in rural areas where RT-PCR test laboratories are not present. A study by Finch and Finch (2020) also showed that individuals with a low socioeconomic background had a higher risk of contracting COVID-19. (Finch & Hernández Finch, 2020) This is due to inequality and lack of testing capability towards those in poverty, considering the fact that RT-PCR test is relatively costly (IDR 900.000) even when the price has already been subsidized by the government. Therefore, new means of screening is necessary to be proposed, bearing in mind the limitation of facilities and budget held by various groups of individuals with different socioeconomic backgrounds.

An affordable, practical, and easily accessible screening method that could be developed is a questionnaire type screening. Development of the UCSS is based on previous study on COVID-19 symptoms and features. (Jiang et al., 2020; Kerboua, 2021; Zheng et al., 2021) This type of screening method could be immediately implemented due to its practical nature, and do not require any specific facilities, instruments, nor human capitals. Questionnaire-based screening also allows for quick result, leading to a more efficient and prompt treatment decision on whether a patient needs to be isolated not. A quick and decisive treatment would prevent said at risk patient to unknowingly spread the disease to other individuals from lack of awareness. Questionnaire-based screening also eliminates cost problem for patients with low socioeconomic background, ensuring access and equality to all levels of societal groups. An affordable screening means also encourages patient to check on themselves as needed without worrying about financial restriction, thus eases prompt findings and indirectly facilitates better restriction of COVID-19 spread. (Gostic et al., 2020; Hur & Chang, 2020; Kwon et al., 2020; Tassis et al., 2020)

However, research on the development of such screening method is still lacking. Therefore, we developed Udayana COVID-19 Screening System (UCSS) for early detection. This study aims to explore the sensitivity and specificity of the scoring system.

2. Methodology

Study Design

This study is an observational cross-sectional study conducted to find a cutoff score using Udayana COVID-19 Screening System (UCSS) which contains an adequate specificity and sensitivity level to be used as a screening method on suspected COVID-19 patients.

Population and Setting

A total of 150 participants were observed from June 2020 to July 2020. Participants were patients admitted to the isolation room of Udayana University Hospital suspected for contracting COVID-19. A majority (n = 137) of these participants were below 60 years old while only 13 patients were above 60 years old.

Exactly half of total samples were individuals with negative findings of COVID-19 while the other 75 individuals were tested positive for COVID-19. All participants have been carefully selected through control variables, resulting in a homogenous sample to ensure validity of the research result. The exclusion criteria were patients who refused to participate. Ethical approval was granted by Udayana University Ethical Committee (No 1010/UN14.2.2.VII.14/LT/2020).


Variables

The free variables in this study are the patients' condition while the leading variable is the variation in score.

Instruments

Instrument used in this study is the Udayana COVID-19 Scoring System (UCSS) showed in figure 1. We conducted a preliminary study on 150 patients admitted to Udayana University Academic Hospital. We performed bivariate and multivariate logistic regression on demographic characteristics, baseline symptoms, radiographic findings, and basic laboratory results towards RT-PCR results as the gold standard. Variables found to be significant in the multivariate analysis were included into the scoring system, with odds ratio serving as the score weight (Sastroasmoro & Ismael, 2011).

Table 1 - Udayana Scoring System for COVID-19.

