Epidemiology of Febrile Diseases in the Emergency Department of a Caribbean Island: The Curaçao Experience

M Limper[1, 3], I Gerstenbluth[2], AJ Duits[3], ECM van Gorp[1, 4]

ABSTRACT

Objective: *The aetiology of febrile diseases in tropical countries often remains poorly characterized. We aim to describe the aetiology and outcome of febrile illnesses at the Emergency Department (ED) in Curaçao.*

Methods: *From April 2008 – April 2009, all adult febrile patients (T > 38.5°C) at the ED of the St Elisabeth Hospital, Curaçao, Netherlands Antilles, were included. Clinical data were recorded, routine laboratory measurements and blood cultures were taken. Final diagnoses were made at discharge by an independent physician and in retrospect by the main investigator.*

Results: *Four hundred and three patients were included: 223 patients (55.6%) were hospitalized, 32 patients (7.9%) died and 18 patients (4.5%) were admitted to the Intensive Care Unit. In 129 febrile patients (32.0%), infection was proven; 84.4% of patients had bacterial (29.0% urinary tract infection, 23.2% pneumonia infection), 5.6% viral and 10.0% parasitic or fungal infections. Twenty-one patients (5.2%) were discharged with a non-infectious diagnosis and 172 patients (42.7%) without a clear diagnosis.*

Conclusion: *A high mortality rate of 7.9% was observed. We found a high prevalence of bacterial infections, with pneumonia and urinary tract infections as the most common causes of fever. One in 20 patients did not have an infectious disease.*

Keywords: Caribbean region, emergency medicine, epidemiology, fever

Epidemiología de las Enfermedades Febriles en el Departamento de Emergencias de una Isla Caribeña: la Experiencia de Curazao

M Limper[1, 3], I Gerstenbluth[2], AJ Duits[3], ECM van Gorp[1, 4]

RESUMEN

Objetivo: *La etiología de las enfermedades febriles en los países tropicales posee aún una pobre caracterización. El presente trabajo se propone describir la etiología y la evolución clínica de las enfermedades febriles en el Departamento de Emergencias (DE) de Curazao.*

Métodos: *De abril 2008 – abril 2009, todos los pacientes febriles adultos (T > 38.5°C) en el DE del Hospital Saint Elisabeth, de Curazao, Antillas Holandesas, fueron incluidos. Se registraron los datos clínicos, se tomaron las medidas de rutina de laboratorio y los cultivos de sangre. Los diagnósticos finales se hicieron a la hora del alta por un médico independiente y en retrospectiva por el investigador principal.*

Resultados: *Se incluyeron cuatrocientos tres pacientes: 223 pacientes (55.6%) fueron hospitalizados, 32 pacientes (7.9%) murieron, y 18 pacientes (4.5%) fueron ingresados en la Unidad de Cuidados Intensivos. En 129 pacientes febriles (32.0%) se comprobó la infección; 84.4% de los pacientes tenían infección bacteriana (29.0% infección de las vías urinarias, 23.2% infección por pneumonia), 5.6% viral y 10.0% infección parasitaria o fúngica. Veintiún pacientes (5.2%) fueron dados de alta con un diagnóstico no infeccioso, y 172 pacientes (42.7%) sin un diagnóstico claro.*

From: [1]Slotervaart Hospital, Department of Internal Medicine, Louwesweg 6, 1066 EC Amsterdam, The Netherlands, [2]Medical and Public Health Service (GGD) of Curaçao, Epidemiology and Research Unit, Piscaderaweg 49, Curaçao, Netherlands Antilles, [3]Red Cross Blood Bank Curaçao, Pater Euwensweg 36, Curaçao, Netherlands Antilles and [4]Department of Virology, Erasmus Medical Centre, PO Box 2040, 3000 CA Rotterdam, The Netherlands.

