Fever and Human Immunodeficiency Virus Infection as Sentinels for Emerging Mycobacterial and Fungal Bloodstream Infections in Hospitalized Patients ≥15 Years Old, Bangkok

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To determine the etiology of bloodstream infections (BSIs) in hospitalized patients ≥15 years old in Thailand, prospectively enrolled, consecutive febrile (≥38°C) patients were admitted to one hospital during February–April 1997. After a patient history was taken and a physical examination was performed, blood was obtained for comprehensive culture and human immunodeficiency virus (HIV) testing. Of 246 study patients, 119 (48%) had BSIs, and 182 (74%) were infected with HIV. The 2 most common pathogens were Cryptococcus neoformans and Mycobacterium tuberculosis (30 and 27 patients, respectively). HIV-positive patients were more likely to be HIV-negative patients to have mycobacteremia (57/182 vs. 0/64, P < .0001), fungemia (38/182 vs. 2/64, P < .001), or polymicrobial BSIs (19/182 vs. 0/64, P < .002). Clinical predictors of BSIs included HIV infection, chronic diarrhea, lymphadenopathy, or splenomegaly. Mortality was higher among patients with than those without BSIs (P < .001). Cohort-based microbiologic studies are critically important to diagnose emerging pathogens and to develop algorithms for empirical treatment of BSIs in developing countries.

The etiology of bloodstream infections (BSIs) in febrile hospitalized adult (≥15 years old) patients in Southeast Asia remains unclear. In Thailand, the incidence and prevalence rates of Cryptococcus neoformans, Mycobacterium tuberculosis, and Mycobacterium avium complex BSIs remain largely unknown because there have been no prospective studies (using comprehensive microbiologic techniques) of BSIs in a febrile hospitalized adult population. The emergence of M. tuberculosis as a cause of fever and BSIs in patients infected with the human immunodeficiency virus (HIV) is an important issue to assess in view of recent published reports that M. tuberculosis has now become a predominant cause of BSIs in adult febrile HIV-infected populations in Tanzania and Brazil [1, 2]. Data from such studies are necessary to make decisions regarding directed empirical and prophylactic therapy for BSIs, particularly in countries with limited resources. Unpublished studies of BSIs in Thailand to date have been retrospective, used limited microbiologic techniques, and identified non–typhi Salmonella species and Streptococcus pneumoniae as the predominant organisms causing BSIs in febrile hospitalized adults.

Therefore, we initiated a study at a hospital in Bangkok to determine the incidence of BSIs in a cohort of febrile hospitalized patients ≥15 years old and to ascertain clinical predictors and risk factors for BSIs in this cohort, evaluate the association between HIV infection and acquisition of BSIs, and determine the clinical outcome of hospitalized patients with BSIs.

Methods

Patients. Bamrasnaradura Hospital, a 500-bed facility located in northern Bangkok, is one of the largest infectious diseases hospitals in the region and is a major referral center for HIV-infected patients. During November through April, there are ~10 admissions to the adult medical service per day, and >50% of these patients are usually febrile. The hospital microbiology facilities include an automated blood culture system that is adequate for bacterial cultures but does not accommodate mycobacterial blood cultures and is insensitive in the detection of fungemia.

For each 24-h period from 11 February through 12 April 1997 (study period), all febrile (oral temperature ≥38°C within 12 h of admission) adults (≥15 years old) admitted to the medical service at Bamrasnaradura Hospital were seen by 1 of the principal investigators. A detailed history was obtained, and a physical examination was conducted. Data obtained included age, sex, medical
history of acute and chronic symptoms, antimicrobial therapy before hospital admission, clinical findings, and hospital course and outcome (e.g., discharged or died). Fever and diarrhea were deemed chronic if present >1 month. Chronic weight loss was defined as weight loss ≥10% of usual body weight. Data were entered on standardized forms.

Before antimicrobial therapy was begun and after the patient’s skin was cleaned with povidone-iodine, 25 mL of venous blood was obtained for culture and HIV testing. All patients received counseling before and after HIV testing. The ward was notified as soon as an organism was isolated from the blood and again when the organism was identified. Additional diagnostic tests, such as chest radiographs, sputum smears for acid-fast bacilli (AFB), and complete blood cell counts, were requested when deemed appropriate by the attending physician.