RUMAH SAKIT UNIVERSITAS UDAYANA			
		UDAYANA SKOR SKRINING PASIEN COVID-19 (untuk penapisan awal pasien)	
NO	PARAMETER	NILAI*	KETERANGAN
ANAMNESIS			
1	Tidak Batuk	0	
	Batuk Produktif	1	
	Batuk Kering	2	
2	Tidak Fatigue	0	
	Fatigue dalam 1 hari terakhir	1	
	Fatigue \geq 2 hari	2	
3	Tidak Mual, Muntah atau Penurunan daya penciuman/perasa ataupun diare	0	
	Mual, Muntah atau Penurunan daya penciuman/perasa	1	
	Diare atau nyeri perut	2	
4	Tidak sesak	0	
	Sesak	2	
PEMERIKSAAN FISIK DAN LABORATORIUM			
5	Tidak Demam	0	demam atau riwayat demam dalam 14 hari
	Demam $<$ 37,5 C	1	
	Demam 37,5 – 38 C atau $>$ 38 C	2	
6	Neutrofil Limfosit Rasio		
	NLR $<$ 3.13	1	
	NLR 3.13- 5	2	
	NLR $>$ 5	3	
7	Limfosit (N:1000-3900/ μ l)		
	$>$ 1500	1	
	1000-1500	2	
	$<$ 1000	3	
8	Abnormalitas pada xray thoraks:		
	Tidak Pneumonia	0	
	Pneumonia Unilateral	1	
	Pneumonia Bilateral	2	
TOTAL NILAI			
Keterangan :			
Bila total skor \geq 7 maka harus dicurigai sebagai COVID-19 lanjutkan pemeriksaan PCR bila tersedia			

Source: Analysis.

This figure contains significant variables in multivariate analysis done in the preliminary study. This scoring system is to be validated in this study.

Data Collection

The UCSS is obtained by evaluating of 4 objective and 4 subjective score. Subjective score is obtained via anamnesis, while objective score is obtained by observing clinical, laboratory, and radiographic features. The UCSS were given to suspected COVID-19 patients while awaiting their RT-PCR test result. All evaluation was administered by the researcher without missing a data, which took around 5 minutes. Each score is then summed and evaluated.

Data Analysis

A descriptive analysis was performed to present demographic variable. To prove the validity of the scoring system, a comparison between participant's UCSS total score and RT PCR test result was performed with Mann Whitney analysis ($p < 0.01$). Receiving-Operating Characteristic (ROC) analysis was performed to evaluate the optimal cut off score. All statistical analysis was carried out with IBM SPSS Statistics 22 software.

3. Results

Table 1 present participants' social demographic and RT-PCR test result. Mean age of participants were 42 ($SD \pm 15.7$). Participants in 65 years or more age group were 8.7%, while the remaining 91.3% were in less than 65 years age group. Male participants comprised 49.3% of total sample and female subjects were 50.7%. All participants undergo RT-PCR testing in which 50% of them showed positive test result, while the remaining 50% showed negative test result.

Table 2 - Demographic and RT-PCR testresult.

Variable	n = 150 (%)
Age in years	
≥ 65	13 (8.7)
< 65	137 (91.3)
Sex	
Male	74 (49.3)
Female	76 (50.7)
RT-PCR test result	
Positive	75 (50)
Negative	17 (50)

Source: Analysis.

This table shows the basic demographic and RT-PCR results of the subjects used for validating the scoring system. Correlation between the UCSS total score and RT-PCR test result was performed to evaluate the validity of the scoring system. The UCSS revealed adequate validity evidenced by statistically significant ($p < 0.001$) the UCSS total score median difference between patients declared COVID-19 positive (8, IQR=3) or negative (5, IQR=5) by RT PCR test results (Table 2). This is further proven by correlation in the increase of the UCSS total score is proportional to RT PCR positive test results on Figure 2.

