

Title: COVID-19 and Misinformation: How an Infodemic Fueled the prominence of Vitamin D

Short Title: COVID-19 Misinformation

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None

COVID-19 and Misinformation: How an Infodemic Fueled the prominence of Vitamin D

We read with a great interest of a preprint paper[1] allegedly written by an Indonesian Author entitled “Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study”, which has taken the internet by a storm. According to the PlumX Metrics[2], this article has been used more than 100,000 times, downloaded more than 17,000 times, and mentioned in social media over 8000 times. Through google scholar[3], we found that this article has been cited nine times, six of which are indexed in Pubmed. We also found an article in the British medical journal (BMJ)[4] that cited this article, which was not detected by the google scholar, through a conventional google search. The manuscript has been cited in COVID-19 rapid evidence summary: vitamin D for COVID-19, an evidence review by National Institute of Health and Care Excellence (NICE)[5]. Thus, we believe that the impact on scholarly fields is far more prominent. Nevertheless, it is just the tip of an iceberg compared to the astronomical impact on laypeople.

Social media, such as Facebook, Twitter, and Reddit and messaging applications can facilitate rapid dissemination of new information, whether good or bad and thus, they are the centre of infodemic warfare. For example, a Reddit[6] section that discussed this paper has involved 330 comments and generated 857 upvotes, which reflects positive response on this article discussion. Then, through twitter[7] search, we have found that this article has been tweeted 1552 times and retweeted 875 times starting from 27 April, with the latest tweet on 29 June.

Furthermore, this finding has been reported in major news outlet including the DailyMail[8] and the Sun[9]. A news section of the British Heart Foundation[10], “Coronavirus: Which news stories can you trust” also discussed this preprint paper. This responsible media provided disclaimer that the study was a preprint and yet to be peer-reviewed, while also revealing a lack

of information relating to all researchers. However, other news outlets or social media users may not follow the suit.

A fraudulent publication for public consumption may spread faster and overwhelm the measures to contain it. Nevertheless, preprint papers do not necessarily mean a “not to be trusted” source, since various researches conducted by prominent researchers, collaborations, or NIH (National Institute of Health) funded publication may supply us with critical information for patients care. An example of this is the RECOVERY (Randomised Evaluation of COVID-19 Therapy) Trial which enables us to provide the best treatment that will be otherwise delayed by peer-reviews. A more critical approach is needed when reading preprints article.

The authors of the current paper are from Indonesia. We launched an independent investigation to look for the Raharusuna et al. track record. Firstly, we performed a search in the Google Scholar, SCOPUS, and PubMed for any prior publications by the authors. We found no records concerning the authors. Secondly, we performed a search in the Indonesian Medical Doctor Council Database[11] and found none of the authors. Thirdly, we searched using the Google Search Engine with keywords "Rumah Sakit Umum Daerah Kabupaten Sukamara" AND "Prabowo Raharusuna"; we did not find any related content. Alternately we performed similar search method for “Prabowo Raharusun”. On searching Indonesian Medical Council database, we run second search with keyword “Prabowo” and third search with keyword “Raharusun”; and found no potential author for the aforementioned preprint paper.

Since we could not find the authors' profile, we assess the preprint manuscript for validity and found several issues: 1) the authors did not mention specifically the name of the hospitals (or the number of hospitals) and how do they obtain the confidential data for their manuscript (similar to the Surgisphere incident). None of the authors is affiliated to the Ministry of Health/other governmental hospitals, and they did not acknowledge any of them. 2) the name of the ethical/institutional review board was not mentioned, and there is no ethical clearance for the study. 3) Vitamin D is not routinely checked in Indonesia; the data collection method was retrospective, which is suspicious. Finally, we called the COVID-19 administration for Sukamara's Regional Public Hospital, which allegedly affiliated with the authors. Upon confirmation, the administrator told us that no authors' names that we mentioned worked in this hospital.

In conclusion, we have taken several steps to investigate the identity and existence of the authors to no avail. As of the time this article is written (1 July 2020), a link to the Raharusuna et al. preprint at SSRN Electronic cannot be accessed. However, the misinformation has been spread through various media and cited by several publications, and believed by many to be true.