Blood cultures. Venous blood (10 mL) was inoculated at the bedside into a biphasic bacterial blood culture bottle (Septi-Chek [SC]; Becton Dickinson Microbiology Systems [BDMS], Cockeysville, MD) to which an agar slide paddle (BDMS) was attached in the laboratory. The blood culture bottle was then momentarily inverted so that the contents covered the agar paddle. An additional 10 mL of blood was added to an isolator tube (Wampole Laboratories, Cranbury, NJ) for lysis and centrifugation within 8 h of venesecration. A portion of the lysis-centrifugation concentrate was inoculated into a biphasic mycobacterial blood culture bottle (Myco-Chek [MC]; BDMS) containing Middlebrook 7H9 broth to which AFB culture supplement (BDMS) was added and to which an AFB agar paddle (BDMS) was attached in the laboratory. The remainder of the concentrate was inoculated onto Middlebrook 7H11, heated blood (chocolate), and inhibitory mold agar slants (BDMS).

The bacterial and mycobacterial blood culture bottles and agar slants were incubated aerobically at 35°C; the inhibitory mold agar slants were incubated at 30°C. Chocolate agar slants were incubated in a 5% carbon dioxide atmosphere. The SC blood culture bottles were examined twice in the first 24 h after incubation for signs of growth and then daily for the next 7 days. Broth from SC bottles that remained clear after 7 days were terminally subcultured onto sheep blood agar plates. Preliminary identification of organisms was made on site, by use of standard microbiologic tests. If an enteric organism was suspected on the basis of colony morphology and Gram’s stain results, a standardized inoculum of the organism was incubated in the BBL Crystal Enteric/Nonfermenter Identification System (BDMS) for identification. Coagulase-negative staphylococcus bacteria isolated from blood cultures were considered to be contaminants.

All MC blood culture bottles were inverted and rotated daily to cover the agar paddle during the first week; thereafter, they were rotated once weekly for 8 weeks or until growth was observed. All isolates (bacteria, fungi, and mycobacteria) were frozen and transported to the Clinical Microbiology Laboratory at Duke University Medical Center (Durham, NC), where they were identified to the species level. M. tuberculosis complex and M. avium complex were identified by use of DNA probes (AccuPROBE; Gen-Probe, San Diego) and biochemical tests; the identities of uncommon Mycobacterium species (e.g., M. simiae and strains of the SAV group [Mycobacterium organisms that resemble M. avium complex by conventional biochemical tests but have high-performance liquid chromatography (HPLC) profiles that are more consistent with M. simiae) were confirmed by use of HPLC. All strains of M. tuberculosis were genotyped by use of restriction fragment length polymorphism (RFLP).

HIV serology. Serum samples were assayed in batches by use of ELISA kits (Enzygnost anti-HIV 1/2 Plus [Behring, Marburg, Germany] and ACCESS HIV 1/2 [Sanofi Diagnostics Pasteur, Marne-La Coquette, France]). HIV ELISA tests were repeated if the first test was positive.

Antimicrobial susceptibility testing. Antimicrobial susceptibility tests and interpretations were performed at Duke University Medical Center according to the recommendations and guidelines proposed by the National Committee for Clinical Laboratory Standards [3, 4]. The antimicrobial panel chosen included affordable drugs that are readily available to patients in Bamrasnaradura Hospital. Susceptibilities of gram-negative organisms to the selected antimicrobials were tested by use of the Microscan Walkaway (Baxter Diagnostics, Deerfield, IL). Other susceptibilities were tested by disk diffusion procedures. The E-test (AB BIODISK, Culer City, CA) was used to test the susceptibility of S. pneumoniae to penicillin. Susceptibility testing of M. tuberculosis isolates was done by use of the BACTEC radiometric method (Becton Dickinson Diagnostics Instrument Systems, Sparks, MD).

Statistical analysis. All data were collected on standardized forms, entered into a computer, and analyzed by use of Epi Info (version 6.02; CDC, Atlanta). We calculated the population sample size for the study on the basis of published prevalence rates of BSIs in studies conducted in Tanzania, Kenya, and Côte d’Ivoire [1, 5, 6]. The χ2 test with Mantel-Haenszel and Yates’s correction or Fisher’s exact test, where appropriate, were used to compare categorical variables. Relative risks and 95% confidence intervals were calculated. Multivariate analysis and logistic regression were performed by use of statistical software (SAS, Cary, NC).

