Dear BPG Editorial Office, Science Editor, and Reviewers, thank you for accepting our manuscript. First, We would like to explain the situation that we are currently dealing. We decided to make this paper based on the situation in Indonesia (July 2021). At that time, high population of fully-vaccinated Indonesian People were infected by B.1.617.2 (delta) variant of SARS-CoV-2, including our staff, residents, and students. Because the demographic statistic and clinical presentation of the delta variant infection after the second dose of vaccine in Indonesia were unknown and few journal discussed about it, We quickly decided to retrospectively collected the data and made a manuscript so that we can also contribute to society about this ongoing pandemic and help other country to understand this disease. After it was completed, We decided to check for possible submission and World Journal of Clinical Case became our top priority choice. After checking the requirement for submission, We are quite upset because We couldn't meet one of the criteria, that is Institutional Review Board Statement. We didn't make it because in our country, Institutional Review Board Statement is not mandatory, especially for a case series in which the patient's personal information are obfuscated and there are no risk in conducting the study. Therefore, We choose manuscript type as review so it can be more suitable and still can be submitted to Would Journal of Clinical Case. Even though We didn't have Institutional Review Board Statement, We still have a written informed consent from our subjects. We hope that this can be applicable and We still can submit the manuscript to World Journal of Clinical Case.

Reviewer #1: Scientific Quality: Grade C (Good) Language Quality: Grade B (Minor language polishing) Conclusion: Accept (General priority) Specific Comments to Authors: Nil

Reviewer #2: Scientific Quality: Grade D (Fair) Language Quality: Grade C (A great deal of language polishing) Conclusion: Major revision Specific Comments to Authors: This paper stands major revision from my point of view. Some of the few observations have been noted below.

1. Objectives were not clearly mentioned in the paper.

Our main objective is to describe the demographic statistics and clinical presentation of the delta variant infection after the second dose of vaccine in Indonesia.

#### 2. What is the logic behind data collection of two days only in the paper?

We apologize for making such confusion. In July, Indonesia became the new epicentre of delta variant and confirmed cases were raising around the country. So in order to help government and clinicians to diagnose delta variant infection based on only clinical symptoms, We decided to take sample as soon as possible. Due to

urgent circumstances, Our sample based on our availability to collect data and since Our Staff, Resident, and Student were also infected by delta variant after they had second dose of vaccine, We decided to retrieve data from them and make a case series as it would be faster. We decided to send 2 days of collecting swab sample from our Clinical Microbiology Laboratory and did the whole genome sequencing. From the result, we acquired 15 samples that were B.1.617.2 (delta) variant from fully vaccinated subjects.

3. Consent from the patients must be included along with the manuscript as Annexure. Please do it immediately.

Thank you for the suggestions. We already had the written informed consent and we will submit it along with the revised version of our manuscript.

4. Literature survey papers should be included in a separate section. Each survey paper should include their limitation in a tabular form. 5. Where is the research gap analysis with numerical data? 6. No comparative study with earlier papers was given. Please mention in a different sub-section and justify with tabular format.

Since our study population were subject with delta variant infection after second dose of vaccination, we couldn't find research that could matched with our criteria. Therefore, we couldn't make a literature review and comparison with our study, but we could used few journal that discussed about clinical characteristics of Delta Variant. We will add this to our revised manuscript.

The common clinical manifestations of COVID-19 patients in this case series were fever in 10 (66.67%), rhinorrhea in 9 (60%), anosmia in 8 (53.34%), and cough in 7 (46.67%). A recent study by Park *et al*<sup>[22]</sup>, also strengthen our findings, from a total of 108 delta variant subjects that were enrolled, common symptoms for the delta variant are fever (73.7%), myalgia (51.5%), cough (49.5%), sore throat (43.4%), and cephalgia (34.3%). In comparison, Myalgia was more common in the delta group (51.5%) than in the non-delta group (26.9%). Non-delta variant also showed significant symptoms of loss of taste (26.9%) and loss of smell (15.4%) compare to delta group with loss of taste (2.0%) and loss of smell (7.1%). <sup>[22]</sup> Another study by Hu Z *et al*<sup>[23]</sup> with 156 full vaccinated delta variant patients that admitted at Yangzhou, China in 2021 also indicate that most common symptoms are cough (48.7%), fever (34.6%), sore throat (25.6%), fatigue (19.2%), and expectoration (8.3%). Another study also showed that between delta variant and alpha variant are quite similar, except patients with

delta variant could become rapidly ill and have higher viral loads in the respiratory tract. Delta variant could also cause auditory impairment and gangrene from worse blood clots. <sup>[24]</sup> Viral infection triggers an inflammatory pathway in the human body. Various inflammatory factors produced by the inflammatory storm can cause systemic immune damage and manifest as high temperatures. It explains why the most common symptom was fever. SARS-CoV-2 also binds to the ACE2 receptor, which is mainly distributed in the respiratory tract, cardiovascular, kidneys, and colon. It causes multiple symptoms, such as dyspnea, cough, anosmia, ageusia, diarrhea, and sore throat<sup>[9]</sup>.

