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Relationship between clinical, laboratory, and radiological parameters with polymerase chain reaction positivity sputum in adult HIV patients with suspicion of pneumocystis jirovecii pneumonia

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Abstract: *Pneumocystis jirovecii pneumonia* (PCP) is a fungal infection of the lungs caused by P. jirovecii, usually affecting patients with Human Immunodeficiency Virus (HIV). The polymerase chain reaction (PCR) test is used in the diagnosis of PCP and has good sensitivity, but it is not available in all healthcare facilities. Clinical, laboratory, and radiological parameters can serve as alternatives to support the diagnosis of PCP in HIV patients. This study is an analytical observational study with a cross-sectional design. The assessment of clinical, laboratory, and radiological parameters of PCP patients was conducted from June to December 2024. Variables were compared using an independent t-test if normally distributed or the Mann-Whitney test if not normally distributed. Nominal variables were compared using the Chi-square test. Multivariate analysis employed logistic regression analysis. A total of 80 patients participated in the study. From the multivariate analysis, clinical parameters such as low-grade fever (PR 23.9; 95% CI 4.086-141.01; $p < 0.001$), non-productive cough (PR 7.108; 95% CI 1.25–40.1; $p = 0.027$), and oral candidiasis (PR 8.81; 95% CI 1.62–47.8; $p = 0.012$) were significant. Laboratory parameters such as lymphocyte count $\leq 1.2\times10^3/\mu L$ (PR 19.4; 95% CI 2.5–149.3; $p = 0.004$), albumin ≤ 3.1 g/dL (PR 5.59; 95% CI 1.062–29.4; $p = 0.042$), and CD4 count ≤ 200 cells/μL (PR 14.3; 95% CI 2.06–99.69; $p = 0.007$) were also significant. Typical radiological parameters (PR 20.6; 95% CI 2.9–144.2; $p = 0.02$) and atypical radiological parameters (PR 5.43; 95% CI 1.47–20.05; $p = 0.02$) showed a significant relationship with sputum PCR positivity for PCP in HIV patients. Low-grade fever, non-productive cough, oral candidiasis, lymphocyte count $\leq 1.2\times10^3/\mu L$, albumin ≤ 3.1 g/dL, CD4 count ≤ 200 cells/μL, and typical and atypical chest X-ray images are associated with sputum PCR positivity in HIV patients suspected of having PCP.

Keywords: *Human immunodeficiency virus (HIV), PCR sputum PCP, Pneumocystis jirovecii pneumonia (PCP).*

1. Introduction

Pneumocystis jirovecii pneumonia (PCP) is a fungal infection of the lungs caused by *Pnemocystis jirovecii*, usually affecting immunocompromised individual, such as Human Immunodeficiency Virus (HIV) patients. However, reports on the incidence of PCP are still very few due to difficulties in diagnosis, although this condition can be life-threatening. The prevalence of PCP was estimated 5% in HIV patients with overall mortality 3.3% [1]. Microscopic examination and smear staining to detect cysts or immunofluorescence techniques is the gold standard in PCP diagnosis, but have very low

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sensitivity and require bronchoalveolar lavage (BAL) samples to increase sensitivity. Several studies have reported that the polymerase chain reaction (PCR) test in PCP diagnosis has good overall sensitivity with samples not only from BAL, but also sputum and oral mucosa. PCR test can also detect smaller number of pathogens than standard conventional smears with high sensitivity (94%-100%) and specificity (70%-96%). Delays in the management of PCP due to late diagnosis increase the morbidity and mortality. Several alternatives such as clinical, laboratory, and radiological parameters might aid diagnosis of PCP in HIV patients. Tang [2] found that routine indicator examinations such as lymphocytes, monocytes, red blood cells, total protein, albumin were significantly lower in PCP patients compared to non-PCP, while LDH was significantly higher in PCP patients compared to patients without PCP. The combination of decreased lymphocyte cells and increased LDH was able to distinguish PCP patients compared to those without PCP with an AUC of 0.941 (95% CI 0.892-0.990).[2]

This study aims to assess the relationship between clinical, laboratory, and radiological parameters with PCR positivity in sputum in HIV patients with suspicion of PCP.