Results

During the study period, 246 patients met the study entry criteria; 171 (69.5%) were male. The median age of the study population was 32 years (range, 15–87). A total of 119 (48%) had BSIs, and 19 (16%) of these had polymicrobial (≥1 pathogen) BSIs; 133 clinically important organisms were isolated from patients (table 1). Of the 246 study patients, 182 (74%) were HIV seropositive; of the 119 patients with BSIs, 114 (96%) were HIV seropositive.

The most frequently isolated BSIs pathogens were C. neoformans (30 patients), M. tuberculosis (27), M. avium complex (24), non–typhi Salmonella (16), Staphylococcus aureus (7), Histoplasma capsulatum (4), Penicillium marneffei (4), Candida species (2), Mycobacterium scrofulaceum (2), M. simiae (2), and the SAV group (2). Two blood culture samples grew coagulase-negative staphylococcus, yielding an overall blood culture contamination rate of 0.8%. RFLP analysis of M. tuberculosis isolates demonstrated 25 different electrophoretic band patterns among the 27 M. tuberculosis isolates.

HIV-positive patients were significantly more likely than HIV-negative patients to have BSIs (relative risk, 8; 95% con-
Febrile, HIV-infected patients presenting with chronic diarrhea, chills and rigors, an absolute lymphocyte count <1200/mm³, and a total white blood cell count >13,000/mm³ or <4000/mm³ had a .91 estimated probability of having a BSI caused by any pathogen. Febrile, HIV-infected patients presenting with lymphadenopathy and an abnormal white blood cell count >13,000/mm³ or <4000/mm³ had a .5 estimated probability of having a BSI caused by *Mycobacterium* species. Any febrile patient with a history of chronic diarrhea alone had a .71 estimated probability of having bacteremia. A febrile, HIV-infected patient with a history of chronic diarrhea and findings of splenomegaly and oral candidiasis on physical examination had a .81 estimated probability of having a polymicrobial BSI.

Of 46 patients with fever and chronic diarrhea, 31 (67%) had BSIs. Of these 31 patients, 6 (19%) had bacteremia only, 7 (23%) had fungemia only, 10 (32%) had mycobacteremia only, and 8 (26%) had polymicrobial BSIs. Similarly, of 125 patients with fever, lymphadenopathy, and HIV infection, 76 (61%) had BSIs. Of these 76 patients, 10 (13%) had bacteremia, 15 (20%) had fungemia, 37 (49%) had mycobacteremia, and 14 (18%) had polymicrobial BSIs.

Several pathogens demonstrated significant antimicrobial resistance. All 6 *Salmonella typhimurium* isolates were resistant to both ampicillin and trimethoprim/sulfamethoxazole (TMP-SMZ), and 3 (50%) of the *Salmonella choleraesuis* isolates were resistant to ampicillin but not to TMP-SMZ. All 3 *Salmonella enteritidis* isolates were susceptible to both ampicillin and TMP-SMZ, and all 16 *Salmonella* species isolates were susceptible to ceftriaxone and ciprofloxacin. All 7 *S. aureus* isolates were resistant to penicillin, 2 (29%) were resistant to erythromycin, and 1 was methicillin resistant but susceptible to vancomycin and clindamycin. Of the 27 *M. tuberculosis* isolates, 7 (26%) were resistant to isoniazid, 8 (30%) to rifampin, 6 (22%) to both isoniazid and rifampin, 6 (22%) to streptomycin, and 4 (15%) to isoniazid, rifampin, ethambutol, and streptomycin. No *M. tuberculosis* isolate was resistant to pyrazinamide.

### Discussion

Basic microbiology services are an essential element in recognizing new and emerging pathogens, monitoring changes in antimicrobial resistance, and assisting clinicians in clinical decision-making. Such services are often unavailable in countries with limited resources, where many laboratories lack personnel or equipment or inappropriately use available resources. As a consequence, the nature of BSIs in febrile hospitalized adults remains unknown in many areas of the world, particularly where HIV is prevalent, and empirical therapy for BSIs in these patients may be misdirected because of limited available data on the prevalence, etiology, and epidemiology of BSIs.