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Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study

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April 26, 2020

Data Availability:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statement of Conflict of Interest:

The authors declare no conflict of interest.

Source of Funding:

The study was not funded by external sources.

KEY FINDINGS:

- Majority of the COVID-19 cases with insufficient and deficient Vitamin D status died.
- The odds of death was higher in older and male cases with pre-existing condition and below normal Vitamin D levels.
- When controlling for age, sex, and comorbidity, Vitamin D status is strongly associated with COVID-19 mortality.
- Randomized controlled trials are warranted to investigate the role of vitamin D supplementation on COVID-19 outcomes and to establish the underlying mechanisms.

ABSTRACT

This is a retrospective cohort study which included two cohorts (active and expired) of 780 cases with laboratory-confirmed infection of SARS-CoV-2 in Indonesia. Age, sex, co-morbidity, Vitamin D status, and disease outcome (mortality) were extracted from electronic medical records. The aim was to determine patterns of mortality and associated factors, with a special focus on Vitamin D status. Results revealed that majority of the death cases were male and older and had pre-existing condition and below normal Vitamin D serum level. Univariate analysis revealed that older and male cases with pre-existing condition and below normal Vitamin D levels were associated with increasing odds of death. When controlling for age, sex, and comorbidity, Vitamin D status is strongly associated with COVID-19 mortality outcome of cases.

INTRODUCTION

The Coronavirus-2019 (COVID-19) pandemic remains a pressing problem in the world and will continually surface as more than 30 different mutations of the disease strain, severe acute respiratory syndrome-coronavirus (SARS-CoV-2), were detected from the latest study in China.¹ With the increasing number of novel strains, researchers across the world are driven to conduct clinical trials for potential anti-viral treatments. However, the likelihood of potential vaccines for the disease went down, due to more evidence debuting previous claims on the efficacy of the tested drugs. Scientists continue to search for effective treatments, with efforts focused on several existing drugs.

Vitamin D has been proven to enhance expression of anti-oxidation-related genes, modulates adaptive immunity, and improves cellular immunity.^{2,3,4,5} With the remarkable potential of Vitamin D, several researchers proposed Vitamin D supplementation could possibly treat COVID-19 or reduce severity, at least.^{6,7,8,9,10,11,12}

In a previous report, a significant association between vitamin D status and severity of COVID-19 disease has been documented in Southeast Asia.¹¹ The report suggests that serum 25(OH)D level was lowest in critical cases, but highest in mild cases which thereby increase the odds of having a mild clinical outcome rather than a critical outcome by approximately 19.61 times. The result further fortified initial hypotheses of Vitamin D proponents that a decrease in serum 25(OH)D level in the body could worsen clinical outcomes of COVID-19 patients while an

increase in serum 25(OH)D level in the body could either mitigate worst outcome or improve clinical outcomes.

Existing literature provides evidence that pre-hospitalization serum 25(OH)D is linked to outcomes of respiratory diseases. Using cross-sectional data from 6789 participants in the nationwide 1958 British birth cohort who had measurements of 25(OH)D, Berry et al.¹³ reported that vitamin D status had a linear relationship with respiratory infections and lung function. Pre-admission 25(OH)D deficiency was also predictive for short-term and long-term mortality.^{14,15}

This study has focused on identifying patterns of mortality among patients infected with Covid-19 and the possible association between serum 25(OH)D level and mortality outcomes. In this study, age, sex, and co-morbidity were added as factors and an outcome variable, mortality, was analyzed to further provide strong evidence of Vitamin D potency for SARS-CoV-2.

METHODS

Study Design and Participants

This is a retrospective cohort study which included two cohorts (active and expired) of 780 cases with laboratory-confirmed infection of SARS-CoV-2. Data between March 2, 2020 (start of outbreak in Indonesia) and April 24, 2020 were obtained from medical records of Indonesia government hospitals. The requirement for informed consent was waived by the Ethics Commission. To ensure anonymity, all names were preserved

throughout the analysis.