Correspondence: Dr M Limper, Slotervaart Hospital, Department of Internal Medicine, Louwesweg 6, 1066 EC Amsterdam, The Netherlands, and Red Cross Blood Bank Curaçao, Pater Euwensweg 36, Curaçao, Netherlands Antilles. E-mail: maarten.limper@slz.nl

Conclusión: *Se observó una alta tasa de mortalidad de 7.9%. Se halló una alta prevalencia de infecciones bacterianas, siendo la pneumonía y las infecciones de las vías urinarias las causas más comunes de fiebre. Uno de cada 20 pacientes no tenía una enfermedad infecciosa.*

Palabras claves: Región del Caribe, medicina de emergencia, epidemiología, fiebre

West Indian Med J 2012; 61 (1): 77

INTRODUCTION

Febrile illness is one of the most frequent causes for attendance at emergency departments (EDs) worldwide (1). Among the most frequently reported specific principal reasons for visiting an ED in the United States of America (USA) in 2005, fever was the third reported complaint, accounting for 4.4% of all ED consultations (2).

Although febrile diseases may be even more prevalent in tropical areas of the world, the aetiology of febrile diseases in these countries remains poorly characterized, due to lack of resources – *ie* diagnostic tools – and suitable infrastructure. Only few studies have focussed on the epidemiology of fever in tropical areas (3−5).

Curaçao is a small island in the Caribbean Sea, 40 miles off the coast of Venezuela, with a population of 150 000 inhabitants. The island's population consists of many persons of different ethnic backgrounds, with an Afro-Caribbean majority and with sizeable minorities such as Dutch, Latin American, French, South- and East-Asian, Portuguese and Levantine people. One public hospital, the St Elisabeth Hospital, serves as the primary hospital for Curaçao and the neighbouring islands.

Curaçao is a relatively rich Caribbean island, with a GDP per capita of US$20 500 in 2008. Main industries include oil refining, tourism and financial services. Curaçao has a semi-arid climate with a dry season from January to September and a wet season from October to December. Temperatures are constant over the year, varying from an average of 26.5˚C (80˚F) in January to an average of 28.9˚C (84˚F) in September. Coinciding with the wet season, yearly outbreaks of dengue fever are observed in Curaçao. Although malaria is endemic in surrounding countries, the sporadic malaria cases on the island seem to be imported.

The purpose of this study is to describe the aetiology and outcome of all adult patients with febrile illnesses in the ED of the St Elisabeth Hospital, a 500-bed teaching hospital with approximately 25 000 ED consultations each year, during a one year period. A better insight in the epidemiology of febrile diseases in Curaçao will not only lead to better clinical practice for the local situation and understanding of part of the epidemiology on surrounding islands and countries, but will also provide unique data for travel and tropical medicine worldwide.

SUBJECTS AND METHODS

Patients

From April 2008 to April 2009, we prospectively included all febrile patients between 18 and 80 years old who presented at the ED of the St Elisabeth Hospital. Inclusion criterion was a rectal temperature of ≥ 38.5˚C (only at this cut-off, blood cultures were routinely taken at the St Elisabeth Hospital), measured at the ED at presentation.

Patient data (history and physical examination) were recorded in case record forms. No interference with standard care was made; therefore, no informed consent was obtained. Laboratory and supplementary diagnostics were ordered at the discretion of the attending physician. In the St Elisabeth Hospital, bacterial diagnostics (*ie*, cultures of body fluids and faeces) can be ordered routinely; viral diagnostics were limited to serology only. Regular imaging by means of X-ray, ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI), could be performed but no nuclear imaging could be done.

Final diagnoses were made at discharge by an independent physician and again in retrospect by the main investigator, using all available data, including culture results, serology, radiology and pathology data. In case of a discrepancy between discharge diagnosis and the diagnosis in retrospect, an independent senior internist was asked to give a final clinical diagnosis.

Definitions

When a causative bacterium or virus could be identified, either by culture or viral serology, in concordance with patient history and clinical signs and symptoms, patients were confined to the 'proven bacterial' or 'proven viral' group. Confirmed parasites and fungi were classified as 'proven infectious – other'.