2. Methods

This study is an observational analytic study with cross-sectional design conducted at Ngoerah Hospital, Denpasar, from June 2024 to December 2024. This study evaluate the clinical (fever, cough, shortness of breath, oral candidiasis, Spo2/FiO2 ratio), laboratory (Hemoglobin, Platelet, Lymphocytes, Neutrophyl Lymphocyte Ratio, Monocyte Lymphocyte Ratio, Eosinophil, Albumin, CD4 and AaDo2), typical chest X-ray parameters (interstitial infiltrate, ground glass opacity, and atypical chest X-ray parameters (infiltrate, consolidation, pneumothorax,) of PCP patients with HIV. PCR sputum results then analysed in relation to these parameters.

2.1. Inclusion Criteria

Patients with age above 18 years, andd HIV patients with suspected PCP based on clinical, laboratory, or radiological criteria, that confirmed by tropical and infectious medicine consultant specialist or pulmonologist.

2.2. Exclusion Criteria

Having pulmonary tuberculosis disease or Incomplete medical records.

2.3. Data Analysis

Descriptive analysis presents sample characteristics using tables and narratives. Normality test analysis uses Kolmogorov-Smirnov test. Numeric variables (laboratory parameters) are compared using Independent T-test, if data was normally distributed, or Mann Whitney test if data not normally distributed. Nominal variables (clinical and radiological parameters) are compared using Chi-square test. Multivariate analysis was carried out to control confounding variables using logistic regression. The whole analysis process was using statistical software statistical package for the social sciences (SPSS) version 26.0.

3. Results

Total 192 HIV patients with suspected PCP was obtained from medical record data. Of this, 80 subjects met the inclusion criteria, 92 subjects were excluded because of pulmonary tuberculosis, and 20 subjects were excluded because of incomplete data.

In this study, the mean age of HIV subjects with positive PCR PCP was 41.46 years and negative PCR PCP was 37.7 years (Table 1). Male was found to be more common in both groups. Majority of the subjects were diagnosed with PCP for the first time in both groups as well. Meanwhile, more than half of the patients were not receiving ARV therapy either in positive PCR PCP group (84%) or negative PCR PCP group (53.3%).

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Table 1.
Study subjects' characteristics.

Characteristics	Sputum PCR		*P value*
	Positive (n = 50)	**Negative (n = 30)**	
Age (years)			
Mean ± SD	41.46 ± 10.3	37.70± 11.046	0.87
Gender			
Male	36 (72%)	22 (73.3%)	0.94
Female	14 (28%)	8 (26.7%)	
HIV diagnosis			
First time	48 (96%)	20 (66.7)	
< 5 years	2 (4%)	5 (16.7%)	0.21
≥ 5 years	0 (0%	5 (16.7%)	
ARV duration			
Not receive	42 (84%)	16 (53.3%)	0.71
< 6 months	8 (16%)	7 (23.3%)	
≥ 6 months	0 (0%)	7 (23.3%)	
PCP prophylaxis			
Yes	1 (2%)	2 (6.7%)	
No	49 (98%)	28 (93.3%)	0.28
Pneumonia			
Yes	30 (60%)	16 (53.3%)	0.56
No	20 (40%)	14 (46.7%)	

Note: SD= Standard Deviation

ROC analysis was performed to determine the cut off value of SpO2/FiO2. We found the cut off was 450 with AUC 0.692 (95%CI 0.573-0.811; p 0.004). Detailed clinical parameters with sputum PCR positivity presented in Table 3. logistic regression analysis on clinical parameters found that low-grade fever and oral candidiasis demonstrated a significant relationship with sputum PCR positivity. The risk for positive sputum PCR in subjects with low-grade fever was 23.9 times greater than those without low-grade fever. Subjects with oral candidiasis were 8.81 times at risk having positive sputum PCR result than those without oral candidiasis, and subjects with non-productive cough were at risk of having positive sputum PCR result 7.108 times greater than patients with productive cough. The Nagelkerke R Square value of 0.803 showed the ability of the total clinical parameters score to explain PCR positivity of 80.3%, meanwhile the rest (19.7%) was influenced by other factors outside the model.

