

https://dspace.org/

The use of a quantitative assay to differentiate between Pneumocystis jirovecii colonisation and disease among hospitalised patients, South Africa 2015-2016

Yun, Jessica Ann Lai

2021

https://hdl.handle.net/10539/32171

Downloaded from a DSpace repository. https://dspace.org/

The use of a quantitative assay to differentiate between *Pneumocystis jirovecii* colonisation and disease among hospitalised patients, South Africa 2015-2016

Abstract

Background: *Pneumocystis jirovecii* pneumonia (PJP) is responsible for infant and adult mortality predominantly among those who are immunocompromised. Due to the use of quantitative real-time polymerase chain reaction (qPCR) yielding a high sensitivity, distinguishing between *P. jirovecii* colonisation and active clinical disease is challenging because *P. jirovecii* DNA is detected regardless of its association with illness. By establishing *P. jirovecii* qPCR DNA load cut-off value using beta-D-glucan (BDG) levels a biomarker of fungal infection, *P. jirovecii* colonisation and disease could be differentiated. This could prompt healthcare providers to initiate treatment in a timely manner as well as to assess the "true" prevalence of PJP.

Aim: *To establish P. jirovecii* qPCR DNA load cut-off value for the differentiation between *P. jirovecii* colonisation and disease among hospitalised patients admitted for severe respiratory illness in South Africa, using BDG level as a biomarker of fungal infection.

Methodology: The study was a cross-sectional study design utilizing secondary data. Study population included hospitalised patients enrolled in the pneumonia surveillance programme from two of the five participating sentinel sites (KwaZulu-Natal and North West provinces) from 2015-2016. A univariable and multivariable random effect (on surveillance hospital) logistic regression was used to evaluate the demographic and clinical factors associated with patients with and without available BDG level results. To determine the optimal *P. jirovecii* DNA load cut-off value of the qPCR, using the BDG as the gold standard for fungal infection, a receiver operating characteristic (ROC) analysis was conducted. Descriptive analysis to describe the demographic, clinical and epidemiological characteristics of those who were *P. jirovecii* diseased, colonised and negative was conducted.

Results: The total study population was 1542 patients enrolled in the pneumonia surveillance programme who had sputum samples tested for *P. jirovecii* and had available qPCR results. HIV was the most prevalent underlying condition with 70.43% (131/186) of patients living with HIV had BDG results as compared to those without BDG results (51.48%, 680/1321). A qPCR load cut-off value of 550 copies/5 µL was established which correctly classified 75% of patients with PJP. This yielded a high specificity of 91.67% and a moderate sensitivity of

57.14%, respectively. The positive and negative predictive values were 100.0% and 81.6%, respectively. Overall, the PJP prevalence was 5.12% and the prevalence of *P. jirovecii* colonisation was 11.28% from 2015 to 2016. On multivariable analysis adjusting for surveillance hospital clustering, patients who were infected with *P. jirovecii* compared to those who were colonised with *P. jirovecii* were more likely to be female (Adjusted relative risk ratio (aRRR) 1.91; 95% CI:1.04-3.49; p=0.04), to be living with HIV (aRRR 4.30; 95% CI:1.82-10.16; p<0.01) and receive cotrimoxazole at time of hospital admission (aRRR 5.19; 95% CI:2.24-12.06; p<0.001). Interestingly, patients who were negative for *P. jirovecii* compared to those who were colonised with *P. jirovecii* were more likely to present with fever (aRRR, 1.44; 95% CI:1.01-2.05; p=0.04). Furthermore, patients infected with *P. jirovecii* compared to those who were colonised with *P. jirovecii* were at an increased risk of in-hospital death (aRRR 2.63; 95% CI:0.98-7.05; p=0.05); therefore, indicating the severity of PJP.

Conclusions & recommendation: The cut-off value cannot be universally applied but rather it may only be used in pilot studies with a similar population that consists of adults who are living with HIV. Irrespective of not establishing a true gold standard for diagnostic tests to diagnose PJP, the established cut-off value could be used in conjunction with clinical presentation as well as to ruling in patients who have PJP (ruling diagnoses). Although the PCR assays are considered to yield a higher sensitivity, more intensive specimen collection is needed to estimate the true burden of PJP in South Africa.