Our study indicates that the prevalence of BSIs among febrile adults (persons >15 years old) admitted to a large infectious diseases hospital in Bangkok was 48% and that *C. neoformans,*

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Table 1. Distribution of pathogens causing bloodstream infections in patients >15 years old, Bamrasnaradura Hospital, Bangkok.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV⁺ (n = 182)</td>
</tr>
<tr>
<td><strong>Enterobacteriaceae</strong></td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>1</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>1</td>
</tr>
<tr>
<td>non-typhi Salmonella</td>
<td>16</td>
</tr>
<tr>
<td><strong>Other gram-negative bacilli</strong></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter johnsonii</td>
<td>1</td>
</tr>
<tr>
<td>CDC Group 03</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas stutzeri</td>
<td>1</td>
</tr>
<tr>
<td><strong>Gram-positive organisms</strong></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>7</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>0</td>
</tr>
<tr>
<td>Streptococcus Group A</td>
<td>1</td>
</tr>
<tr>
<td>Norcardia species</td>
<td>1</td>
</tr>
<tr>
<td>Rhodococcus equi</td>
<td>1</td>
</tr>
<tr>
<td><strong>Yeasts</strong></td>
<td></td>
</tr>
<tr>
<td>Candida parapsilosis</td>
<td>1</td>
</tr>
<tr>
<td>Cryptococcus laurentii</td>
<td>1</td>
</tr>
<tr>
<td>Cryptococcus neoformans</td>
<td>30</td>
</tr>
<tr>
<td>Histoplasma capsulatum</td>
<td>4</td>
</tr>
<tr>
<td>Penicillium marneffei</td>
<td>4</td>
</tr>
<tr>
<td><strong>Mycobacteria</strong></td>
<td></td>
</tr>
<tr>
<td><em>M. avium</em> complex</td>
<td>24</td>
</tr>
<tr>
<td><em>M. scrofulaceum</em></td>
<td>2</td>
</tr>
<tr>
<td><em>M. simiae</em></td>
<td>2</td>
</tr>
<tr>
<td><em>M. tuberculosis</em></td>
<td>27</td>
</tr>
<tr>
<td>Total no. of patients with blood pathogens</td>
<td>114</td>
</tr>
</tbody>
</table>

NOTE: CDC, Centers for Disease Control and Prevention; SAV, *Mycobacterium* species. Any febrile patient with a history of chronic diarrhea alone had a .71 estimated probability of having bacteremia. A febrile, HIV-infected patient with a history of chronic diarrhea and findings of splenomegaly and oral candidiasis on physical examination had a .81 estimated probability of having a polymicrobial BSI.

* >1 organism was isolated from blood of 19 patients.
M. tuberculosis, and M. avium complex were the three pathogens most commonly isolated from the bloodstream of these patients. In addition, certain fungi (H. capsulatum and P. marneffei) and mycobacteria (M. simiae, M. scrofulaceum, and mycobacteria of the SAV group) emerged as important causes of BSIs in this population. Three-quarters of adults with fever hospitalized at this Bangkok hospital and 96% of patients with BSIs were HIV seropositive. Multivariate analysis suggested specific clinical parameters that were strongly predictive for bacteremia, mycobacteremia, and fungemia. Approximately 22% of M. tuberculosis isolates showed multidrug resistance.

In the Western world, M. tuberculosis and M. avium complex BSIs have been recognized and reported both in HIV-seropositive [7–11] and HIV-seronegative patients [12]. In the Western setting, however, M. tuberculosis BSIs are less common than M. avium complex BSIs, which are more frequently observed in patients with advanced HIV infection [9, 13]. Nonetheless, M. tuberculosis BSIs have been reported in 15%–56% of HIV-infected patients clinically suspected to have extrapulmonary tuberculosis [8, 10, 11, 14–16].

The association between HIV-1 infection and tuberculosis has been well described for HIV-endemic regions in Africa [17–20]. More recently, studies have established the importance of M. tuberculosis BSIs in febrile HIV-infected adult patients in HIV-endemic regions in Tanzania [1] and Brazil [2], where 19 (58%) of 33 HIV-infected patients with a final diagnosis of tuberculosis had M. tuberculosis BSIs. Thus, M. tuberculosis is a common bloodstream pathogen in HIV-infected patients, and it is imperative that laboratories in areas of the world with a high prevalence of HIV use methods that enhance recovery of M. tuberculosis so that these infections can be diagnosed early and appropriately.