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Table 3.
Relationship of of clinical parameters with sputum PCR positivity in study subjects.

Clinical parameters	Sputum PCR		Bivariate analysis		Multivariate analysis	
			p-value	PR (95%CI)	p-value	PR (95%CI)
	Positive (n = 50)	Negative (n = 30)				
Low grade fever						
Yes	44 (88%)	4 (13.3%)	< 0.001	4.88 (2.36 – 10.1)	<0.001	23,9 (4,06-141,01)
No	6 (12%)	26 (86.7%)				
Cough						
Non-productive	22 (44%)	18 (60%)	< 0.001	8.28 (2.92 – 23.48)	0.027	7,108 (1,25 – 40,1)
Productive	28 (56%)	12 (40%)				
Dyspnoea						
Yes	45 (90%)	22 (73.3%)	0.65	1.75 (0.86 – 3.54)	0.665	0.55 (0.037 – 8.26)
No	5 (10%)	8 (26.7)				
Oral candidiasis						
Yes	38 (76%)	5 (11.6%)	< 0.001	2.73 (1.69 – 4.39)	0.012	8,81 (1,62-47,8)
No	12 (24%)	25 (67.6%)				
SpO2/FiO2						
≤ 450	34 (68%)	10 (33.3%)	0.005	1.74 (1.17 – 2.59)	0.202	4.36 (0.453-42.13)
> 450	16 (32%)	20 (66.7%)				

Analysis on laboratory marker found that NLR, lymphocytes, albumin, and CD4 was found significant between positive PCR group and negative PCR group (Table 4). Variables with significant mean difference were than analysed in bivariate analysis. NLR and Albumin cut off was obtained from ROC curve, for NLR 7.175 (AUC 0.650, p <0.025); and albumin 3.1 (AUC 0.813; p <0.001); while CD4 cut off ≤200 cells/μL and lymphocytes cut off ≤1.2 x 103/μL were used (Table 5). Laboratory parameters with significant relationship (Table 5) included for multivariate analysis. Multivariate analysis on laboratory parameters demonstrated limphocytes, albumin and CD4 affected sputum PCR positivity. Subjects with albumin ≤3.10 g/dL at risk having positive sputum PCR 5.59 times greater than those with albumin >3.10. Subjects with CD4 ≤200 cells/μL at risk having positive sputum PCR 14.3 times greater than those with CD4 > 200. Subjects with lymphocytes ≤ $1.2x10^3$μ/L at risk having positive sputum PCR 19.4 times greater than those with albumin >3.10. The Nagelkerke R Square value of 0.759 showed the ability of independent variables to explain the dependent variable by 75.9%, the rest (24.1%) influenced other factors outside the model.

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Table 4.
Differences in laboratory parameters with sputum PCR positivity in study subjects.

	Sputum PCR		p-value
	Positive (n = 50)	**Negative (n = 30)**	
Haemoglobin (g/dL)			
Mean± SD	11.49 ± 2.156	11.49 ± 3.082	0.990
Platelet (10^3/µL)			
Mean± SD	294.13 ± 134.946	283.67 ± 131.565	0.736
Lymphocytes(10^3/µL)			
Median (min -max)	0.78 (0.17-1.65)	1.65 (0.60-5.32)	< 0.001
NLR			
Median (min – max)	8.53 (0.91 – 127.65)	5.36 (0.71 – 40.43)	0.025
MLR			
Median (min – max)	0.575 (0.03 – 3.35)	0.550 (0.05 – 2.37)	0.929
Eosinofil (10^3/µL)			
Median (min – max)	0.02 (0 – 0.4)	0.06 (0 – 0.62)	0.086
Albumin			
Mean± SD	2.87 ± 0.456	3.48 ± 0.570	< 0.001
CD4			
Median (min – max)	18.5 (1 – 218)	266.5 (85– 1131)	< 0.001
CD8			
Median (min – max)	327.5 (56 – 2486)	400(47 – 1857)	0.773
AaDo2			
Median (min – max)	37.6 (3.7 – 156.8)	31.6 (11 – 165)	0.243

Table 5.
Relationship of laboratory parameters with sputum PCR positivity in study subjects.