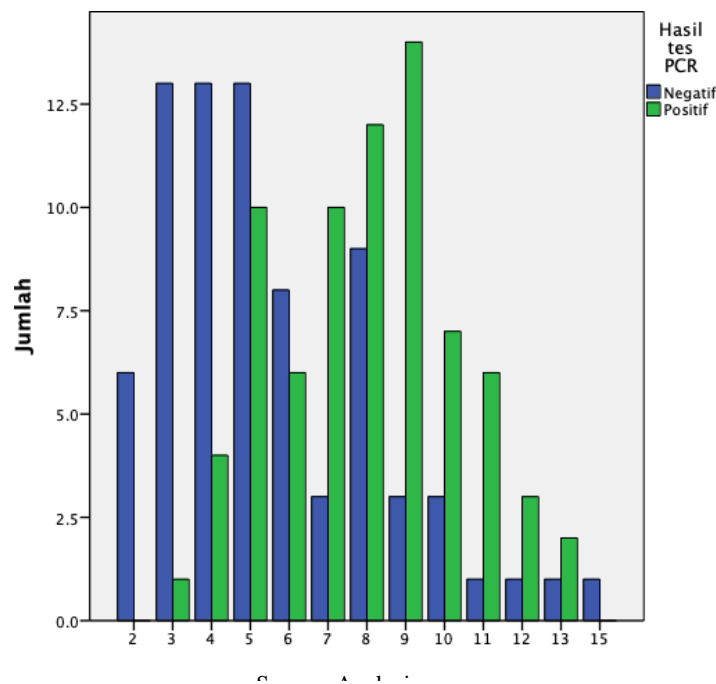
Table 3 - Correlation of total score with RT-PCR test results.

Total Score	RT-PCR		Sig.
	Positive	Negative	
Median (IQR)	8 (3)	5 (5)	<0.001
Mean (SD)	7.9 (2.3)	5.6 (2.8)	
Min-Max	3-13	2-15	
Mean Rank	95.01	55.99	
Sum of Rank	7125,5	4199,5	

Source: Analysis.

This table divides the patient into positive and negative group via gold standard RT-PCR. UCSS results were then calculated. Differences between the two groups were found to be statistically significant.

Figure 1 - Correlation of the UMCCS total score and RT PCR test result.



Source: Analysis.

This figure is a bar chart of the score result between the two groups. It must be noted that the positive group differs significantly and may be visually seen to have higher score value within the UCSS. The ROC curve analysis revealed an acceptable area under curve (AUC) for COVID- 19 positive (AUC 0.76; Figure 3). Table 3 shows the UCSS' cut-off points for diagnosing COVID-19. Based on the ROC curve analysis, the optimal cut-off score for maximum value of sensitivity and specificity 7, with sensitivity of 72% and specificity of 71%. Therefore, the UCSS' accuracy is at the moderate level.

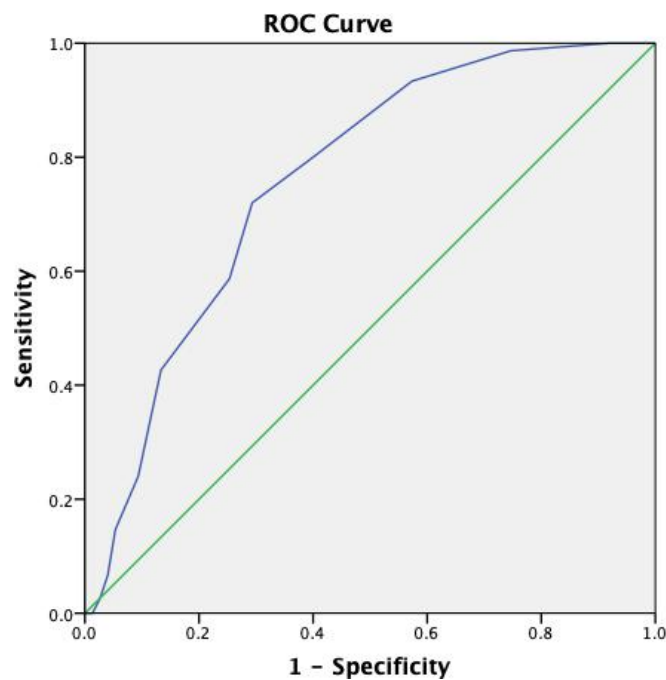
Table 4 - Cut-points of Udayana Modified COVID Scoring System (UMCSS) as COVID-19 diagnosis.

Cut Point	Sensitivity	Specificity
1.00	1.00	0.00
2.50	1.00	0.18
3.50	0.99	0.25
4.50	0.93	0.43
5.50	0.80	0.60
6.50	0.72	0.71
7.50	0.59	0.75
8.50	0.43	0.87
9.50	0.24	0.91
10.50	0.15	0.95
11.50	0.07	0.96
12.50	0.03	0.97
14.00	0.00	0.99

Source: Analysis.