In contrast with studies in developed countries, studies conducted in certain sub-Saharan countries with high HIV endemicity suggest that, although M. tuberculosis BSIs are common in febrile adult HIV-infected patients, M. avium complex BSIs remain relatively uncommon [1, 21]. Our study suggests, unlike findings in these sub-Saharan studies, that BSIs due to C. neoformans, M. tuberculosis, or M. avium complex are relatively common in febrile adult HIV-infected patients in Bangkok. That the prevalence rate of M. avium complex BSIs in Bangkok is so different from the rates in similar study populations in HIV-endemic regions in sub-Saharan Africa underscores the variation in the epidemiology of BSIs in different countries and the importance of ensuring that regional reference laboratories have the capacity to culture blood (and other specimens) comprehensively for bacteria, mycobacteria, and fungi. In addition, our results demonstrate the inherent risk of extrapolating data from one HIV-endemic region of the world to another for the implementation of clinical or public health policies.

Our multivariate analyses provide a statistical model that highlights which febrile hospitalized adults in a large Bangkok hospital are at greatest risk of BSIs and should, therefore, be strongly considered for having blood samples cultured. Our data suggest that (1) any adult HIV-infected patient presenting with chronic diarrhea, chills and rigors, and an absolute lymphocyte count < 1200/mm³ would have a >90% chance of having a BSI and should be considered for bacterial, mycobacterial, or fungal blood cultures; (2) any adult patient with fever and a history of chronic diarrhea should, at the least, be considered for bacterial blood cultures; and (3) patients clinically suspected to be HIV infected, with lymphadenopathy and an abnormal white blood cell count, should be considered for mycobacterial and bacterial blood cultures. If blood culture services are unavailable, empirical therapy alone may be appropriately based on these probabilities. Development and use of such algorithms, after discussion between microbiologists, clinicians, and epidemiologists, might facilitate better use of scarce laboratory resources and improve patient outcomes.

In some countries or regions, decisions have been made about empirical antimicrobial therapy on the basis of limited laboratory results. Of importance, BSIs prevalence rates might vary by country, and clinical predictors of BSIs might vary from setting to setting. This may preclude extrapolation of data from one country to another, and clinical algorithms developed for one specific site or country might not be applicable to other sites. Hence, countries that wish to implement public health policy should conduct appropriate BSI studies within their own setting or exercise care when extrapolating data from other sources. Cohort-based microbiologic studies, such as we have conducted, could guide development of appropriate empirical antimicrobial therapy.

RFLP analysis of the M. tuberculosis isolates in our study demonstrated a heterogeneity of strains, suggesting that our findings were neither a result of an outbreak of M. tuberculosis infection among hospitalized patients nor a result of inadvertent contamination in the microbiology laboratory. Our decision to treat coagulase-negative staphylococcus as a contaminant was based on the results of BSI studies that have demonstrated the clinical insignificance of these organisms as BSI pathogens in the absence of invasive devices [22]. None of the patients in our study had intravascular devices at the time blood was obtained for culture. Thus, even if a significant number of blood samples had yielded growth of coagulase-negative staphylococcus in culture, their clinical significance as true BSI pathogens would still have remained doubtful. Our results also demonstrate that if blood samples are obtained by trained personnel using appropriate skin preparation and these specimens are handled appropriately in the laboratory, contamination of blood cultures should occur infrequently (<1%).

Our data show a 100% resistance rate among S. typhimurium isolates to ampicillin and TMP-SMZ and a 22% prevalence rate of multidrug resistance among the M. tuberculosis isolates. These results demonstrate the value of antimicrobial susceptibility data in the clinical selection of antimicrobial therapeutic...
regimens and underscore the importance of surveillance of antimicrobial resistance among pathogens that commonly cause BSIs in HIV-endemic developing countries.

*C. neoformans* was the most common pathogen causing BSIs in our study, and only 4 patients had BSIs due to the fungal pathogen *P. marneffei*, which is one of the most common pathogens causing opportunistic infections in HIV-infected patients in northern Thailand [23, 24]. The prevalence of *P. marneffei* infections among HIV-infected patients from areas outside the northern regions appears to be considerably lower [24], which may be due to the fact that the HIV epidemic has been most severe in the northern provinces of Thailand [25]. In a study spanning a 4-year period, Chariyalertsak et al. [24] demonstrated that HIV-infected patients presenting with *P. marneffei* infection were more likely to be seen in the rainy season in each year; these investigators did not observe seasonal variation in the incidence of disseminated *C. neoformans* infections. Our study was conducted during the height of the dry season in Thailand. Thus, the low incidence of *P. marneffei* BSIs in our Bangkok patient population could have been a manifestation of seasonal variation.