Laboratory parameters	**Sputum PCR**		**Bivariate analysis**		**Multivariate analysis**	
			p-value	**PR (95%CI)**	**p-value**	**PR (95%CI)**
	Positive (n = 50)	**Negative (n = 30)**				
Lymphocytes					0.004	19.4 (2.5 - 149,3)
≤ 1.2 x10^3/µL	43 (86%)	5 (16.7%)	< 0.001	4.09 (2.11 -7. 93)		
> 1.2 x10^3/µL	7 (14%)	25 (83.3%)				
NLR						
≥ 7.175	20 (40%)	18 (60%)	0.107	0.737 (0.516 – 1.053)	0.94	22.4 (0.42 - 19.48)
< 7.175	30 (60%)	12 (40%)				
Albumin					0.042	5,59 (1,062 –29,4)
≤ 3.1 g/dL	48 (96%)	11 (18.6%)	< 0.001	8.542 (2.27 – 32.103)		
> 3.1 g/dL	2 (4%)	19 (63.3%)				
CD4					0.007	14,3 (2.06 – 99.69)
≤ 200 cells/µL	48 (96%)	20 (66.7%)	< 0.001	4.235 (1.184 – 15.148)		
> 200 cells /µL	2 (4%)	10 (33.3%)				

Analysis on radiology parameters demonstrated that typical radiological group, subjects were at risk of having positive sputum PCR results 20.6 times greater than those with normal radiology, while subjects with atypical radiological results were at risk of having positive sputum PCR results 5.43 times greater than those with normal radiology. The Nagelkerke R Square value of 0.39 indicates the ability of independent variables to explain the dependent variable by 39%, the rest (71%) is influenced by other factors outside the model.

4. Discussion

The mean age of patients with positive sputum PCR in this study was 41.46 ± 10.3 years. Male predominance was found in both groups (positive and negative PCR results). These results are in line

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with previous study by Yustin, et al. [3] where the mean age of HIV patients was 36.79 ± 10.45 with male predominance as well. Majority of the subjects suspected with PCP were first diagnosed with HIV. This might occur because most subjects only seek for medical attention after having PCP symptoms such as shortness of breath and worsening cough to the point of disrupting their activities. Therefore, majority of the subjects also had not received ARV therapy and PCP prophylaxis. HIV patients have a higher prevalence of PCP colonization than immunocompetent individuals (68% vs. 24%). In addition, PCP colonization rate will increase in HIV patients with CD4 ≤ 50/μL, and have not received prophylaxis [4].

Positive sputum PCR was found higher in HIV subjects with pneumonia in this study. Clinical characteristics of PCP in HIV patients includes fever, shortness of breath, and non-productive cough. Symptoms become progressive 3-4 weeks before hospitalization [5]. On physical examination, PCP patients classically have tachypnea, tachycardia, and abnormalities on lung auscultation. Weight loss, recurrent bacterial pneumonia, and oral thrush are also common findings [6]. This is supported by a study in three government hospitals in Jakarta that found all PCP patients had clinical manifestation of fever, cough, shortness of breath, rhonchi, and weight loss [7]. A systematic review and meta-analysis by Wills, et al. [8] reported HIV patients with PCP have interstitial infiltrates (59%; 95% CI, 52%–66%; 36 studies, n = 1380; I2 = 85%) and GGO pattern (48%; 95% CI, 15%–83%; 4 studies, n= 57; I2= 86%) on chest x-ray examination.