If a specific micro-organism could not be identified, but clinical signs and symptoms were consistent with clear radiological or pathology findings – for instance, a clear history of fever, productive cough and dyspnoea, abnormal pulmonary auscultation and an infiltrate on the chest X-ray, a clinical diagnosis was assigned and patients were confined to the 'suspected bacterial' or 'suspected viral' group. If patients were discharged with a clinical suspicion of infection, but without objective findings, they were confined to the 'rest' group. If a non-infectious cause of the fever, without the presence of pathogenic micro-organisms, was identified, patients were confined to the 'non-infectious' group.

'Pneumonia' was defined as an acute episode of fever with an infiltrate on the chest X-ray as confirmed by a radiologist, or as fever and auscultatory findings consistent with pneumonia and at least two of the following criteria: cough, purulent sputum, C-reactive protein > 3 times the higher cut-off value or PO_2 < 60 mm Hg, in the absence of any other focus for fever.

'Urinary tract infection' (UTI) was defined as an acute episode of fever with a positive urine culture and/or a urine sediment with > 100 000 bacteria per mL and > 5 leukocytes per high power field.

'Urosepsis' was defined as UTI combined with one or more of the following: tachycardia (heart rate > 100 beats/minute), tachypnoea (respiratory rate > 20 breaths/minute) and leukocyte count < 4.0 or > 12.0 cells/mm^3.

A blood culture was considered to be contaminated if one or more of the following organisms were identified in only one of a series of blood culture specimens: coagulase-negative *Staphylococcus* species, *Propionibacterium acnes*, *Micrococcus* species, "viridans"-group streptococci, *Corynebacterium* species, or *Bacillus* species. A blood culture series was defined as one or more specimens collected serially within a 24-hour period to detect a bacteraemic episode.

Data analysis

Data are presented as numbers with percentages and medians with interquartile ranges (IQR). Predictors of mortality were identified by means of logistic regression. A p-value < 0.05 was considered statistically significant.

RESULTS

Between April 2008 and April 2009, we identified 403 patients (207 males, 51.4%) with fever, presenting at the ED. Median age was 52 years (IQR 32 − 71 years). A total of 223 patients (55.6%) were hospitalized, 32 patients (7.9%) died and 18 patients (4.5%) were admitted to the Intensive Care Unit. Of the deceased patients, 20 (62.5%) died from a proven bacterial infection, 2 (6.3%) of a suspected bacterial infection and one of a viral infection (HIV; no positive bacterial cultures, no other indication of bacterial infection). Six patients (18.6%) died without a clear diagnosis. Except for older age, no predicting factors for mortality could be identified. Mortality was not correlated with specific pathogens or diseases.

In 129 febrile patients (32.0%), infection was proven. Most of the proven infections were bacterial infections (84.4%); a small number of viral infections (5.4%) and parasitic or fungal infections (10.0%) could be identified. When combining proven and suspected infections, 257 patients (48.6%) were diagnosed with an infectious cause of fever. The majority of the patients with a suspected but non-confirmed infectious cause of fever were discharged with suspected viral syndromes.

Twenty-one patients (5.2%) were discharged with a certain non-infectious diagnosis. In these patients, the most frequently observed cause of fever was malignancy. One hundred and seventy-two patients (42.7%) were discharged without a clear diagnosis.

Table: Patient characteristics of a cohort of febrile patients presenting at the emergency department of the St Elisabeth Hospital, Curaçao

Characteristic	n = 403
Median age (IQR) – yrs	52 (32 – 71)
Female sex – n (%)	196 (49)
Race or ethnic group – n (%)	
Black	340 (84)
Hispanic	29 (7)
White	27 (7)
Asian	7 (2)
Hospitalized – n (%)	223 (56)
Mortality – n (%)	32 (8)
Intensive Care admission – n (%)	18 (4)
Proven infection – n (%)	150 (37)
Proven + suspected infection – n (%)	257 (64)
Patients receiving antibiotics – n (%)	171 (42)

The most frequently reported diagnosis, both at presentation and at discharge, was bacterial pneumonia, caused by *Klebsiella pneumoniae* in 92% of cases when a pathogen could be isolated. At presentation, 'viral syndromes not otherwise specified' were reported in 34 patients (8.4%), in particular during the wet season. Most of the patients presenting with suspected viral syndromes were not hospitalized and were lost to follow-up; therefore, a certain final diagnosis could not be made. On clinical grounds, dengue fever was suspected in almost all of these cases; however, only one case was serologically proven. Urinary tract infections and urosepsis, mostly caused by *Escherichia coli* (*E coli*), *Proteus mirabilis* and *K pneumoniae* were the third most common diagnoses at presentation and accounted for 29% of all final diagnoses. Four patients were diagnosed with HIV. Malaria was reported in three cases; tuberculosis was not seen.