The mortality rate among study patients with BSIs was significantly higher than that among patients without BSIs; mortality was particularly high among patients with bacteremia or fungemia. The blood culture system in the clinical microbiology laboratory of our study hospital could detect bacteremia but was less sensitive for recovery of mycobacteria or fungi. Without comprehensive blood cultures, BSIs in our study population would not have been detected. Data from our study suggest that the initial priority of other hospitals in Thailand ought to be the development of microbiology services to diagnose BSIs and the identification, through clinical predictors, of patient populations most at risk of having BSIs. By focusing available resources on performing blood cultures for high-risk patient populations, using comprehensive methods to detect bacteria, mycobacteria, and fungi, clinicians could initiate directed empirical therapy, which could then be tailored once the results of cultures are available.

In many countries, resources are limited; therefore, cultures of patient blood samples are not done or, if they are done, the microbiologic methods (e.g., type of media available, duration of incubation, quality control) are inadequate. The Western style inpatient-based culture methods cannot be established or sustained in such settings. Cohort-based microbiologic surveillance studies, such as this one, focus on quality-controlled diagnostic testing over a finite period and are performed on patients who have similar symptoms or signs and who meet simple, objective entry criteria, such as having a fever. Such studies could be conducted at sentinel hospitals that provide a natural gathering point to obtain samples from patients meeting these entry criteria.

These “probe” studies could be conducted, in the form of periodic surveys of cohorts of patients meeting the aforementioned defined entry criteria, by use of quality-controlled tests with a high positive predictive value for infection, such as cultures of blood, cerebrospinal fluid, or stool samples. A comprehensive cohort-based study acting as a surveillance probe over a finite period may be more feasible and effective than individual patient-directed laboratory testing in providing useful clinical and public health information: such studies may provide better estimates of true incidence and prevalence rates of emerging pathogens and antimicrobial resistance and better determination of clinical predictors of infection. In addition, these studies would provide the opportunity to increase capacity in basic clinical microbiology in sentinel regional hospitals or laboratories where there is an inadequate critical public health infrastructure.

Our study had some limitations. First, only 1 blood sample was obtained for culture from each patient: 2 blood cultures would probably have yielded a larger number of organisms [26]. Thus, the true rate of BSIs in the febrile adult population that we studied is probably higher than our observed rate of 48%. Second, we did not culture samples from different body sites and body fluids for pathogens. Thus, we could not correlate BSIs with a concurrent positive culture for the same organism from another site. Third, the results of a 2-month survey from one hospital might not be representative of the situation in other regions in Thailand because clinical predictors of BSIs, as determined by use of logistic regression analysis, will vary highly on the basis of geography, available diagnostic resources, and the nature of the patient population. For such predictors to be useful, they would have to be assessed for the area in which they would potentially be used. Thus, the predictors developed in this study are useful primarily as an example. Appropriate clinical algorithms would have to be developed from studies conducted in the respective regions.

For this study, ELISA HIV results were not confirmed by Western blot analysis. Data from Thailand have shown that the use of two ELISA tests to confirm the presence of HIV antibodies produces results comparable to those of the Western blot [27]. Thus, in a country with a high prevalence of HIV infection and limited financial resources, Western blot analysis is not necessary.

The results of this study suggest that the HIV pandemic has led to high rates of BSIs among febrile hospitalized patients in Southeast Asia. We conclude that (1) the scope of clinical microbiology services offered by hospitals serving HIV-endemic areas in Thailand may need to be widened to include blood cultures for bacteria, mycobacteria, and fungi; (2) development of clinical algorithms may be useful to more effectively use limited resources and improve patient care; and (3) cohort-based microbiologic surveillance studies used as “probes” for emerging infections in sentinel hospitals can provide important clinical and public health information, such as the identities of emerging pathogens, prevalence rates of these pathogens and
their resistance profiles to commonly used antimicrobials, and clinical predictors.

The daunting task remains to define the role of new and emerging pathogens causing BSIs in a variety of patient populations presenting to hospitals in Southeast Asia and developing countries elsewhere. Continued recommendation of individual patient-directed culturing in developing countries is likely to fail because of insufficient laboratory personnel, resources, and expertise. The cohort-based methods used here could be implemented at regional referral laboratories in developing countries. In this way, cultures could be done, by use of quality-controlled methods, for larger numbers of patients. With the demonstrated utility of cohort-based microbiologic studies used as surveillance probes for emerging infections, there is hope that patient therapy can be improved and national and international surveillance of new and emerging pathogens and antimicrobial resistance can be enhanced.

Acknowledgments

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