This table specify possible cutpoints within the UCSS. A cut off point of 6.5 yields 72% sensitivity and 71% specificity.

Figure 2 - Receiver operating characteristic (ROC) curve analysis for COVID-19 diagnosis.



Source: Analysis.

This figure shows the ROC curve to validate the accuracy of UCSS as a diagnostic instrument.

4. Discussion

In this study we found that the UCSS has the potential in diagnosing COVID-19. The Udayana COVID-19 Scoring

System (UCSS) was correlated with RT PCR, the gold standard of COVID 19 diagnosis. This study also proved adequate sensitivity and specificity of the UCSS, with a cut-off score of 7.

COVID-19 diagnosis is key to contain the disease spread. Among all COVID-19 testing kit available, RT PCR is considered the gold standard for diagnosis because of highly accurate test result. However, several studies have claimed RT PCR has several weaknesses. Molecular testing equipment needed for the RT PCR test is not available in every region, including sub urban areas of developing countries.(Galea-Pace, 2020) This condition compels local health facility to deliver samples to fully-equipped laboratory, causing longer waiting time. In the midst of this global pandemic, there is severe shortage of RT PCR testing reagent.(Chu et al., 2020; Purwa & Sucahya, 2020) This “equipment sensitive” weakness of RT PCR cause testing to be highly expensive therefore disrupting early diagnosis and containment (Cohen et al., 2020; Surkova et al., 2020). Equipping healthcare facilities in sub urban areas of low resource and developing countries proved to be a burden. This study proved that the UCSS have adequate COVID-19 diagnosis ability compared with RT PCR. Therefore, the UCSS has the potential to be used as an alternative diagnostic aid.

UCSS would also be useful in re-testing evaluation for COVID-19 patients waiting for release from hospitalization. RT PCR has been reported to present a number of false positive results due to the detection of viral shed, although the virus itself is no longer actively infecting the patients’ system.(Cohen et al., 2020; Surkova et al., 2020) This problem has been noticed and considered by the World Health Organization (WHO), which then revise the criteria for patient release from two negative RT PCR swab on sequential samples taken at least 24 hours apart to ten days from clinical onset, keeping in mind an additional criterion of three days without symptoms for symptomatic patients (Foppiani et al., 2020; Lyons-Weiler, 2021). UCSS could be used as a supportive instrument along with the revised WHO release recommendation for better documentation and a more structured data keeping. Using UCSS along with WHO revised isolation release recommendation would help decreasing budget or cost and patients waiting time, as well as a more effective hospital resources management. (Lyons-Weiler, 2021; Surkova et al., 2020) The sooner recovered patients able to be released from hospital isolation, the sooner there would be space availability for next patients in need. It would also mean hospital resources, including human capitals and facilities, could be more efficiently allocated to new patients.(Cao et al., 2020; Peiffer-Smadja et al., 2020)

The UCSS result has much shorter waiting time compared with the RT PCR. The UCSS results only takes approximately 2 hours if we include the simple blood test and chest X-Ray evaluation, while RT PCR may take 3-5 days or even more in sub urban region. Based on this finding, development the UCSS is in the array of this study purpose, which is to develop a quick, simple, and cost effective COVID-19 screening tool for disease containment in the sub urban areas of low resource and developing country. Further study with a massive sample size and diverse area is needed to further evaluate the results obtained from this study.

5. Conclusion

The UCSS showed acceptable validity and accuracy. The UCSS has the potential to be used as a diagnostic aid for COVID-19 early detection. We suggest further studies to be conducted in diverse areas and greater sample size is recommended. External validation may also be done in different clinical and population settings to explore the generalizability potential of the instrument.

The author acknowledges the limits of this study, where the sample size was not big enough to conclude a widely-applicable result. This scoring system must also be studied on other healthcare centers to provide a wider scope of demographic variation in patients.