Data Collection

Age, sex, co-morbidity, Vitamin D status, and disease outcome (mortality) were extracted from electronic medical records. Co-morbidity status was classified as with or without pre-existing condition.

For Vitamin D status, cases were classified based on their serum 25(OH)D levels: (1) normal - serum 25(OH)D of > 30 ng/ml, (2) insufficient - serum 25(OH)D of 21-29 ng/ml, and (3) deficient - serum 25(OH)D of < 20 ng/ml. This classification was based on existing literature.¹⁶ The pre-admission serum 25(OH)D levels were considered for the analysis. Serum 25(OH)D level was checked by two physicians based on the available clinical data of the patients.

Statistical Analysis

Analysis was carried out using SPSS 21.0 statistical software. Mean was used for continuous variable (age), while frequency and percentage were employed for categorical variables. To compare differences in the outcomes, Mann-Whitney U and χ^2 tests were used. Meanwhile, univariate logistics regression was used to determine the association between each predictor variable and mortality outcome. The odds ratio (OR) associated with the effect of a one standard deviation increase in the predictor was used in the interpretation of data. To determine the association of Vitamin D status and mortality outcome, all ORs were adjusted

for age, sex, and comorbidity using a generalized linear model. A p-value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Descriptive Statistics

The demographic and clinical characteristics of two cohorts (active and expired) are presented (**Table 1**). Mean overall age was 54.5 years, mean age for expired cases was 65.2 years, higher compared to active cases (46.3 years). Of the 780 sample, majority (58.8%) aged below 50 years, most of the them (83.0%) are still admitted in the hospital. Of the 321 samples aged 50 years and above, majority (66.6%) died due to the disease. Females (51.3%) outnumbered males (48.7%); however, there were more male cases who died (66.6%) than female (33.4%). Patients with existing condition (84.9%) comprised majority of the death cases. Interestingly, majority of the cases had normal Vitamin D status (49.7%), most of them (93.0%) are still hospitalized. Of the 213 cases with insufficient Vitamin D status, majority (49.1%) died. The same distribution was observed in Vitamin D deficient cases where majority (46.7%) died due to the disease.

A total of 179 cases had Vitamin D deficiency (Vitamin D < 20 ng/ml), mean level of serum 25(OH)D and mean age for this group were 18.2 ± 0.6 ng/ml and 66.9 ± 13.8 years, respectively (**Table 2**). 213 cases had Vitamin D insufficiency (Vitamin D 20–30 ng/ml), mean level of serum 25(OH)D and mean age for this group were 26.7 ± 1.3 ng/ml and 62.9 ± 14.7 years, respectively. 388 cases

had normal Vitamin D levels (Vitamin D > 30 ng/ml), mean level of serum 25(OH)D and mean age for this group were 32.2 ± 1.2 ng/ml and 46.6 ± 12.6 years, respectively. 80.0% of Vitamin D deficient cases had pre-existing conditions (comorbidity). 73.8% of Vitamin D insufficient cases had pre-existing conditions (comorbidity). 18.8% of cases with normal Vitamin D levels had pre-existing conditions (comorbidity). 98.9% of Vitamin D deficient cases died while only 1.1% of them were active cases. 87.8% of Vitamin D insufficient cases died while only 12.2% of them were active cases. Only 4.1% of cases with normal Vitamin D levels died while 95.9% of them were active cases.

Univariate Analysis

Each predictor was separately analyzed using univariate logistic regression (**Table 2**). Older cases (50 years and above) were approximately 10.45 times more likely to die than younger cases (at most 50 years) (OR=10.45; $p < 0.001$). Male cases were approximately 5.73 times more likely to die from the disease than female cases (OR=5.73; $p < 0.001$). Meanwhile, cases with pre-existing condition had increased odds of mortality compared to cases without (OR=11.24; $p < 0.001$). With reference to normal cases, Vitamin D insufficient cases were approximately 12.55 times more likely to die (OR=12.55; $p < 0.001$) while Vitamin D deficient cases were approximately 19.12 times more likely to die from the disease (OR=19.12; $p < 0.001$).

