Original Report

Tropical Diabetic Hand Syndrome: Risk Factors in an Adult Diabetes Population

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ABSTRACT

Objectives: To determine risk factors for the tropical diabetic hand syndrome, a condition associated with significant morbidity and mortality in Africa.

Methods: This was a case-control study of a Tanzanian diabetes population presenting with the syndrome during February 1998 to March 2000. A case patient was defined as any patient with diabetes presenting with hand cellulitis, ulceration, or gangrene. Control patients were randomly selected patients with diabetes who had no hand symptoms.

Results: Thirty-one case patients and 96 control patients were identified. The median age of case patients was 52 years (range, 28–76 y); 58% were male; 4 patients (16%) died. Precipitating events included papule (n = 6), insect bites (n = 6), boils (n = 5), burns (n = 2), or trauma (n = 3). Case and control patients were similar for presence of micro- and macrovascular disease and occupation. On logistic regression analysis, independent risk factors were body mass index of 20 or less (odds ratio [OR] = 18.0; 95% confidence interval [CI] = 4.3–97.0; P < 0.001), peripheral neuropathy (OR = 23.0; 95% CI = 5.3–124.0; P < 0.001), or type I diabetes, (OR = 6.7; 95% CI = 2.0–24.0, P < 0.01).

Conclusion: The major risk factors for the tropical diabetic hand syndrome are intrinsically related to the underlying disease. Thus, prevention of hand infections may require aggressive glucose control, and education on hand care and the importance of seeing a doctor promptly at the onset of symptoms.

Key Words: *diabetes, hand infections, hand sepsis, Tanzania, sub-Saharan Africa*

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Hand infections among patients with diabetes have long been recognized by clinicians in developed and less developed countries. However, it was not until 1977 that the phenomenon of hand sepsis was first described in the published medical literature for a diabetes population in a developed country,[1] and in 1984 for a diabetes population in an African country.[2] Although relatively uncommon and not generally recognized as a specific diabetes complication, hand infections are now seen most frequently in tropical countries, are commonly associated with mild preceding trauma, and may rapidly progress to extensive gangrene of the limb, resulting in significant morbidity or mortality.[3] Recently, the term tropical diabetic hand syndrome has been used to describe patients who meet this case definition of progressive, fulminant hand sepsis.[4,5]

Various risk factors for diabetes hand sepsis have been postulated. These include insect bites or a history of hand trauma, type II diabetes, female sex, poor glycemic control, low socioeconomic status, residence in coastal areas, or late presentation to hospital.[2–6] However, these reported associations either were based on data from descriptive studies or were not validated. Thus, a case-control study was undertaken, to characterize the epidemiology and clinical characteristics of the tropical diabetic hand syndrome in an adult diabetes outpatient population in sub-Saharan Africa, and to document risk factors associated with the syndrome in this diabetes population.

PATIENTS AND METHODS

Study Population

Tanzania is a developing country in East Africa with a low gross national product. Dar es Salaam, the capital, has a population of about 3 million people. The prevalence of diabetes in Tanzania is variable: low (0.9%) in rural areas and high (8.8–12.2%) in urban Dar es Salaam.[7,8] Nearly all the African diabetes patients in this population attend the specialist diabetes outpatient services at

Muhimbili Medical Centre (MMC) a large teaching hospital located in Dar es Salaam, and the main referral medical center in Tanzania. When patients attend the MMC diabetes clinic, weight and height are measured and urine specimens are routinely checked. Glycosylated hemoglobin levels are not routinely done because of prohibitive costs. Thereafter, a physician conducts a physical examination with special attention to the eyes, limbs, and blood pressure. In 1994, a standardized form was introduced for systematic collection of risk factor data in the MMC diabetes outpatient population. No new patient interventions were introduced. During the study period, June 1998 to March 2000, patients who attended the MMC diabetes outpatient clinic were questioned by doctors and nurses regarding hand symptoms or hand-related problems.

Case Definition

A case was defined as any adult (≥18 y) diabetes patient presenting to the MMC diabetes outpatient clinic with signs of cellulitis, suppuration, ulceration, or gangrene in the hand during the study period.