Although subjects with two-dose vaccination can still be infected with SARS-CoV-2, the results from a current trial suggest that there is a 90% reduction in symptomatic COVID-19 with vaccine. However, it remains unknown whether this efficacy is mediated by decreasing SARS-CoV-2 infection susceptibility (VE<sub>SUSC</sub>) or the development of symptoms after infection (VE<sub>SYMP</sub>)<sup>[25]</sup>. In our case series, symptoms that developed in COVID-19 patients were mild to moderate according to the Indonesian COVID-19 Guideline. In addition, vaccination decreased the symptom duration of COVID-19 patients (7.73 d, ± 5.444), increased the recovery time from the first positive swab to negative swab (17.93 d,  $\pm$  6.364), and prevented the subjects from needing hospitalization. A recent study revealed that VE in terms of protection against deaths was 72%, with a lower reduction of mortality for B.1.1.7 vs non-B.1.1.7 variants (70% vs 78%, respectively)<sup>[26]</sup>. A study from a hospital in New Delhi, India showed that among those fully vaccinated, there was 12.5% (23/184) mortality compared to 31.45% (309/984) among the unvaccinated (odds ratio: 0.3, 95%CI: 0.2-0.5; P <  $(0.0001)^{[27]}$ .

7. Sufficient number of mathematical tests were not carried out to prove the efficacy of the paper. 8. All the statistical results were explained in paragraphs. Represent all those results in graphical methods and tabular formats only. 9. Please improve the Result section with advanced statistical tests.

We already submitted the tabular formats but in different file. Since we used filipodia to check our manuscript and to acquire the language certificate. They provide us with final files in which manuscript and supplementary file were separated. Here, we attached the tabular format of our manuscript results section.

Demographic factor	All
Subjects, n	15
Age class, n (%)	
21-25	3 (20)
26-30	5 (33.34)
31-35	4 (26.67)
35-40	3 (20)
Age in yr, mean ± SD	$29.87 \pm 5.097$
Sex	
Male	10 (66.67)
Female	5 (33,33)
Height in cm, mean ± SD	$167.00 \pm 8.384$
Weight in kg, mean ± SD	$69.20 \pm 11.706$
Body mass index as $kg/m^2$ , mean $\pm$ SD	$24.768 \pm 3.531$
Occupation, <i>n</i> (%)	
Employee	11 (73.34)
Medical students	1 (6.67)
Residents	3 (20)
Comorbidity, n (%)	2 (13.34)
Chronic respiratory disease	1 (6.67)
Obesity	1 (6.67)
Vaccination type, , n (%)	
CoronaVac (Sinovac)	14 (93.34)
ChAdOx1 nCoV-19 (Oxford-AstraZeneca)	1 (6.67)

Table 1 Demographic statistics of the subjects enrolled

SD: Standard deviation.

## Table 2 Clinical characteristics of the subjects enrolled

Characteristic	All					
Reinfection, n (%)	1 (6.67)					
Predicted source of infection, <i>n</i> (%)						
Family	3 (20)					
Patient	3 (20)					
Coworker	7 (46.67)					
Unknown	2 (13.34)					
Mask usage during outside activity, $n$ (%)						
Surgical mask	11 (73.34)					
N95 mask	3 (20)					
KN95 mask	1 (6.67)					
Symptoms, n (%)						
Fever	10 (66.67)					
Cough	7 (46.67)					
Rhinorrhea	9 (60)					
Headache	5 (33.34)					
Sore Throat	2 (13.34)					
Anosmia	8 (53.34)					
Ageusia/Dysgeusia	4 (26.67)					
Diarrhea	3 (20)					
Fatigue	4 (26.67)					
Myagia	4 (26.67)					
Dyspnea	1 (6.67)					
Nausea	1 (6.67)					
Time in d of symptom duration, mean ± SD	$7.73 \pm 5.444$					
Time in d of PCR conversion, mean ± SD	$17.93 \pm 6.364$					
Time in d that elapsed from second dose of vaccine to a positive						
PCR result, median IQR	87 (86-128.00)					
In-home isolation, <i>n</i> (%)	15 (100)					
Drug treatment, n (%)						
Vitamin C	14 (93.34)					

Vitamin D	12 (80)
Paracetamol	8 (53.34)
Azithromycin	5 (33.34)
Oseltamivir	1 (6.67)
Favipiravir	3 (20)
Phytopharmaca	1 (6.67)

IQR: Interquartile range; PCR: Polymerase chain reaction; SD: Standard deviation.