Generalized Linear Model

To control for possible confounding of age, sex, and comorbidity on the association of Vitamin D status and mortality outcome, a generalized linear model was employed (**Table 3**). After accounting for these variables in the model, a significant association has been obtained between Vitamin D status and mortality. In particular, the odds of death was higher in cases with insufficient Vitamin D status (OR=7.63; $p<0.001$). When compared to cases with normal Vitamin D status, death was approximately 10.12 times more likely for Vitamin D deficient cases (OR=10.12; $p<0.001$).

Table 1. Demographic and clinical characteristics of sample

Variables	Total (N=780)	Expired (N=380)	Active (N=400)	p- value
Age, mean	54.5	65.2	46.3	
< 50 years	459 (58.8%)	127 (33.4%)	332 (83.0%)	<0.001
≥ 50 years	321 (41.2%)	253 (66.6%)	68 (17.0%)	
Sex				
Female	400 (51.3%)	128 (33.4%)	332 (83.0%)	<0.001
Male	380 (48.7%)	252 (66.6%)	68 (17.0%)	
Comorbidity				
Yes	383 (49.1%)	323 (84.9%)	60 (15.0%)	<0.001
No	397 (50.9%)	57 (15.1%)	340 (85.0%)	
Vitamin D Status				
Normal	388 (49.7%)	16 (4.2%)	372 (93.0%)	<0.001
Insufficient	213 (27.3%)	187 (49.1%)	26 (6.5%)	
Deficient	179 (23.0%)	177 (46.7%)	2 (0.5%)	

Table 2. Dynamics of Vitamin D status

	Vitamin D < 20 ng/ml (18.2 ± 0.6)	Vitamin D 20-30 ng/ml (26.7 ± 1.3)	Vitamin D > 30 ng/ml (32.2 ± 1.2)
Overall, N	179	213	388
Mean age	66.9 ± 13.8	62.9 ± 14.7	46.6 ± 12.6
Comorbidity, %	80.0	73.8	18.8
Death, %	98.9	87.8	4.1
Active, %	1.1	12.2	95.9

Table 3. Univariate analysis for factors associated with mortality

Variables	OR	p-value
Age, mean		
< 50 years	-	
≥ 50 years	10.45	<0.001
Sex		
Female	-	
Male	5.73	<0.001
Comorbidity		
Yes	11.24	<0.001
No	-	
Vitamin D Status		
Normal	-	
Insufficient	12.55	<0.001
Deficient	19.12	<0.001

Table 4. Association between Vitamin D status and mortality (adjusted for age, sex, and comorbidity)

Variable	OR	p-value
Vitamin D Status		
Normal	-	
Insufficient	7.63	<0.001
Deficient	10.12	<0.001

CONCLUSION

To the best of the researchers' knowledge, this is the first retrospective study which determines the association of Vitamin D status and COVID-19 mortality outcome. Older and male cases with pre-existing condition and below normal Vitamin D levels were associated with increasing odds of death. When controlling for age, sex, and comorbidity, Vitamin D status is strongly associated with COVID-19 mortality outcome of cases. Randomized controlled trials are warranted to investigate the role of vitamin D supplementation on COVID-19 outcomes and to establish the underlying mechanisms.

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Sukamara, 29 Juli 2020

Nomor : 445 /1115/ RSUD
Sifat : Biasa
Lampiran : -
Hal : Balasan Surat Komplain

Kepada:
Yth. Joshua Henrina
Michael Antonius Lim
Raymond Pranata
di-
JAKARTA

Menindaklanjuti Surat Komplain yang dikirim oleh saudara Joshua Henrina melalui email joshuahenrina@gmail.com perihal Pencatutan RSUD Kab Sukamara di dalam salah satu artikel yang ditulis oleh Prabowo Raharusun, dkk. Pada tanggal 28 Juli 2020. Dengan ini menyatakan bahwa:

