Diagnostic Utility of Blood (1- >3)-β-D-Glucan Testing in Patients with HIV in Arkansas

Gayathri Krishnan, MD; Lana S Hasan, MD; Michael Saccente, MD

Department of Internal Medicine

University of Arkansas for Medical Sciences, Little Rock, Arkansas

BACKGROUND

- Blood (1- > 3)-β-D-Glucan (BDG) is a sensitive marker for *Pneumocystis jirovecii* pneumonia (PJP) in patients with AIDS (PWA).
- However, other fungal infections, including progressive disseminated histoplasmosis (PDH), cause high levels of BDG.
- At our hospital, PDH is a common diagnosis in PWA with fever and respiratory complaints, making it difficult to differentiate PJP from PDH based on clinical features alone.
- The objective of this study was to assess BDG as a diagnostic test for PJP in Arkansas where histoplasmosis is endemic.

METHODS

- We performed a retrospective review of patients with confirmed PJP and confirmed PDH who had BDG testing between January 1, 2014 and December 31, 2019.
- Positive cytological or histological evidence of *P. jirovecii* in bronchoalveolar lavage (BAL) or lung biopsy, or positive PCR on sputum or BAL confirmed PJP.
- Identification of *Histoplasma capsulatum* in culture of blood or other normally sterile site, histology showing typical yeast forms, or a positive urine *H. capsulatum* antigen assay (MiraVista Diagnostics) confirmed PDH.
- The Fungitell Assay (Associates of Cape Cod) determined BDG levels as follows: negative,< 60 pg/mL; indeterminate, 60-79 pg/mL, and positive ≥ 80 pg/mL. Values below 31 pg/mL and those above 500 pg/mL were censored at 30 and 500, respectively
- Respiratory symptoms were defined as the presence of cough, shortness of breath, or dyspnea on exertion.

RESULTS

- 53 episodes of PDH occurred in 46 patients. 42 were accompanied by a BDG result. Of these, 38 (90%) were positive; 3 (7%) were negative; and 1 (2%) was indeterminate.
- 44 (83%) of the PDH episodes were associated with respiratory symptoms. 36 of these had a BDG result. 34 (94%) were positive; 1 (3%) was negative; and 1 (3%) was indeterminate.
- 44 episodes of PJP occurred in 40 patients. All had a BDG result. 43 (98%) were positive.
- Concomitant opportunistic infections were diagnosed during 10 (23%) of 44 episodes of PJP, including 6 episodes of concomitant PDH.
- The mean BDG level was significantly higher in the PJP group compared to those with PDH and respiratory symptoms (P=.002).
- However, values overlapped substantially, and BDG positivity was not significantly more frequent in the PJP group (P=.586).

Results of (1->3)-β-D-Glucan Testing by Diagnosis

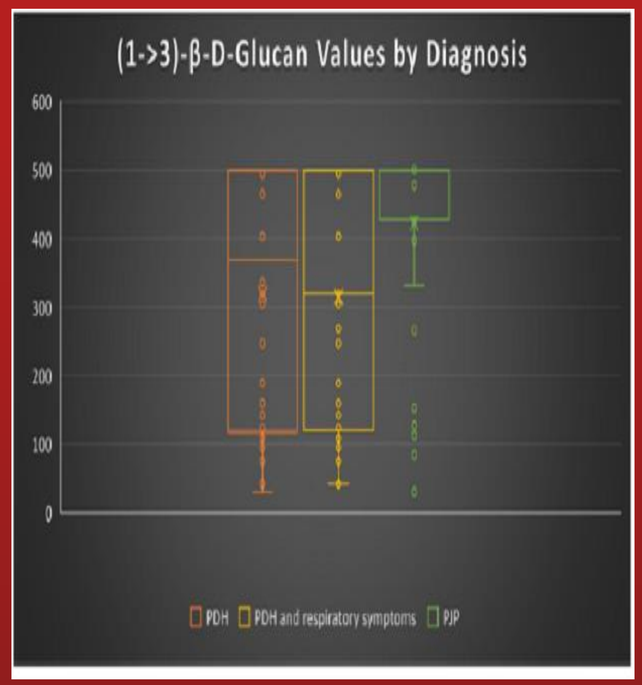
BDG level (pg/mL)	PDH (N=42)	PDH and respiratory symptoms (N=36)	PJP (N=44)	P*
Mean (SD)	322.5 (185.3)	315.6 (184.5)	422.5 (146.5)	0.002[a]
Min, max	30, 500	30, 500	30, 500	
Median (Q1-Q3)	369.5 (122-500)	320 (120-500)	500 (427-500)	
Negative <60	3 (7%)	1 (3%)	1 (2%)	0.586[b]
Indeterminate 60-79	1 (2%)	1 (3%)	-	
Positive ≥80	38 (90%)	34 (94%)	43 (98%)	

Note: BDG, (1-> 3)-β-D-Glucan; PDH, progressive disseminated histoplasmosis; PJP, *Pneumocystis jirovecii* pneumonia; SD, standard deviation; Q1, first quartile; Q3, third quartile

*Comparing PDH and respiratory symptoms to PJP

[a] Student's t-test

[b] Fisher's exact test (for calculation, indeterminate values were classified as negative)



CONCLUSIONS

- BDG is a highly sensitive marker both for PJP, and for PDH, including a subset of subjects with PDH and respiratory symptoms.
- In Arkansas and perhaps in other regions where histoplasmosis is endemic, BDG positivity is not a reliable marker of PJP because it cannot distinguish between PJP and PDH.
- In this setting, attributing an elevated BDG to PJP without additional evaluation (i.e. diagnostic bronchoscopy) risks misdiagnosis.

REFERENCES

- Sax PE, Komarow L, Finkelman MA, Grant PM, Andersen J, Scully E, Powderly WG, Zolopa AR; AIDS Clinical Trials Group Study A5164 Team. Blood (1->3)-beta-D-glucan as a diagnostic test for HIV-related Pneumocystis jirovecii pneumonia. Clin Infect Dis. 2011 Jul 15;53(2):197-202. doi: 10.1093/cid/cir335. PMID: 21690628; PMCID: PMC3165964.
- Wood BR, Komarow L, Zolopa AR, Finkelman MA, Powderly WG, Sax PE. Test performance of blood beta-glucan for Pneumocystis jirovecii pneumonia in patients with AIDS and respiratory symptoms. *AIDS*. 2013;27(6):967-972. doi:10.1097/QAD.0b013e32835cb646
- Corsi-Vasquez G, Ostrosky-Zeichner L, Pilkington EF 3rd, Sax PE. Point-Counterpoint: Should Serum β-d-Glucan Testing Be Used for the Diagnosis of Pneumocystis jirovecii Pneumonia?. *J Clin Microbiol*. 2019;58(1):e01340-19. Published 2019 Dec 23. doi:10.1128/JCM.01340-19

Contact gayathrik@wustl.edu or saccentemichael@uams.edu with further questions