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Evaluación de la notificación del dengue durante una epidemia, Colombia

ABSTRACT

OBJECTIVE: To assess the validity of dengue fever reports and how they relate to the definition of case and severity.

METHODS: Diagnostic test assessment was conducted using cross-sectional sampling from a universe of 13,873 patients treated during the fifth epidemiological period in health institutions from 11 Colombian departments in 2013. The test under analyses was the reporting to the National Public Health Surveillance System, and the reference standard was the review of histories identified by active institutional search. We reviewed all histories of patients diagnosed with dengue fever, as well as a random sample of patients with febrile syndromes. The specificity and sensitivity of reports were estimated for this purpose, considering the inverse of the probability of being selected for weighting. The concordance between reporting and the findings of the active institutional search was calculated using Kappa statistics.

RESULTS: We included 4,359 febrile patients, and 31.7% were classified as compatible with dengue fever (17 with severe dengue fever; 461 with dengue fever and warning signs; 904 with dengue fever and no warning signs). The global sensitivity of reports was 13.2% (95%CI 10.9;15.4) and specificity was 98.4% (95%CI 97.9;98.9). Sensitivity varied according to severity: 12.1% (95%CI 9.3;14.8) for patients presenting dengue fever with no warning signs; 14.5% (95%CI 10.6;18.4) for those presenting dengue fever with warning signs, and 40.0% (95%CI 9.6;70.4) for those with severe dengue fever. Concordance between reporting and the findings of the active institutional search resulted in a Kappa of 10.1%.

CONCLUSIONS: Low concordance was observed between reporting and the review of clinical histories, which was associated with the low reporting of dengue fever compatible cases, especially milder cases.

DESCRIPTORS: Dengue, epidemiology. Epidemics, statistics & numerical data. Disease Notification. Sensitivity and Specificity. Epidemiological Surveillance.

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RESUMEN

OBJETIVO: Evaluar la validez de la notificación de casos de dengue y su correspondencia con las definiciones de caso y de gravedad.

MÉTODOS: Evaluación de prueba diagnóstica con muestreo transversal a partir de un universo de 13.873 pacientes atendidos durante quinto periodo epidemiológico en instituciones de salud de 11 departamentos de Colombia, en 2013. La prueba en evaluación fue la notificación al Sistema Nacional de Vigilancia en Salud Pública y el estándar de referencia fue la revisión de historias identificadas mediante búsqueda activa institucional. Se revisó todas las historias de pacientes con diagnóstico de dengue y una muestra aleatoria de pacientes con síndromes febriles. Se estimó especificidad y sensibilidad de notificación ponderando por el inverso de la probabilidad de ser seleccionado. Se calculó la concordancia entre notificación y los hallazgos de la búsqueda activa institucional usando el estadístico Kappa.

RESULTADOS: Se incluyeron 4.359 pacientes febriles, 31,7% fueron clasificados compatibles con dengue (17 con dengue grave; 461 con dengue y signos de alarma; 904 con dengue sin signos de alarma). La sensibilidad global de la notificación fue 13,2% (IC95% 10,9;15,4) y la especificidad 98,4% (IC95% 97,9;98,9). La sensibilidad varió de acuerdo con la gravedad: 12,1% (IC95% 9,3;14,8) en pacientes con dengue sin signos de alarma; 14,5% (IC95% 10,6;18,4) en aquellos con dengue y signos de alarma y 40,0% (IC95% 9,6;70,4) en aquellos con dengue grave. La concordancia entre la notificación y los hallazgos de la búsqueda activa institucional mostró Kappa de 10,1%.

CONCLUSIONES: Se observó baja concordancia entre la notificación y la revisión de historias clínicas, que estuvo asociada a baja notificación de los casos compatibles con dengue, especialmente aquellos menos graves.

DESCRIPTORES: Dengue, epidemiología. Epidemias, estadística & datos numéricos. Notificación de Enfermedad. Sensibilidad y Especificidad. Vigilancia Epidemiológica.

INTRODUCTION

Dengue fever is an arthropod-transmitted viral disease having the greatest epidemiological, social, and economic impact. It is an increasing threat to global public health.[8,9] Since the 1980s, the incidence of dengue fever has increased in America, with a mortality rate that has tripled every decade.[5,17] Colombia is not unfamiliar with this situation and has a continuous epidemic, affecting the population residing ≤ 2,200 meters above sea level.[a]

To determine the magnitude of the problem and to guide and evaluate public health interventions, a reliable surveillance system is required to allow valid estimation of the damage caused by the disease, as well as the changing patterns of morbidity and mortality. However, previous studies have identified problems that may affect the notifications of dengue fever cases, thus compromising the validity of the information obtained by the system.[3,11,12] The lack of consensus between clinical and laboratory diagnosis,[11,12] as well as the poor compliance to the severity classifications,[3] has been particularly suggested.