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Conflict of Interests

The author declared that there are no conflict of interests.

References

- Cao, Y., Li, Q., Chen, J., Guo, X., Miao, C., Yang, H., Chen, Z., Li, C., & Li, L. (2020). Hospital Emergency Management Plan During the COVID-19 Epidemic. In *Academic Emergency Medicine*, 27(4), 309–311. <https://doi.org/10.1111/acem.13951>
- Chu, A. W. H., Chan, W. M., Ip, J. D., Yip, C. C. Y., Chan, J. F. W., Yuen, K. Y., & To, K. K. W. (2020). Evaluation of simple nucleic acid extraction methods for the detection of SARS-CoV-2 in nasopharyngeal and saliva specimens during global shortage of extraction kits. *Journal of Clinical Virology*, 129, 104519. <https://doi.org/10.1016/j.jcv.2020.104519>
- Cohen, A. N., Kessel, B., & Milgroom, M. G. (2020). Diagnosing SARS-CoV-2 infection: The danger of over-reliance on positive test results. In *medRxiv* (p. 2020.04.26.20080911). medRxiv. <https://doi.org/10.1101/2020.04.26.20080911>
- Finch, W. H., & Hernández Finch, M. E. (2020). Poverty and Covid-19: Rates of Incidence and Deaths in the United States During the First 10 Weeks of the Pandemic. *Frontiers in Sociology*, 5, 47. <https://doi.org/10.3389/fsoc.2020.00047>
- Foppiani, A., Bertoli, S., Battezzati, A., & Zuccotti, G. (2020). Data to guide the application of the new WHO criteria for releasing COVID-19 patients from isolation. In *Pharmacological Research* (Vol. 160). Academic Press. <https://doi.org/10.1016/j.phrs.2020.105063>
- Galea-Pace, S. (2020, July). *McKinsey: Overcoming Supply Chain Shortages due to COVID-19 | Digital Supply Chain | Supply Chain Digital*. Supply Chain Digital.
- Gostic, K. M., Gomez, A. C. R., Mummah, R. O., Kucharski, A. J., & Lloyd-Smith, J. O. (2020). Estimated effectiveness of symptom and risk screening to prevent the spread of COVID-19. *ELife*, 9. <https://doi.org/10.7554/eLife.55570>
- Hur, J., & Chang, M. C. (2020). Usefulness of an Online Preliminary Questionnaire under the COVID-19 Pandemic. In *Journal of Medical Systems* (Vol. 44, Issue 7, pp. 1–2). Springer. <https://doi.org/10.1007/s10916-020-01586-7>
- Jiang, F., Deng, L., Zhang, L., Cai, Y., Cheung, C. W., & Xia, Z. (2020). Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19). In *Journal of General Internal Medicine* (Vol. 35, Issue 5, pp. 1545–1549). Springer. <https://doi.org/10.1007/s11606-020-05762-w>
- Kerboua, K. E. (2021). NLR: A Cost-effective Nomogram to Guide Therapeutic Interventions in COVID-19. In *Immunological Investigations* (Vol. 50, Issue 1, pp. 92–100). Taylor and Francis Ltd. <https://doi.org/10.1080/08820139.2020.1773850>
- Kwon, K. T., Ko, J. H., Shin, H., Sung, M., & Kim, J. Y. (2020). Drive-through screening center for covid-19: A safe and efficient screening system against massive community outbreak. *Journal of Korean Medical Science*, 35(11), 123. <https://doi.org/10.3346/jkms.2020.35.e123>
- Lauer, S. A., Grantz, K. H., Bi, Q., Jones, F. K., Zheng, Q., Meredith, H. R., Azman, A. S., Reich, N. G., & Lessler, J. (2020). The incubation period of coronavirus disease 2019 (CoVID-19) from publicly reported confirmed cases: Estimation and application. *Annals of Internal Medicine*, 172(9), 577–582. <https://doi.org/10.7326/M20-0504>