Case and Control Patients

Patients who met the case definition underwent further evaluation that included a comprehensive history and physical examination. Details of the history included data on demography; region of residence; type and duration of diabetes; family history of diabetes; medical history of hand problems; precipitating causes, such as insect bites or hand injury; symptoms associated with peripheral neuropathy, alcohol, and tobacco use; and occupation. The physical examination included objective evaluation for peripheral neuropathy, peripheral vascular disease, and severity of hand sepsis, using the Wagner classification that has been used to classify the severity of foot ulcers.[9] Control patients with no history of hand symptoms were randomly selected from the MMC diabetes outpatient population during the study period. Three control patients were chosen for each case patient; case and control patients were matched for age and gender.

Statistics

Data were collected on a standardized form and analyzed using Epi Info, version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA). Categorical variables were compared using the chi-squared or Fisher's exact test, where appropriate. Continuous variables were compared using the Wilcoxon rank sum test. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. To identify independent risk factors, a logistic regression model was constructed using SAS software, version 6.12, for personal computers (SAS Institute, Cary, NC). All risk factors with $P < 0.2$ that were identified by univariate analysis were evaluated by stepwise logistic regression analysis.

RESULTS

Patients

During the study period, 31 patients met the case definition; 96 control patients were selected. The median age of case patients was 52 years (range, 28–76 y). Of the 31 case patients, 18 (58%) were male and 29 (94%) were of African race. The median duration of diabetes in case patients was 72 months (range, 0.5–228 mo). Only one (3%) case patient smoked tobacco. Four (16%) case patients developed diabetic ketoacidosis and were admitted to the MMC medical service. On presentation, all 31 case patients had severe pain; 25 (81%) had a purulent ulcer; 26 (84%) had cellulitis in the hand; and 29 (94%) had significant hand swelling. All case patients resided in the Dar es Salaam area. Occupations of case patients included housewife (n = 11, 35%), retired (n = 8, 26%), street vender (n = 4, 13%), laborer (n = 1, 3%), cook (n = 1, 3%), policeman (n = 1, 3%), lorry driver (n = 1, 3%), or priest (n = 1, 3%). Precipitating factors putatively associated with hand sepsis varied (Table 1).

Case-Control Study

Case and control patients were similar for region of residence, the presence of microvascular and macrovascular disease, alcohol or tobacco use, or occupation. In

Table 1. Potential Precipitating Factors Associated with the Tropical Diabetic Hand Syndrome, Dar es Salaam, Tanzania

Lesion or Event	*Number of Cases (n = 31) (%)*
Papule	6 (19.4)
Insect bite associated with skin irritation through scratching	6 (19.4)
Boils	5 (16.1)
No obvious cause	5 (16.1)
Trauma	3 (9.7)
Burns	2 (6.5)
Scabies (aggravated by itching)	1 (3.2)
Cutting finger nails too deep	1 (3.2)
Following insertion of intravenous catheter for antimalarial therapy	1 (3.2)
Unexplained swelling of the hand	1 (3.2)

contrast, case patients were more likely than controls to have a lower median body mass index (23 vs. 28; $P < 0.001$), a higher median duration of diabetes (72 vs. 24 mo; $P < 0.01$), a higher median random blood glucose at the time of clinic visit (19.4 mmol/L vs. 14.9 mmol/L; $P < 0.05$), peripheral neuropathy ($P < 0.001$), a family history of diabetes ($P < 0.05$), or type I diabetes ($P < 0.001$). On logistic regression analysis, independent risk factors for hand sepsis were a body mass index of 20 or less (OR = 18.0; 95% CI = 4.3-97.0; $P < 0.001$), presence of peripheral neuropathy (OR = 23.0; 95% CI = 5.3-124.0; $P < 0.001$), or type I diabetes (OR = 6.7; 95% CI = 2.0-24.0; $P < 0.01$).

Severity of Hand Sepsis, Intervention, and Patient Outcome

All 31 case patients had hand ulceration or gangrene (Table 2). Sixteen (52%) case patients required surgical incision and drainage, or débridement; four case patients (13%) required arm amputation for progressive gangrene despite receiving antimicrobial and insulin therapy; and another four (13%) died from overwhelming sepsis despite prolonged courses of parenteral antimicrobial and insulin therapy in the MMC inpatient medical service.

Seasons

Five case patients presented to the MMC outpatient clinic during the 1998 wet season (January-May) and five patients during the 1998 dry season (June-December). The corresponding numbers for the 1999 wet and dry seasons were ten and nine patients, respectively. Thus, there was no discernible seasonal variation in the incidence of hand sepsis among the diabetes patients attending the MMC outpatient diabetes clinic during the study period.

