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Original Research

Bayesian evaluation of two conventional diagnostic methods for pathogenic fungal infections

Mahesh C. Sahu [a,c], Rabindra N. Padhy [b,*]

[a] *Microbiology Department, IMS and Sum Hospital, Siksha 'O' Anusandhan University, Kalinga Nagar, Bhubaneswar, Odisha, India*
[b] *Central Research Laboratory, IMS and Sum Hospital, Siksha 'O' Anusandhan University, Kalinga Nagar, Bhubaneswar, Odisha, India*
[c] *Department of Botany, B.J.B. Autonomous college, Bhubaneswar 751014, Odisha, India*

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Abstract

Background/Aims: To evaluate two pathogenic fungal diagnostic methods, the staining and the culture tests with Bayes rule, for quantifying errors in each method.
Methods: With 10% potassium hydroxide (KOH) mounting for soft tissues and 20% KOH mounting for hard tissues and with lactophenol cotton blue (LCB), a staining test with microscopy was done for 1310 samples. Each sample was cultured in Sabouraud dextrose agar (SDA) and potato dextrose agar (PDA); tubes were incubated at room temperature, 25°C, and 37°C for growth.
Results: There were 365 true positive (TP), 42 false positive (FP), 815 true negative (TN) and 88 false negative (FN) cases. The *a priori probability* value of infections was 0.3458 in the population, the *sensitivity* value was 0.8057, and the *specificity* value was 0.9510. The FP rate was 0.0490, the *FN rate* was 0.1943, and the *positive predictivity* and the *negative predictivity* values were 0.8968 and 0.9025, respectively. The computed value of *a posteriori probability* or post-test arithmetic computation for diagnostic efficiency was 0.5617. The area under the receiver operating curve (ROC) characteristic was 0.72.
Conclusion: The staining test was efficient by 34–89% in arriving at a positive result with a sample, when its culture test was positive; alternately, it was efficient by 90–95% for a negative result, when its culture test result was negative. Both staining and culture test results were dependable by 56–72% for prognosis.

Keywords: Bayes rule; fungal diagnostic test results; receiver operating characteristic curve; sensitivity; specificity

1. Introduction

Immunodeficiency and hyperglycemic conditions have been considered as root causes of aggressive/invasive fungal infections; nevertheless, diabetes mellitus type 2 has predisposing factors for the initiation of nonsystemic fungal infections. The most dominating fungal species are *Candida* and *Aspergillus*; for example, in a study, 50% patients were diagnosed with candidiasis.[1] Indeed, *Candida albicans* was originally a harmless colonizer in healthy persons, but its aggressive strains could cause superficial to life-threatening systemic infections. In the past few decades, overuse and inappropriate prescription of antifungal agents have contributed to the emergence of antifungal resistance, which slowly causes potentially grievous, uncontrollable systemic infections.[2]

The prognosis of fungal infections involves two basic procedures: (1) direct microscopy with 10/20% potassium hydroxide (KOH)-treated excised tissue/concentrated clinical samples stained with lactophenol cotton blue (LCB) for a wet mount, called the 'staining test'[3]; and (2) fungal culture on

* Corresponding author. Central Research Laboratory, IMS and Sum Hospital, Siksha 'O' Anusandhan University, Kalinga Nagar, Bhubaneswar 751003, Odisha, India.
E-mail addresses: rnpadhy54@yahoo.com, rnpadhy54@gmail.com (R.N. Padhy).

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Sabouraud dextrose agar (SDA) and potato dextrose agar (PDA) media, called the "culture test". The inherent difficulty of the staining test is that an insufficient amount of hyphae or fungal spores in a clinical sample would land at "staining-negativity and culture-positivity", known as *false negative* (FN) cases. By contrast, clinical samples with dead hyphae from patients with ongoing antifungal treatment indicate "staining-positivity and culture-negativity", which are referred to as *false positive* (FP) cases. These two types of situations cause loss of confidence in *true positive* (TP) cases, with positive results of both methods, and true negative (TN) cases, with negative results of both methods. The results of the staining procedure are instantly available, but it takes 3–7 days for the culture test results. Eventually, the staining test is sought after for the start of empiric antifungal treatment.