## 10. English is poor with plenty of mistakes. Correct those.

We used filipodia to polish the language for our manuscript. All files will be uploaded after their final revision.

## (1) Science editor:

## 1. Methodology lacks details on the study population / how sample was chosen

We conducted a retrospective study based on a combination of author recall, reverse transcription-polymerase chain reaction (RT-PCR), and whole genome sequencing (WGS) results from the Clinical Microbiology Laboratory, Faculty of Medicine, Universitas Indonesia (Depok, Indonesia). Due to urgent circumstances, Our study population were consist of Staff, Resident, and Student who worked or studied at Faculty of Medicine, Universitas Indonesia.

After collecting samples from Staff, Resident, and Student for two days, whole genome sequencing were conducted and we retrieved 15 samples confirmed with delta variant. This sample were all included in our study.

### 2. Results are not available in table

We already submitted the tabular formats but in different file. Since we used filipodia to check our manuscript and to acquire the language certificate. They provide us with final files in which manuscript and supplementary file were separated. Here, we attached the tabular format of our manuscript results section.

Demographic factor	All
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Phytopharmaca	1 (6.67)

IQR: Interquartile range; PCR: Polymerase chain reaction; SD: Standard deviation.

## 3. Comparison to other variants to document disease severity would strengthen the data presented

The common clinical manifestations of COVID-19 patients in this case series were fever in 10 (66.67%), rhinorrhea in 9 (60%), anosmia in 8 (53.34%), and cough in 7 (46.67%). A recent study by Park *et al*<sup>[22]</sup>, also strengthen our findings, from a total of 108 delta variant subjects that were enrolled, common symptoms for the delta variant are fever (73.7%), myalgia (51.5%), cough (49.5%), sore throat (43.4%), and cephalgia (34.3%). In comparison, Myalgia was more common in the delta group (51.5%) than in the non-delta group (26.9%). Non-delta variant also showed significant symptoms of loss of taste (26.9%) and loss of smell (15.4%) compare to delta group with loss of taste (2.0%) and loss of smell (7.1%). <sup>[22]</sup> Another study by Hu Z et al<sup>[23]</sup> with 156 full vaccinated delta variant patients that admitted at Yangzhou, China in 2021 also indicate that most common symptoms are cough (48.7%), fever (34.6%), sore throat (25.6%), fatigue (19.2%), and expectoration (8.3%). Another study also showed that between delta variant and alpha variant are quite similar, except patients with delta variant could become rapidly ill and have higher viral loads in the respiratory tract. Delta variant could also cause auditory impairment and gangrene from worse blood clots. <sup>[24]</sup> Viral infection triggers an inflammatory pathway in the human body. Various inflammatory factors produced by the inflammatory storm can cause systemic immune damage and manifest as high temperatures. It explains why the most common symptom was fever. SARS-CoV-2 also binds to the ACE2 receptor, which is mainly distributed in the respiratory tract, cardiovascular, kidneys, and colon. It causes multiple symptoms, such as dyspnea, cough, anosmia, ageusia, diarrhea, and sore throat<sup>[9]</sup>.

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Language Quality: Grade B (Minor language polishing) Scientific Quality: Grade C (Good)

#### (2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted.

I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Before its final acceptance, please upload the primary version (PDF) of the Institutional Review Board's official approval in official language of the authors' country, and the Signed Consent Form(s) or Document(s) to the system; for example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Before final acceptance, when revising the manuscript, the author must supplement

and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <u>https://www.referencecitationanalysis.com/</u>.

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## Literature survey papers should be included in a separate section. Each survey paper should include their limitation in a tabular form.

**Sources :** a comprehensive search of PubMed was performed for all studies published prior from March 2020 to April 2022, using the search terms "COVID-19", "Delta Variant OR B.1.617.2 Variant", "Fully vaccinated OR Full-Dose Vaccine", and "Case Series" which yielded 26 results. A systematic review of these papers were performed, and after the full text of all articles were evaluated to determine whether results were included. There were no language restrictions. 2 results were used for our paper.



Figure 1. Flow Chart outlining the selection of articles.

Table 1. Literature Survey Papers

Ref.	Publication	Journal	Sample	Subjects	Limitations
	Date		Size		
Park S et	01/04/2022	Clinical	108	Delta	Statistic of Fully
al		Infection		Variant	Vaccinated Sample not
		Disease			included, Sample from
					Different Ethnic

Hu Z et al	03/01/2022	Frontiers	156	Delta	Sample from Different
		in		Variant	Ethnic
		Medicine		Fully	
				Vaccinated	