DISCUSSION

This study documented that the tropical diabetic hand syndrome in Tanzanian patients with diabetes may result in significant morbidity and mortality, and that on presentation to the diabetes clinic at a teaching hospital in Dar es Salaam, over 80% of the affected patients already had purulent hand ulceration and 29% had actually progressed to gangrene. In addition, independent risk factors for the tropical diabetic hand syndrome in this study population included body mass index of 20 or less, peripheral neuropathy, and type I diabetes.

There have been few published reports of hand sepsis affecting diabetes patients in Africa. The first, in 1984, highlighted the problem in Nigeria: 5 (3.2%) of 152 consecutive diabetes patients developed hand ulceration and sepsis that were associated with gangrene.[2] All five patients had type I diabetes and had suffered antecedent trivial hand injuries that rapidly progressed to sepsis following delayed presentation to hospital; none had clinical evidence of peripheral neuropathy or peripheral vascular disease. In a 1991 report from Nairobi, Kenya, researchers characterized ulcers from various anatomic sites in 100 patients with diabetes, and identified 15 patients with hand ulcers.[10] Although nine of these ulcers were described as neuropathic, the report did not suggest underlying risk factors, possible etiologies, or whether the patients had diabetes. During a 6-month period in 1992, 150 patients with hand infections presented to a Khartoum teaching hospital.[11] The majority of these patients were manual workers, trauma was the main cause of hand sepsis, and 15 (10%) patients had diabetes. However, the clinical characteristics of these 15 diabetes patients were not delineated in the report. In more recent studies of hand sepsis among diabetes patients in Tanzania and Libya, female patients predominated, none of the affected patients had peripheral vascular disease, and prolonged hospital stays were common.[3,6] Whereas the morbidity rate was high among the Libyan patients, the mortality rate remained high among the Tanzanian patients. All these published studies of hand sepsis in African patients were based on numerator data only. In contrast, results reported here stem from the first case-control study of the hand sepsis problem, using both numerator and denominator data. Thus, the risk factor analysis more accurately reflects the reality.

Most of the published reports describe a predominance of women among diabetes patients who develop hand sepsis.[2,3,6] In rural areas in Africa, where many women are responsible for farming and planting crops (tasks that require manual labor), those women with diabetes remain at risk of acquiring various kinds of hand trauma that may progress to hand sepsis. This may explain the predominance of women in these published reports. In this study, case patients resided mainly in urban Dar es Salaam and were not at risk of hand trauma as an occupational hazard. In fact, only one of the case patients in

Table 2. Severity of Hand Sepsis among Diabetes Patients, Muhimbili Medical Center, Tanzania

Clinical Description	*Number of Patients (n = 31) (%)*
Deep ulcer with no bone involvement (Wagner grade 2)	19 (61)
Deep ulcer with bone involvement (Wagner grade 3)	3 (10)
Localized hand gangrene (Wagner grade 4)	8 (26)
Extensive hand gangrene (Wagner grade 5)	1 (3)

this study was a manual laborer. Thus, urban and rural risk factors may be different.

Although univariate analysis of the data demonstrated that case patients had a significantly higher median random blood glucose than the controls, random blood glucose by itself did not remain an independent risk factor for hand sepsis after multivariate analysis. This suggests that other underlying factors associated with poor glycemic control, such as peripheral neuropathy (an independent risk factor in this study), might be playing a more significant role in the pathogenesis of hand sepsis. Peripheral neuropathy may commonly manifest as loss of sensation in the feet, and is an important factor in the pathogenesis of foot ulcers, which can progress to infection, necrosis, gangrene, loss of the limb, or death. Published data suggest that foot ulcers in diabetes patients in sub-Saharan Africa are more likely attributable to peripheral neuropathy or infection rather than to peripheral vascular disease.[7,12] Thus, it is plausible that reduced sensation in the hands of patients with diabetes who have peripheral neuropathy might predispose them to sustain and tolerate seemingly innocuous hand injuries that would otherwise not be tolerated with normal sensation. Against this hypothesis are data from previously published reports in which peripheral neuropathy and peripheral vascular disease did not appear to be of significant importance in the pathogenesis of hand sepsis in Libyan, Nigerian, or Tanzanian patients.[2,3,6,13]