This paper evaluates data from 1310 clinical samples to resolve the bivalence of both prognostic methods in an attempt to digitalize the pervasive errors in each method, using the Bayes rule. This analysis would help a clinician in assessing errors of occurrence of FN and FP cases in the systemic fungal infections that could prevent or allow starting antifungal treatment. Clearly, FN cases would not be treated ordinarily, whereas FP cases would be unnecessarily treated for long durations, considering the chronicity of the fungal infections. Untreated FN cases would cause the stability of the infection, whereas treatment of FP cases would result in systemic side effects.

2. The Bayesian concept

During prognosis, a clinician becomes eager to know how many staining and culture test results are dependable. The Bayesian concept would be appropriate in digitally resolving the pervasive errors in results of clinical samples in staining and culture tests. Customarily, the culture test is regarded as the "gold standard", i.e., ideal, with which the second, i.e., the staining test, is to be compared. Thus, the staining test is to be accessed using the Bayesian concept. However as noted, the culture test also has a degree of fallibility of "staining positivity and culture negativity" with dead hyphae/spores. Obviously, both tests are independent by themselves, but remain critical in examining the status of the staining test. Thus, with prudence, the Bayesian analysis of recorded data as evidence could measure the degree of belief/assumption for what percent of the culture test could be taken as of the gold standard, and also, how dependable the staining test would be numerically. To evaluate the inherent probability of each, the prior probability (*a priori probability* or *prevalence,* or the prevalence of infection in the targeted population, the total number of samples) is determined prior to using data, prevalence = [(TP + FN)/*N*], with $N =$ number of total samples. Further, there are two essentially associated test statistics: the *sensitivity* (*TP rate*) − this is the portion of people with the infection, who will have positive staining test results, computed by [TP/(TP + FN)], and the *specificity* (*TN rate*) − this is the portion of people without the infection, who will have negative staining test results, computed by [TN/(FP + TN)]; these two test statistics are the basis of Bayesian analysis.[4,5]

Several other associated test statistics are computed. These include: the FP rate, which is the probability of errors of the culture test, computed by [FP/(FP + TN)]; the *FN rate,* the probability of errors of the staining test, computed by FN/(TP + FN); the *positive predictivity,* the post-test probability of the infection that gives a positive test result or the portion of people with positive test results, who actually have a fungal infection, computed by [TP/(TP + FP)], which would predict positivity by the staining test; the negative predictivity, the post-test probability of the infection that gives a negative test result, or the portion of people with negative test results, who actually do not have the infection, computed by [TN/(FN + TN)], which would predict negativity by the staining test; the *diagnostic accuracy* (*inherent validity* or *predictive validity*), which is the ability of the staining test to be correctly positive or negative, among binary results of the culture test, computed by [(TP + TN)/N]; the *positive likelihood ratio* (LR), the ratio between the TP rate and FP rate, computed by [*sensitivity*/(1-*specificity*)], when the staining test result is positive; and the *negative* LR, the ratio between the FN rate and TN rate, computed by [(1-*sensitivity*)/*specificity*], when the staining test result is negative. Indeed, the larger the *positive* LR value the greater would be the likelihood of infection, and similarly, the lesser the *negative* LR value the lesser would be the likelihood of infection, in a population.

In addition, *a posteriori probability* is the value from post-test arithmetic computation of the data for diagnostic efficiency and it specifically analyzes how good (numerically) each test is in independently arriving at the truth, which is the desired conclusion from the tests. At length, the area under the *receiver operating characteristic* (ROC) curve, drawn with values of *sensitivity* and *specificity,* as a graphical analysis for diagnostic efficiency, additionally examines the predictive capability as another value of *a posteriori probability,* independent of the arithmetic computation. Thus with a double-check, post-test analysis of the data can be done for numerical assessments with two values of *a posteriori probability.* Moreover, additional values of associated test statistics generated in the Bayesian analysis clump around the data-set facilitating a holistic or rather a multiple evaluation of the ambivalence. Thus, this analysis would provide a methodological framework of qualitative assessment of two test results of diagnosis of a fungal infection.

3. Materials and methods

A prospective cross-sectional study was undertaken over a period of 5 years, from January 2009 in the Department of Microbiology of IMS and Sum Hospital. Clinical samples from patients attending the outpatient department, designated as community acquired (CA), and from inpatients, designated as hospital acquired (HA), such as skin swabs and skin scrapings, wound swabs, nail cuttings, blood, urine, vaginal swabs, surgical wound abscesses, hair from scalp, etc., were tested for fungal infections. Samples taken from patients suspected as having fungal infections attending the outpatient department were categorized as CA samples, whereas samples