1. Kami tidak pernah membuat atau terlibat dalam penulisan artikel yang berjudul *Patterns of Covid-19 Mortality and Vitamin D: An Indonesian Study*.
2. Kami tidak pernah memiliki pegawai atas nama Prabowo Raharsun dan nama-nama sebagaimana yang tercantum dalam artikel tersebut.
3. RSUD Sukamara untuk saat ini tidak memiliki website resmi dan email resmi kami hanya satu, yaitu rsud_sukamara@yahoo.com. Kami memiliki facebook atas nama RSUD Sukamara, tetapi sudah tidak aktif lagi.
4. Kami juga mendapatkan pertanyaan mengenai apakah kami pernah mengirim email resmi mengenai "berpulanganya Prabowo Raharusun", menanggapi pertanyaan tersebut, kami dapat memastikan bahwa kami tidak pernah mengeluarkan pernyataan atau email tersebut.
5. Kami dapat memastikan bahwa Joshua Henrina, Michael Anthonius Lim, and Raymond Pranata sebelumnya pernah menghubungi RSUD Kabupaten Sukamara tentang perihal yang tertuang pada surat ini sebelum dipublikasikannya artikel "COVID-19 and Misinformation: How an Infodemic Fueled the prominence of Vitamin D" pada *British Journal of Nutrition*.

Demikian hal ini kami sampaikan untuk dapat dipergunakan sebagaimana mestinya.

Direktur RSUD Sukamara,

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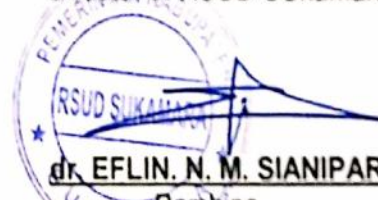
Sukamara, 29th July 2020

Responding to the Inquiry Letter (Complaint) sent by dr. Joshua Henrina through electronic mail (email) from joshuahenrina@gmail.com regarding the misuse of "RSUD Kabupaten Sukamara" as an alleged institution in an article written by Prabowo Raharusun et al., on 28th July 2020. Through this letter, we officially state that:

1. We have never conducted or participated in the writing of the article titled "Patterns of Covid-19 Mortality and Vitamin D: An Indonesian Study".
2. We do not have an employee named Prabowo Raharusun and the names lists on the articles.
3. RSUD Sukamara did not have any official website and our official email address is only rsud_sukamara@yahoo.com. We do have an official facebook account, but it is not active anymore.
4. We have also received inquiries whether we have ever sent an official email regarding the supposed "Prabowo Raharusun death", responding to this inquiry, we can assure that we have never released such statement or email.
5. We confirmed that the authors Joshua Henrina, Michael Anthonius Lim, and Raymond Pranata have previously contacted RSUD Kabupaten Sukamara regarding this matter, prior to the publication of "COVID-19 and Misinformation: How an Infodemic Fueled the prominence of Vitamin D" in the British Journal of Nutrition.

Hereby we release this statement to be used accordingly.

Director of RSUD SUKAMARA


dr. EFLIN, N. M. SIANIPAR
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Surat Komplain kepada RSUD Kabupaten Sukamara

Jl. Tjilik Riwut No.kM. 5.5, Natai Sedawak,

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Kalimantan Tengah 74171

28 Juli 2020

Hal: Pencatutan RSUD Kab Sukamara di dalam salah satu artikel yang ditulis oleh Prabowo Raharusun, dkk.