The other two independent risk factors for hand sepsis in the case patients (type I diabetes and body mass index ≤ 20) are likely surrogate markers for the patient's propensity for developing ketoacidosis, which has a recognized association with impaired phagocytosis and altered white cell chemotactic ability in patients with diabetes.[14] In this respect, however, the results should be interpreted with caution. For example, in the published report of four Tanzanian patients with fatal hand sepsis, all had type I diabetes,[3] whereas type II diabetes was predominant among the patients from Nigeria and Libya who had hand sepsis.[2,6] In the United States, too, the role of diabetes type in the pathogenesis of hand sepsis remains controversial. For example, in the 1977 report of hand infections in patients with diabetes, all 20 patients had a history of type II diabetes.[1] In contrast, the majority of patients with hand infections followed at the Joslin Clinic for Diabetes in Boston and reported in 1990 had type I diabetes.[15] Thus, the role of type of diabetes in the pathogenesis of hand sepsis remains equivocal.

Nine (29%) of the case patients in the present study had localized or extensive hand gangrene. Although hand cultures were not obtained in these patients, it is plausible that these patients had developed one of the recognized forms of synergistic gangrene. For example, symbiosis of *Staphylococcus aureus* and microaerophilic streptococci can cause a progressive, spreading, synergistic, subcutaneous gangrene (Meleney gangrene) that is confined largely to the superficial fascia; symbiosis of aerobic gram-negative bacteria with various enteric anaerobes commonly results in a polymicrobial synergistic gangrene; and streptococcal gangrene associated with *Streptococcus pyogenes* infection may develop rapidly following massive skin edema, erythema, and skin vesicle formation. In a comprehensive review of the published literature on the bacteriology of hand sepsis, Gill and colleagues noted that the range of pathogens associated with hand sepsis varied and included gram-positive (predominantly *S. aureus* and *Streptococcus* spp) or gram-negative (*Klebsiella* spp, *Enterobacter* spp, *Proteus* spp, and *Escherichia coli*) organisms, anaerobes, or mixed bacterial growth that contained both aerobic and anaerobic organisms.[5] Although the relatively few published reports from Africa confirmed a similar, variable bacteriologic etiology that was commonly polymicrobial in nature,[2,6,10,11] the roles of mycobacteria and fungi as etiologic factors for hand sepsis in African patients have yet to be ascertained. Notwithstanding the underlying etiology of hand infections, the major form of treatment, especially in settings with limited microbiology facilities, is wide surgical excision of infected tissues, and supplementation of such surgery with empirical broad-spectrum antimicrobial chemotherapy.[3,5]

Data from the present study spanned two seasonal cycles and suggest that the incidence of hand sepsis does not vary by season. However, since Dar es Salaam is a coastal city that remains humid throughout the year, and most of the case and control patients from the study resided in the districts around Dar es Salaam, it was not possible to establish whether humidity or living on the coast are themselves underlying risk factors for hand sepsis. A recent survey of clinicians across Africa suggested that hand sepsis might indeed be a phenomenon seen mostly in coastal areas.[5] This hypothesis could be tested by initiating surveillance systems for hand infections in large diabetes clinics in sentinel hospitals across Africa, comprehensively determining the infectious etiologies (i.e., culturing for bacteria, mycobacteria, and fungi), and comparing prevalence rates of hand infections from the various participating institutions. However, such an endeavor would almost certainly require enhancement of hospital microbiology capability to culture tissue, fluid, and blood specimens for bacteria, mycobacteria, and fungi, and might not be feasible or sustainable in some African countries because of prohibitive costs, lack of trained personnel, or inadequate laboratory facilities.

CONCLUSION

The tropical diabetic hand syndrome may cause significant morbidity and mortality in diabetes patients in sub-Saharan Africa. Clinicians should be cognizant of this complication and be prepared to immediately admit these

patients to the acute medical service. Management of patients who develop the syndrome should include aggressive surgical intervention and broad-spectrum antimicrobial therapy. Improperly treated or unrecognized hand infections can lead to disability, limb amputation, or death. In Tanzania, prevention efforts should be focussed on patients with type I diabetes with peripheral neuropathy and low body mass index. Finally, diabetes patients, especially those who carry out manual labor, should be educated on proper hand care and the importance of consulting a doctor immediately following hand trauma regardless of the severity, or at the onset of hand-related symptoms.

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