Based on laboratory parameters characteristic, similar results are reported in previous studies Yustin, et al. [3] and Mulyani, et al. [9]. HIV infection is characterized by a decrease of CD4 T cells, an increase in CD8 T cells, and chronic immune activation that causes immune dysfunction [10]. In this study, hypoalbuminemia (3.41 g/dL) was reported. Tang [2] found serum albumin level differences in PCP patients undergoing immunosuppressive therapy compared to controls. PCP patients had lower albumin than patients with immunosuppressive therapy without PCP (2.87 g/dL versus 3.69 g/dL; P <0.001).

In this study, majority (63.8%) of subjects had atypical chest X-ray (infiltrates and consolidation). This is also in accordance with literature. Radiological findings commonly reported are diffuse and homogeneous bilateral interstitial patterns. Other features that can be found are cystic lesions, central lymphadenopathy, spontaneous pneumothorax, and although rare, pleural effusion. Normal chest X-ray reported in one third cases of PCP [5, 8].

This study found a significant relationship between low grade fever, non-productive cough and oral candidiasis with sputum PCR positivity in HIV patients with suspicion of PCP after other independent variables were controlled. Subjects with low grade fever were at risk of having positive sputum PCR result 23.9 times greater than those without low grade fever (95% CI 4.06 - 141; p< 0.001); meanwhile subjects with non-productive cough have 7.108 times greater risk than patients with productive cough (95% CI 1.25 - 40.19; p= 0.027). This is in line with the study by Siegel, et al. [11] which demonstrated HIV patients infected with PCP are likely to experience slower and less obvious symptoms such as mild fever (>80%), and non-productive cough and dry cough (95%) for several weeks [11]. Patients are likely to experience fever, often no higher than 38.1^{0}C [12]. Oral candidiasis is a common co-infection found in HIV patients with PCP. Oral candidiasis and hairy leucoplakia are highly predictive in patients with CD4 values <200. In this study, subjects with oral candidiasis at 8.81 times greater risk having positive sputum PCR result than group without oral candidiasis (95% CI 1.62 - 47.8; p= 0.012). Oral candidiasis was found in 4.2% HIV and 11.6% in AIDS patients. $CD4^{+}$ plays a role in immunity related to Candida infection, via induction of B lymphocyte IgA secretion and activation of Th17 cells, low CD4 levels interfere with this defense mechanism [13]. Oral candidiasis has been reported associated with an increased likelihood of PCP compared to tuberculosis or bacterial pneumonia in HIV patients.[12] PCP symptoms were varied in each individual and 7% were asymptomatic [14].

This study found no significant relationship between shortness of breath (dyspnea) symptoms and SpO2/FiO2 ratio with sputum PCR positivity. This result may be due to early phase of the disease and/or different individual perceptions of dyspnea. This symptom may not reported in early phase of

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PCP infection, low fungal load values may be found in early phase of disease, especially in HIV patients, thus symptoms develop in the following weeks [15]. The SpO2/FiO2 ratio is an alternative to alveolar-arterial oxygen gradient (AaDO2) parameter. It is a well-known parameter to help increased suspicion of PCP [16, 17]. The SpO2/FiO2 ratio does not require invasive procedure [18]. Clinical studies consistently demonstrated hypoxia and inflammatory or tissue injury markers are associated with poor outcomes in PCP patients [8]. Prognostic implications of the SpO2/Fio2 in pneumonia patients including PCP found that SpO2/Fio2 <236 had a higher risk of mortality compared to control (p = 0.002), in this study although SpO2/FiO2 was found significant on bivariate analysis but not in multivariate analysis, this could be caused by decrease SpO2/FiO2 not only caused by PCP but also in pneumonia [19].

Anemia and thrombocytopenia in HIV patients occur due to hematopoietic process disorders. Thrombocytopenia is caused by decreased platelet survival or ineffective production of platelets and their precursors [20]. Use of myelosuppressive drugs such as zidovudine can decreased haemoglobin levels in HIV patients [21]. This study found no significant difference of both parameters. Variations in subjects, majority of whom were patients newly diagnosed with HIV and had not received ARV may explain the results.