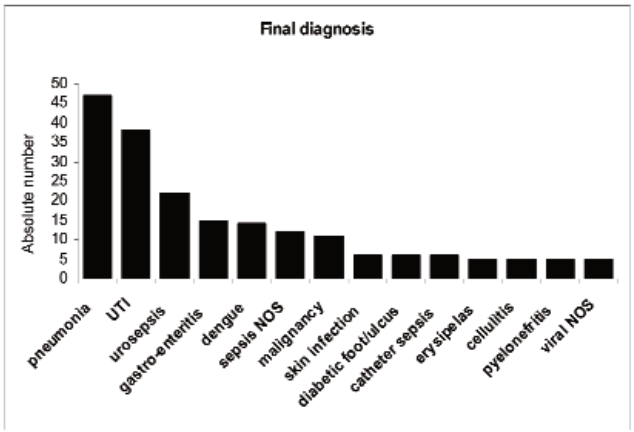

Fig. 1: Most frequently reported final diagnoses in a cohort of febrile patients presenting at the ED of the St Elisabeth Hospital, Curaçao.

In 183 patients (45.4%), blood cultures were obtained. Eighty-three blood cultures (45.4%) showed bacterial growth. However, 33 blood cultures were deemed contamination, leaving 27.3% of the cultures positive with a likely pathogen. Eighty-seven urine cultures were obtained, with 64 (73.6%) positive. Twelve sputum cultures were obtained, with 7 (58.3%) positive.

The most common bacteria in the blood cultures were *E coli*, *Staphylococcus aureus* and *K pneumoniae*, respectively. The most common bacteria in the urine cultures were *E coli*, *K pneumoniae* and *Enterococcus faecalis*, respectively. No extended spectrum β-lactamase (ESBL)-producing bacteria or methicillin-resistant *Staphylococcus aureus* (MRSA) were found.

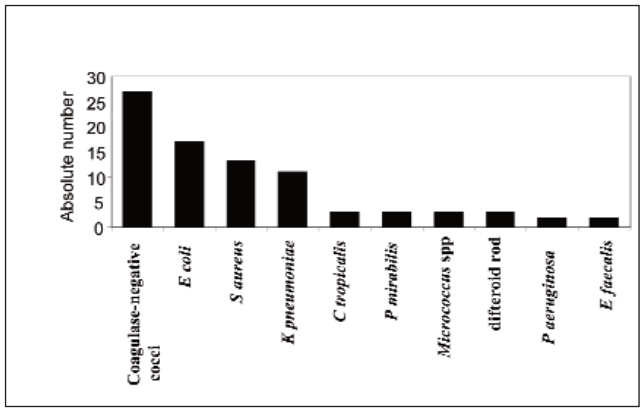

Fig. 2: Top 10 cultured micro-organisms in the blood of patients with infectious fever, presenting at the ED of the St Elisabeth Hospital, Curaçao.

In 163 patients (40.4%), the diagnosis at presentation was similar to the final diagnosis. One hundred and seventy-one (42.2%) patients were prescribed antibiotics. Of these patients, 107 (62.6%) either had a proven or a suspected bacterial infection in retrospect; 14 patients (8.2%) either had a proven or a suspected viral infection also in retrospect. Six patients (3.5%) were prescribed antibiotics, whereas the final diagnosis was non-infectious.