- Lyons-Weiler, J. (2021). Balance of Risk in COVID-19 Reveals the Extreme Cost of False Positives. In *International Journal of Vaccine Theory, Practice, and Research* (Vol. 1, Issue 2).
- Manski, C. F., & Molinari, F. (2021). Estimating the COVID-19 infection rate: Anatomy of an inference problem. *Journal of Econometrics*, 220(1), 181–192. <https://doi.org/10.1016/j.jeconom.2020.04.041>
- McIntosh, K., & Hirsh, M. B. A. (2021). *COVID-19: Epidemiology, virology, and prevention - UpToDate*. Uptodate. <https://www.uptodate.com/contents/covid-19-epidemiology-virology-and-prevention>
- Moghadas, S. M., Fitzpatrick, M. C., Sah, P., Pandey, A., Shoukat, A., Singer, B. H., & Galvani, A. P. (2020). The implications of silent transmission for the control of COVID-19 outbreaks. *Proceedings of the National Academy of Sciences of the United States of America*, 117(30), 17513–17515. <https://doi.org/10.1073/pnas.2008373117>
- Morawska, L., & Milton, D. K. (2020). It Is Time to Address Airborne Transmission of Coronavirus Disease 2019 (COVID-19). In *Clinical Infectious Diseases* (Vol. 71, Issue 9, pp. 2311–2313). Oxford University Press. <https://doi.org/10.1093/cid/ciaa939>
- Park, M., Cook, A. R., Lim, J. T., Sun, Y., & Dickens, B. L. (2020). A Systematic Review of COVID-19 Epidemiology Based on Current Evidence. *Journal of Clinical Medicine*, 9(4), 967. <https://doi.org/10.3390/jcm9040967>
- Peiffer-Smadja, N., Lucet, J. C., Bendjelloul, G., Bouadma, L., Gerard, S., Choquet, C., Jacques, S., Khalil, A., Maisani, P., Casalino, E., Descamps, D., Timsit, J. F., Yazdanpanah, Y., & Lescure, F. X. (2020). Challenges and issues about organizing a hospital to respond to the COVID-19 outbreak: experience from a French reference centre. In *Clinical Microbiology and Infection* (Vol. 26, Issue 6, pp. 669–672). Elsevier B.V. <https://doi.org/10.1016/j.cmi.2020.04.002>
- Purwa, & Suchaya, K. (2020). Barriers to Covid-19 RT-PCR Testing in Indonesia: A Health Policy Perspective. In *Journal of Indonesian Health Policy and Administration* (Vol. 5, Issue 2).
- Rothan, H. A., & Byrareddy, S. N. (2020). The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. In *Journal of Autoimmunity* (Vol. 109). Academic Press. <https://doi.org/10.1016/j.jaut.2020.102433>

Sastroasmoro, S., & Ismael, S. (2011). *Dasar-dasar Metodologi Penelitian Klinis* (4th ed.). Sagung Seto.

Surkova, E., Nikolayevskyy, V., & Drobniowski, F. (2020). False-positive COVID-19 results: hidden problems and costs. In *The Lancet Respiratory Medicine* (Vol. 8, Issue 12, pp. 1167–1168). Lancet Publishing Group. [https://doi.org/10.1016/S2213-2600\(20\)30453-7](https://doi.org/10.1016/S2213-2600(20)30453-7)

Tassis, B., Lunghi, G., Frattaruolo, M. P., Ruggiero, M., Somigliana, E., & Ferrazzi, E. (2020). Effectiveness of a COVID-19 screening questionnaire for pregnant women at admission to an obstetric unit in Milan. *International Journal of Gynecology & Obstetrics*, 150(1), 124–126. <https://doi.org/10.1002/ijgo.13191>

Zheng, Y., Wang, L., & Ben, S. (2021). Meta-analysis of chest CT features of patients with COVID-19 pneumonia. *Journal of Medical Virology*, 93(1), 241–249. <https://doi.org/10.1002/jmv.26218>