The systematic assessment of activities regarding dengue fever surveillance is necessary. Therefore, the purpose of this study was to evaluate the validity of dengue fever case reporting and the relation to case definition and severity.

METHODS

Test diagnostic assessment was performed with cross-sectional sampling. The reporting to the Public

[a] Instituto Nacional de Salud. Informe del evento dengue decimo periodo epidemiológico año 2013. Available from: http://www.ins.gov.co/lineas-de-accion/Subdireccion-Vigilancia/Informe%20de%20Evento%20Epidemiolgico/DENGUE%202013.pdf

Health Surveillance System (PHSS) was considered as the test under evaluation, and the classification of patients according to the criteria by the World Health Organization (WHO)[20] was considered the test of reference (gold standard) by reviewing their medical records obtained by active institutional search (AIS). This type of search provided external data to the reports, as recommended for the evaluation of surveillance systems.[7]

The study population was patients with acute febrile illness (AFI) of unknown origin who visited health institutions from 11 endemic cities of different Colombian states. Such cities were prioritized by the National Institutes of Health and the Ministry of Health and Welfare because they were in an outbreak situation since the first trimester of 2013. In every city, health institutions (primary units for data generation: UPGD) that regularly reported the highest number of dengue fever cases were selected.

The study population was represented by the AFI cases admitted to each institution during the fifth epidemiological period (epidemiologic week, EW 17-20) who met the inclusion criteria: at least one diagnosis checked in the individual records service (RIPS), according to the International Statistical Classification of Diseases and Health Related Problems, tenth revision (ICD-10) ["virosis" or unspecified viral infection (B349), unspecified fever (R509), relapsing fever (A689), Hemorrhagic fever with renal syndrome (A985), dengue fever (A90X) or dengue hemorrhagic fever (A91X)]; and diagnosis of acute illness characterized by fever lasting less than seven days.

In every city, all dengue fever diagnosed cases (A90X and A91X) were selected for the review, and a sample of approximately 400 medical histories among the total identified AFI cases (B349, R509, A689, and A985) was obtained by random simple sampling with proportional distribution to the number of medical appointments in every institution. The probability of inclusion was constant for the institutions within the same city, but it varied among different cities. In addition, the probability of inclusion was inversely proportional to the number of AFI cases reported by the total number of selected institutions.

The clinical history of each selected patient was reviewed, and the signs, symptoms, and CBC findings were recorded using a standardized instrument, including the OMS criteria to define the severity.[20] The patients were organized in one of the following categories: dengue fever with no warning signs (WS) – acute febrile disease, < 7 days, with two or more of the manifestations (including headache, retro-orbital pain, myalgia, arthralgia, rash, or exanthema); dengue fever with WS – patient with at least one of the abovementioned manifestations and any of the WS (including intense and continuous abdominal pain, persistent vomiting, drowsiness and/or irritability, postural hypotension, painful hepatomegalyia > 2 cm, decreased diuresis, temperature drop, mucous hemorrhage, abrupt drop in platelet count (< 100,000) associated with hemoconcentration); severe dengue fever – patient with some of the previous definitions and any of the complications {including severe plasma exudation, which leads to shock syndrome or fluid accumulation with respiratory difficulty, such as pleural effusion, ascites, pericardial effusion, severe hemorrhaging, serious organ damage [including myocarditis, encephalitis, hepatitis (transaminases > 1,000), acalculous cholecystitis, acute kidney failure or damage to other vital organs]}; dengue fever mortality; and patients with no dengue fever (did not meet the criteria of the previous categories).

The definitions above[20] are currently used for the surveillance of dengue fever in Colombia. The application of this classification in the clinical records selected by AIS was considered to be the reference standard regardless of whether there was confirmation of infection by laboratory tests.

The patients included in this study, who were reported for dengue fever, were identified in the PHSS records; if they were reported, the severity groups were identified by reporting institutions. To link the databases, i.e., to identify the individuals reported to PHSS, the identification number was used (citizenship card for adults and the unique personal identification number (UPIN) for individuals under 18 years of age).

The study population was described according to demographic and clinical variables, and the distribution of its origin. The relation between the patterns of dengue fever case reports to PHSS and the classification obtained by reviewing medical records was evaluated.