Many patients received empirical antibiotic therapy, with amoxicillin-clavulanate prescribed in most cases of suspected pneumonia, accounting for 27.4% of all antibiotic prescriptions. Cefuroxime was prescribed mostly in UTI, accounting for 15.0% of all antibiotic prescriptions. Piperacillin-tazobactam was prescribed in almost all febrile cases without a clear initial diagnosis, accounting for 14.2%.

DISCUSSION

This is the first study to systematically describe the aetiology and outcome of febrile illness at the ED on a Caribbean island. We found a high mortality rate of almost 8% in this cohort, underscoring that fever as a symptom at the ED should be taken seriously. Although no studies focussing on mortality in febrile patients have been undertaken in this area of the world, the mortality rate is comparable with earlier findings in a Spanish study and is much lower than found earlier in an African and Asian study (2, 5, 6).

Although Curaçao is a tropical island, not many typical tropical infections were seen. During the wet season, many patients presented to the ED with fever, myalgia, arthralgia and thrombopenia and were diagnosed with probable dengue fever on clinical grounds. Due to the self-limiting character of dengue fever, most often no paired serological samples were obtained. However, in a small parallel study in the same time period, 9 out of 23 patients with clinically suspected dengue fever were diagnosed with dengue fever by means of polymerase chain reaction (PCR) on blood during the acute phase (Limper *et al*, unpublished results), suggesting that some of the 34 patients, diagnosed with 'viral syndromes not otherwise specified', may have been suffering from dengue fever.

No case of tuberculosis was observed. Although malaria is endemic in surrounding countries (8, 9) only three cases of malaria were reported, which were all imported.

In concordance with earlier data, we found a relatively high number of bacterial infections, with pneumonia and urinary tract infections as the most common cause of fever (10). One in 20 patients presenting with fever did not have an infectious disease. As blood cultures were obtained in only 45% of febrile patients at the ED, the number of bacterial infections might be an underestimation. However, an earlier Australian study also showed a considerable amount of non-infectious causes of fever at the ED (1).

We found a surprisingly high number of *K pneumoniae* infections, both in the respiratory and in the urinary tract. Although *K pneumoniae* is a common finding in urinary tract infections, it is a far less common cause of pneumonia worldwide (11). One earlier Caribbean study, focussing on sputum cultures of patients with pneumonia in Trinidad, also showed remarkably low presence of *Streptococcus pneumoniae*, with an incidence of *K pneumoniae* of 1−5% and the highest incidence for other Gram-negative pathogens (12). Ecological studies show that *K pneumoniae* is a commonly found microbe in the neighbouring ocean (13); one might speculate that this results in a higher infection rate with *Klebsiella pneumoniae* compared to other areas. However, no further evidence for this association could be found. Another explanation may be the high and still rising prevalence of diabetes mellitus in the Caribbean, which is known to be associated with *K pneumoniae* infections (14).

Hardly any antibiotics were prescribed for patients with eventual viral infection or non-infectious fever. However, in patients who were not hospitalized, medical therapy was not always recorded, leading to a possible underestimation of antibiotics prescriptions. Furthermore, no information on out-of-hospital antibiotic use was available. Antibiotic guidelines have been developed in the St Elisabeth Hospital, but are not used uniformly and are partly based on European data, due to a lack of local data. This may explain the frequent use of broad spectrum antibiotics.

Some limitations in this study have to be noted. Firstly, a considerable number of patients were discharged without a clear diagnosis. With respect to viral disease, only dengue-serology was obtained on a regular basis. Paired serological samples were often not obtained. Throat swabs for PCR were not performed, resulting in an underestimation of viral airway infections in particular. Nuclear imaging is not possible in Curaçao. Furthermore, the existing diagnostic tools are not being used in an optimal way.

Secondly, a certain diagnosis of non-infectious disease is difficult to make, as such the absence of microbial pathogens either reflects non-infectious disease or a failure of the diagnostic process. Since blood cultures were obtained in less than half of the patients, exclusion of bacterial disease remains difficult.

Although the infrastructure for diagnosing infectious diseases in Curaçao is well-developed, many patients are treated empirically, without a proven final diagnosis. In particular, during the dengue season, patients with systemic viral symptoms are almost uniformly registered as dengue patients, whereas other viral diseases may be present as well.