There was a significant difference in the mean albumin levels between subjects with positive and negative sputum PCR results ($p < 0.05$) in this study. Subjects with albumin ≤3.10 were at risk of having positive sputum PCR result 35.3 times greater than those with albumin >3.10. Tang [2] also found serum albumin levels differences in PCP patients undergoing immunosuppressive therapy compared to controls. Patients with PCP had lower serum albumin levels than patients with immunosuppressive therapy without PCP (2.87 g/dL versus 3.69 g/dL; $P < 0.001$) [2]. Depletion of B lymphocytes and CD4 T cells in mice with Pneumocystis infection, induce strong Th1 inflammatory response, associated with edema and albumin release in the alveoli [22]. In inflammatory conditions, there is an increase of albumin breakdown. Combination of inflammatory responses and increased albumin release through capillaries also causes hypoalbuminemia [23].

This study found no relationship between NLR levels and sputum PCR positivity in HIV patients with suspicion of PCP (PR 0.737, 95% IK 0.516 - 1.053; p value = 0.107). non significant relationship could be caused by neutrophil decrease early in HIV infection but will increase as the infection progresses. Chemotactic agents will attract neutrophils to infected area to kill and phagocytose microorganisms during infection. HIV patients who experience neutrophil dysfunction will be more susceptible to bacterial infections [21]. MLR is often used as an indicator of inflammation. Monocyte count is influenced by GM-CSF which is a hematopoietic growth factor. GM-CSF causes an increase in the number of serum monocytes and PMNs, which are useful in immunity when lung infections occur [24].

There was no significant difference of MLR, between HIV subjects with positive and negative sputum PCR results in this study. However, MLR values in both groups were higher than normal. In HIV patients, there is a disturbance in monocyte activity. When compared with healthy individuals, HIV patients reported have an increase in overall number of monocytes. HIV virus replication, microbial translocation, and co-infection with infectious pathogens can activate monocytes during HIV infection [25].

HIV infection can also cause eosinophilic inflammation. In PCP infection, immune response to beta-D-glucan may be involved in the mechanism of eosinophilia in the lungs [26]. However, this study found no significant difference in eosinophil values between positive and negative PCR results. This result may be because, eosinophils are not the main cells involved in immune response to PCP.

CD4 count is used to assess immunological status at the time of HIV diagnosis [27]. We reported a significant difference and relationship between CD4 values with positive sputum PCR results ($p<0.05$). Progressive CD4 T cells decline is associated with HIV progression, opportunistic infections, and mortality. Increased risk of opportunistic infections in HIV patients is known to occur when CD4 cells fall below 200 cells/mm^3 [28]. Subjects with CD4 ≤200 cells/mm^3 had 12.29 times greater risk of

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having positive sputum PCR results in our study. Previous study have shown that initial CD4 count was significantly lower in PCP patients (14 vs 24 cells/μL; $p < 0.001$) and decreased with increasing severity of PCP [29].

In PCP infection, there is a significant increase in CD8 T cells number in the lungs, especially when there is significant CD4 T cell depletion. In the absence of $CD4^+$ T cells, $CD8^+$ T cells will eliminates Pneumocystis and formed secondary defense against fungi. In PCP, a large number of $CD8^+$ T cells are recruited to the lungs. Elimination of PCP agents by $CD8^+$ T cells facilitated by cytokines such as TNF-α, TNF-β or IFN-γ. Low numbers of $CD8^+$ T cells in peripheral blood are associated with poor prognosis in non-HIV PCP patients with respiratory failure [30, 31]. In this study, there was no significant difference in CD8 values between groups with positive and negative PCP sputum PCR results. However, patients with positive PCP sputum PCR had lower CD8 values (327.5 vs. 400 cells/μL).