Two approaches were considered:

a) Considering the review of histories identified by AIS and the reports to SIVIGILA as two different and independent ways of measuring the frequency of the illness and the classification of its severity, we measured the concordance between these two surveillance strategies by calculating the Kappa statistics. A perfect concordance would be observed if no patients classified as not infected with dengue fever were reported during AIS, and in addition, if all patients compatible with dengue fever were reported, following the same classification obtained by the review of clinical histories. The weighted value of Kappa was calculated, assigning the value of 0.5 to the diagonals adjacent to the main value. Furthermore, the value of Kappa for the classification of the severity was estimated by

considering only the patients reported and included in one of the dengue fever categories during AIS.

b) The second approach followed a design of criterion standard validation study. The classification of cases based on the review of clinical histories was considered as the reference standard; the specificity, sensitivity, and the positive and negative predicted values (PPV and NPV) of reporting to SIVIGILA were estimated. The reports of patients were considered to be valid if they met any of the dengue fever definitions, regardless of whether or not there was consensus on the classification of severity. The probability of being selected varied between cities and was higher for patients with diagnostics of dengue fever; therefore, weights were calculated using the inverse of probability of being selected. The global estimation of validity indicators was performed and 95% confidence intervals (95%CI) were calculated.

The relation between the severity of dengue fever and the probability of being reported was evaluated as secondary analysis. Reporting was considered the dependent variable, whereas severity ratings during the AIS were taken as the independent variable. The reference category was the group with no dengue fever. The hypothesis that the notification of dengue fever is influenced by the severity of the disease was evaluated. Prevalence ratios (PR) were used as a measure of association, and binomial regression was applied to estimate and to adjust for age and sex variables.

RESULTS

In total, 13,873 patients were identified with ICD-10-compatible diagnostics, including 265 with diagnosis of dengue fever (A90X and A91X). From the patients with other diagnosis (n = 13,608), a sample with 4,094 SFA patients was obtained. As a result, 4,359 cases originating from 45 institutions from 11 territorial entities (Table 1) were reviewed. When OMS criteria were applied, 2,977 patients were considered not infected with dengue fever; 904 were classified as having dengue fever with no WS; 461 were classified as having dengue fever with WS; and 17 were classified as having severe dengue fever.

The average age of the patients classified as having dengue fever (including all categories of severity) was 27.1 years (mean of 18 years). Of these, 42.0% presented in patients < 14 years old and 2.4% in patients < 1 year old. A percentage of 40.4% corresponded to women and 59.6% to men. Among the patients, 63.2% scheduled an appointment within the first three days of the illness; 31.1% between the fourth and seventh day; and 5.7% had no information regarding the number of days after fever onset.

The application of OMS criteria revealed 1,382 patients compatible with dengue fever; among them, 210 were reported to SIGIVILA, including 135 who were reported as having dengue fever with no WS, 61 as having dengue with WS, and 14 as having severe dengue fever (Table 2).

Table 1. Distribution of the study population and sample selected by territorial entity. Colombia, 2013.

Territorial entity[a]	Number of selected institutions	ICD-10 Diagnosis[b]		AFI Sample	Revised histories (Dengue fever + AFI Sample)
		Dengue fever (A90X, A91X)	Others AFI (B349, R509, A689, A985)		
Bucaramanga	7	58	1,524	419	477
Magdalena	6	6	1,238	434	440
Cali	5	47	1,007	425	472
Girardot	5	44	1,064	382	426
Villavicencio	5	0	679	325	325
Neiva	4	2	4,652	472	474
Cartagena	4	0	888	332	332
Valledupar	3	2	1,516	325	327
Ibagué	3	0	248	244	244
Cúcuta	2	3	386	339	342
Riohacha	1	103	406	397	500
Total	45	265	13,608	4.094	4,359

[a] Corresponds to the city where the information was obtained, except for the department of Magdalena (which obtained information of 4 municipalities).
[b] Search of medical code records of the tenth version of the International Classification of Diseases (ICD-10) was used in diagnostics: dengue fever (A90X); hemorrhagic dengue fever (A91X); viral infection, unspecified (B349); fever, unspecified (R509), relapsing fever, unspecified (A689), hemorrhagic fever with renal syndrome (A985).

Although there was a global consensus of 69.0%, this was attributed to the high number of unreported non-dengue cases (Table 2), which represented 67.0% of all patients. This corresponded to Kappa statistics of 10.0% and weighted Kappa reaching 11.5%. On the other hand, we observed a concordance percentage of 57.9% and a Kappa value of 20.9% regarding the severity classification of the reported patients.