This study shows that, although infection is often suspected in patients with fever, fever caused by non-infectious disease is common in a Caribbean cohort of ED patients. Furthermore, mortality numbers in patients presenting with febrile disease are considerably high, underlining once more the importance of fast and adequate diagnostics in this population.

This first description of the epidemiology of febrile disease in an ED of a Caribbean island contributes to a better insight into the prevalence of infectious diseases in the region. As thorough knowledge of the epidemiology of infectious diseases and microbial resistance data are the hallmarks of a well-balanced antibiotics policy, this study will hopefully lead to a more restricted use of antibiotics in the area, thus diminishing chances of antimicrobial resistance. Future studies should focus on the continuous monitoring of epidemiology, combined with resistance data. Only by doing this, a sensible antibiotics policy can be established.

REFERENCES

1. Knott JC, Tan SL, Street AC, Bailey M, Cameron P. Febrile adults presenting to the emergency department: outcomes and markers of serious illness. Emerg Med J 2004; **21:** 170−4.
2. Nawar EW, Niska RW, Xu J. National Hospital Ambulatory Medical Care Survey: 2005 emergency department summary. Adv Data 2007; **386:** 1−32.
3. Archibald LK, McDonald LC, Nwanyanwu O, Kazembe P, Dobbie H, Tokars J et al. A hospital-based prevalence survey of bloodstream infections in febrile patients in Malawi: implications for diagnosis and therapy. J Infect Dis 2000; **181:** 1414−20.
4. de Lavaissiere M, D'Ortenzio E, Dussart P, Fontanella JM, Djossou F, Carme B et al. Febrile illness at the emergency department of Cayenne Hospital, French Guiana. Trans R Soc Trop Med Hyg 2008; **102:** 1055−7.
5. Murdoch DR, Woods CW, Zimmerman MD, Dull PM, Belbase RH, Keenan AJ et al. The aetiology of febrile illness in adults presenting to Patan hospital in Kathmandu, Nepal. Am J Trop Med Hyg 2004; **70:** 670−5.
6. Ortega M, Almela M, Martinez JA, Marco F, Soriano A, Lopez J et al. Epidemiology and outcome of primary community-acquired bacteremia in adult patients. Eur J Clin Microbiol Infect Dis 2007; **26:** 453−7.
7. Lin JN, Tsai YS, Lai CH, Chen YH, Tsai SS, Lin HL et al. Risk factors for mortality of bacteraemic patients in the emergency department. Acad Emerg Med 2009; **16:** 749–5.
8. Rodulfo H, de Donato M, Quijada I, Pena A. High prevalence of malaria infection in Amazonas State, Venezuela. Rev Inst Med Trop Sao Paulo 2007; **49:** 79−85.
9. Valero-Bernal MV. Malaria in Colombia: retrospective glance during the past 40 years. Rev Salud Publica (Bogota) 2006; **8:** 141−9.
10. Paran Y, Yablecovitch D, Choshen G, Zeitlin I, Rogowski O, Ben-Ami R et al. C-reactive protein velocity to distinguish febrile bacterial infections from non-bacterial febrile illnesses in the emergency department. Crit Care 2009; **13:** R50.
11. Higgins K, Singer M, Valappil T, Nambiar S, Lin D, Cox E. Overview of recent studies of community-acquired pneumonia. Clin Infect Dis 2008; **47 (Suppl 3):** S150−6.
12. Nagalingam NA, Adesiyun AA, Swanston WH, Bartholomew M. A cross-sectional study of isolates from sputum samples from bacterial pneumonia patients in Trinidad. Braz J Infect Dis 2005; **9:** 231−40.
13. Santoro M, Hernandez G, Caballero M. Aerobic bacterial flora of nesting green turtles (Chelonia mydas) from Tortuguero National Park, Costa Rica. J Zoo Wildl Med 2006; **37:** 549−52.
14. Aschner P. Diabetes trends in Latin America. Diabetes Metab Res Rev 2002; **18 (Suppl 3):** S27−S31.