## Where is the research gap analysis with numerical data?

Table 2. Research Gap Analysis

Ref.	Reasons(s)	Population	Results	Free text of Gap
	for Gap			
Park	D	Delta	A total of 141 patients (Delta	Results may not be
S et		Variant	group, n = 108 [77%]; non- Delta group, n = 33 [23%])	applicable for
al				reference as full
			Delta Group : Median Age 34.5(26.5-46.0)	vaccinated criteria
				not included and Our
			• Hypertension 12 (11.1)	subject only had
			• Hyperlidemia 2(6.1)	Chronic Respiratory
			<ul><li>Diabetes 5 (15.2)</li><li>Psychiatric Illness</li></ul>	Disease 1 (6.67) and
			1(3.0)	Obesity 1 (6.67)
			• Asthma/Rhinitis 1	
			• Cancer 1 (3.0)	
			• Obesity BMI>30 4	
			(12.1)	
Hu Z	D	Delta	A total of 677 patients (Wild	Results may not be
et al		Variant	Type=341; Delta	applicable for
		Fully	Unvaccinated =120; Delta	reference as Median
		Vaccinated	Partially Vaccinated=60;	Age in Our Subject
			Delta Fully Vaccinated =156)	29.87 ± 5.097 with
				Comorbidity Chronic
			Delta Fully Vaccinated :	Respiratory Disease 1
			Median Age 43.0 (33.0-56.8)	(6.67) and Obesity 1
			• Hypertension 31	(6.67)

			(19.9)	
		•	Diabetes 9 (5.8)	
		•	Cardiovascular	
			Disease 5 (3.2)	

- A. Insufficient (no studies/limited number of studies/ small sample size(s)) or imprecise information
- B. Biased information (high risk of bias/suboptimal study design)
- C. Inconsistent or unknown consistency results
- D. Not the right information (results not applicable/optimal outcomes not assessed/studies too short)

# No comparative study with earlier papers was given. Please mention in a different sub-section and justify with tabular format.

The common clinical manifestations of COVID-19 patients in this case series were fever in 10 (66.67%), rhinorrhea in 9 (60%), anosmia in 8 (53.34%), and cough in 7 (46.67%). A recent study by Park *et al*<sup>[22]</sup>, also strengthen our findings, from a total of 108 delta variant subjects that were enrolled, common symptoms for the delta variant are fever (73.7%), myalgia (51.5%), cough (49.5%), sore throat (43.4%), and cephalgia (34.3%). In comparison, Myalgia was more common in the delta group (51.5%) than in the non-delta group (26.9%). Non-delta variant also showed significant symptoms of loss of taste (26.9%) and loss of smell (15.4%) compare to delta group with loss of taste (2.0%) and loss of smell (7.1%). <sup>[22]</sup> Another study by Hu Z et al<sup>[23]</sup> with 156 full vaccinated delta variant patients that admitted at Yangzhou, China in 2021 also indicate that most common symptoms are cough (48.7%), fever (34.6%), sore throat (25.6%), fatigue (19.2%), and expectoration (8.3%). Another study also showed that between delta variant and alpha variant are quite similar, except patients with delta variant could become rapidly ill and have higher viral loads in the respiratory tract. Delta variant could also cause auditory impairment and gangrene from worse blood clots. <sup>[24]</sup> Viral infection triggers an inflammatory pathway in the human body. Various inflammatory factors produced

by the inflammatory storm can cause systemic immune damage and manifest as high temperatures. It explains why the most common symptom was fever. SARS-CoV-2 also binds to the ACE2 receptor, which is mainly distributed in the respiratory tract, cardiovascular, kidneys, and colon. It causes multiple symptoms, such as dyspnea, cough, anosmia, ageusia, diarrhea, and sore throat<sup>[9]</sup>.

	Our Study (n=15)	Park S et al	Hu Z et al (n=156)
		(n=108)	
Age	$29.87 \pm 5.097$	34.5 (26.5-46.0)	43.0 (33.0-56.8)
Comorbidity			
Hypertension		12 (11.1)	31 (19.9)
Hyperlipidemia		4 (3.7)	
Diabetes		7 (6.5)	9 (5.8)
Psychiatric illness		1(0.9)	
Cancer		1 (0.9)	
Obesity (BMI>30)	1 (6.67)	12 (11.1)	
Cardiovascular			5 (3.2)
Disease			
Respiratory Disease	1 (6.67)		
Symptoms			
Fever	10 (66.67)	73 (73.7)	54 (34.6)
Cough	7 (46.67)	49 (49.5)	76 (48.7)
Rhinorrhea	9 (60)	4 (4.0)	
Headache	5 (33.34)	34 (34.3)	
Sore Throat	2 (13.34)	43 (43.4)	40 (25.6)
Anosmia	8 (53.34)	7 (7.1)	
Ageusia/Dysgeusia	4 (26.67)	2 (2.0)	
Diarrhea	3 (20)	3 (3.0)	14 (9.0)
Fatigue	4 (26.67)		30 (19.2)
Myalgia	4 (26.67)		
Dyspnea	1 (6.67)	1 (1.0)	1 (0.6)
Nausea	1 (6.67)		