Jakarta,

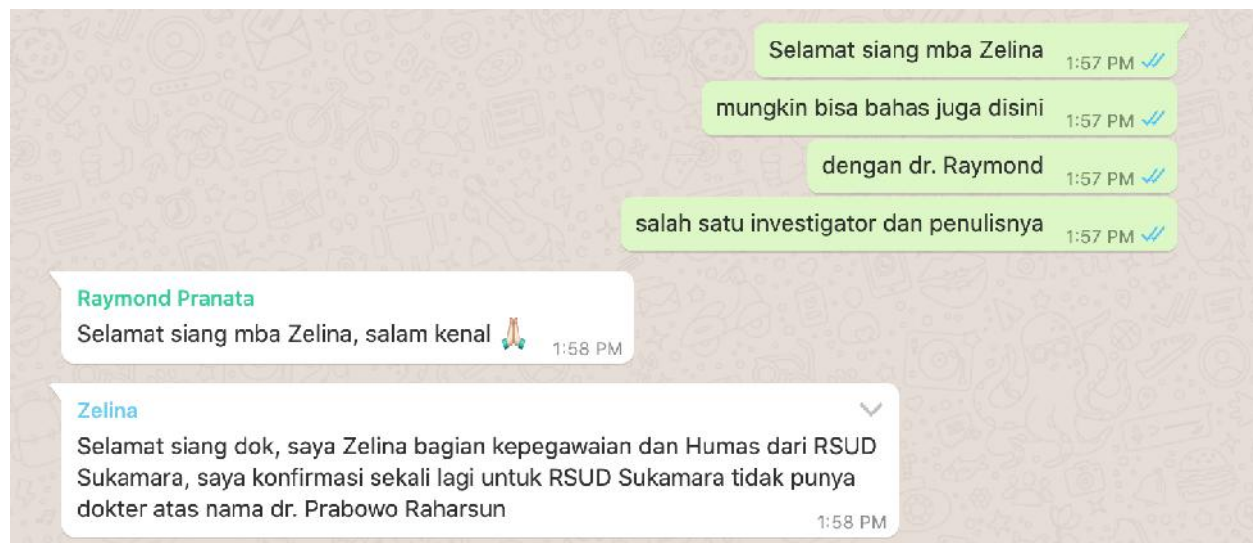
Dengan hormat, kami selaku warga Indonesia dan peneltiti di bidang ilmu kesehatan, telah membaca sebuah artikel yang ditulis oleh Prabowo Raharusun, dkk yang terduga berafiliasi dengan RSUD Sukamara dengan prihatin. Setelah kami membacanya, ada beberapa kejanggalan, yaitu

- (1) Artikel ini mengatakan memeriksakan kadar vitamin D pada pasien COVID-19 di RSUD Kab. Sukamara. Saya sudah mengonfirmasinya ke bagian humas ternyata tidak ada penelitian yang dilakukan mengenai COVID-19 dan tidak ada nama – nama pengarang yang bekerja di RSUD tersebut
- (2) Pemeriksaan vitamin D sangat jarang dilakukan, dan mahal, sangat tidak mungkin diperiksakan di semua orang, dan apalagi bukan di RS umum pusat nasional.
- (3) Kami memeriksakan nama – nama pengarang artikel tersebut di database kedokteran indonesia, dan tidak ditemukan nama dokter – dokter tersebut.
- (4) Track record pengarang tersebut tidak ada di internet, tidak ada di Pubmed, scopus, dll
- (5) Penelitian tentang COVID-19 di Indonesia dilakukan di pusat rumah sakit tipe rujukan. Jadi mustahil apabila ada studi besar yang melibatkan orang banyak hanya di RSUD Sukamara saja
- (6) Artikel tersebut ada di SSRN, tetapi setelah beredar kabar skandal Mehra, yaitu skandal besar yang melibatkan Harvard University dan mengenai COVID-19, artikel oleh Prabowo Raharusun, dkk hilang dari SSRN. Alasan ditariknya artikel ini karena katanya dia meninggal akibat COVID-19.

- (7) Korespondensi emailnya ke RSUD.Sukamara@yahoo.com yang bukan email officialnya, yaitu RSUD_sukamara@yahoo.com. Ada website resmi RSUD Sukamara, yang sebenarnya tidak ada

Berikut adalah bukti-buktinya:

Gambar 1. Tidak ada nama pengarang yang bekerja di RSUD Sukamara



Gambar 2. Link email dan administrasi, serta website palsu RSUD_sukamara

Zelina

Dan untuk email RSUD Sukamara hanya punya satu email yaitu rsud_sukamara@yahoo.com kita juga tidak punya website resmi

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Oleh karena itu, kami memohon kepada RSUD Sukamara untuk memberikan pernyataan resmi, tentang kebohongan artikel ini sehingga dapat memutihkan kembali nama RSUD Sukamara.

Nanti, dari pernyataan resmi yang dikeluarkan, bisa kami publikasikan juga ke *British Journal of Nutrition*.

Salam Hormat,

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