Hypoxemia is one of the criteria for PCP diagnosis and its mortality. In severe pulmonary inflammation, impaired gas exchange will cause hypoxia and decreased lung compliance [7]. In this study, there was no significant difference of AaDo2 values between groups. However, the HIV group with positive sputum PCR had a higher median AaDo2 value (37.6 vs. 31.6). This was also found in a study by Li, et al. [31] where PCP patients had higher AaDo2 values (264.8 mmHg vs. 67.7 mmHg). Furthermore, PCP-related mortality was also associated with PaO2/FiO2 ratio <160 mmHg [31]. Possible reason for our finding may be due to the increase in AaDo2 not only happens in PCP patients but also in other conditions. An increase in the AaDO2 gradient can be caused by diseased that caused increased dead space ventilation, left to right shunt, and perfusion without alveolar ventilation [32].

Chest X-ray of PCP patients can be characterized as diffuse, bilateral peri-hilar interstitial infiltrates and become more homogeneous as disease progression. Other finding such as GGO with perihilar predominance, is an atypical image [33]. This study found a significant relationship between chest X-ray results with sputum PCR positivity in HIV subjects with suspicion of PCP ($p= 0.003$). Subjects with typical radiological results were at risk of having positive sputum PCR results 19.7 times greater than those with normal radiology, while subjects with atypical radiological results were at risk of having positive sputum PCR results 4.87 times greater than those with normal radiology. These results are supported by various studies that found atypical images on chest X-rays of HIV patients with PCP [8, 34].

To the best of our knowledge, this study, it is the first study in Indonesia that evaluates the relationship between clinical, laboratory and radiological symptoms with PCP sputum PCR positivity in HIV patients with suspicion of PCP.

4.1. Limitations

This study has several limitations. First, majority of the subjects were newly diagnosed as HIV; second, laboratory parameters, which is significant for PCP such as LDH, not included in this study; and lastly, this study did not take into account the onset of symptoms the subject had experienced until seeking medical attention.

5. Conclusion

In this study, clinical parameters (low grade fever, non-productive cough, and oral candidiasis), laboratory parameters (lymphocytes $\leq 1.2 \times 10^3$ μ/L, albumin ≤3.1 g/dL, CD4 ≤200 cell/μL), and radiological parameters (typical and atypical chest X-ray images) are related to sputum PCR positivity in HIV patients with suspicion of PCP. This finding could be used for physician for establishing a more systematic PCP diagnosis in HIV patient with suspicion of PCP.

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Transparency:

The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

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Table 2.
Clinical manifestation, laboratory, and radiological parameters.

	N (%)
	Mean ± SD
Clinical manifestation	
Dyspnoea	67 (83.8%)
Oral candidiasis	43 (53.8%)
Non-productive cough	40 (50%)
Low grade fever	47 (40%)
SpO2/FiO2	354.8 ± 14.248
Laboratory	
Haemoglobin (g/dL)	11,49 ± 0,28
Platelet (10^3/µL)	290,2 ± 14,86
WBC (10^3/µL)	8.6 ± 4.5
Lymphocyte(10^3/µL)	1.2 ± 0.89
NLR	12,7 ± 1,95
MLR	0.79 ± 0.07
Albumin (g/dL)	3.41 ± 0.31
Eosinophil (10^3/µL)	0.083 ± 0.012
CD4 (cells/µL)	149.36 ± 21.3
CD8 (cells/µL)	565.11 ± 57.54
AaDo2	48.43 ± 4.34
Radiological	
Typical(ground glass opacity, interstitial infiltrates, reticulogranular)	13 (16.3%)
Atypical (infiltrates, consolidation)	53 (66.3%)
Normal	14 (17.5%)

Note: NLR=Neutrophil lymphocyte ratio); MLR=Monocytes Lymphocyte Ratio).

Table 6.
Relationship of chest X-ray results with sputum PCR positivity in study subjects.

Radiological	**Sputum PCR**		**Bivariate analysis**		**Multivariate analysis**	
			p-value	**PR (95%CI)**	**p-value**	**PR (95%CI)**
	Positive (n = 50)	**Negative (n = 30)**				
Atypical	36 (72%)	17 (56.7%)	0.02	5.21 (1.29-21)	0.02	5.43 (1.47 - 20.05)
Typical	10 (20%)	3 (10%)	0.05	15. (2.28-109.2)	0.01	20.6(2.9 – 144.2)

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