High specificity of 98.4% (95%CI 97.9;98.9) was observed when estimating the indicators of validity. The predictive values were approximately 75.0% (PPV = 74.9%; 95%CI 68.1;81.6; NPV = 75.9%; 95%CI 74.3;77.4). The global report sensitivity was 13.2% (95%CI 10.9;5.4) with values of 12.0% (95%CI 9.3;14.8) for dengue fever with no WS, 14,5% (95%CI 10,6;18,4) for dengue fever with WS, and 40.0% (95%CI 9.6;70.4) for severe dengue fever.

The probability of being reported was multiplied by 7.5 (95%CI 5.2;11.1) for the patient who met the criteria for dengue fever with no WS, by 9.1 (95%CI 6.1;13.6) for the patient who met the criteria for dengue fever with WS, and by 25.1 (95%CI 11.9;52.9) for the patient who met the criteria for severe dengue fever, when compared with patients without dengue. This ratio was maintained after the adjustment to variables of age and gender (Figure).

DISCUSSION

Dengue has become a growing public health problem that exceeds the capabilities of control within endemic countries. This study was conducted in an outbreak situation in different territorial entities of an endemic country where more than 80.0% of the population is at risk of contracting the infection.[a]

The main finding of this study is the low concordance between reporting to the surveillance system and the systematic application of the clinical definitions suggested by OMS to identify and classify dengue fever. If we consider these internationally adopted definitions as a reference standard, the low concordance would be explained by the low sensitivity to reporting, with sub-registration > 85.0% of dengue fever compatible cases.

This problem has already been reported in literature for different scenarios.[4,6,10,15,16,18,19] A study conducted at Ibagué, Colombia, reported a sensitivity of 11.0%, a value approaching the estimation by this study (13.2%), for reporting suspicious dengue fever cases received by the emergency services during the second dengue fever epidemic that occurred between 1995 and 1997.[3] However, the sensitivity varies broadly between endemic countries. To compare them, we used the expansion factor (EF), which is the inverse of sensitivity and corresponds to the value by which the reported cases should be multiplied to obtain a better estimation of such cases.[19]

For Colombia, the EF would be approximately 7.6 (inverse of 13.2%), according to the results of this study. In other Latin American countries, wide variations are reported. In Brazil, the EF is estimated as 1.6 for hospitalized cases, a value that contrasts the EF of > 14 estimated for Nicaragua in the last decade.[18] The EF has also been reported to vary according to the severity of the disease, and its value is found to be higher for milder cases.[6,18] This is in accordance with the observations of this study, where the EF values were 2.5, 6.9, and 8.3, for the groups with severe dengue fever, dengue fever with no WS, and dengue fever with WS, respectively.

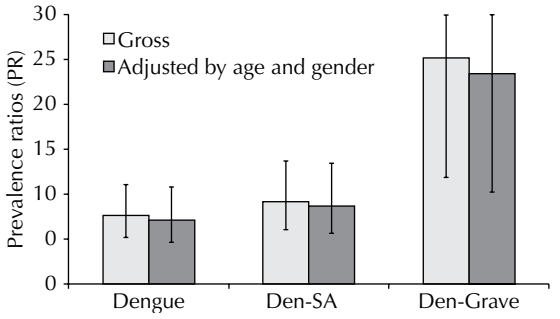
In addition to considering reporting problems, the low concordance could put in question the usefulness of the case definitions and severity proposed by the OMS. The severity classification was recently revised in an attempt to make it more functional and a representative of the need for specialized support.[20] As a result, OMS integrated the concept of severe dengue, which is specific to conditions that require procedures of high complexity, such as

Table 2. Distribution of patients with acute febrile illness according to World Health Organization[20] criteria and notification to Public Health Surveillance System. Colombia, 2013.

Notification status	Classification of patients using WHO criteria				Total
	No dengue fever	Dengue without WS	Dengue fever with WS	Severe Dengue fever	
Not notified	2,926[a]	817	397	9	4,149
Dengue fever without WS	32	64[a]	37	2	135
Dengue fever with WS	18	21	22[a]	0	61
Severe Dengue fever	1	2	5	6[a]	14
Total	2,977	904	461	17	4,359

WS: Warning signs

[a] Percentage of overall agreement: 69.2% (Expected: 65.8%); Kappa: 10.06% (Standard Error: 0.72%); Weighted Kappa: 11.5% (Standard Error: 0.76%).



Den-SA: Dengue fever with warning signs; Den-Grave: Severe Dengue fever
Error bars show the confidence intervals of 95%, which were truncated at 30 for the group of severe dengue fever.

Figure. Relationship between dengue fever severity and the probability of being reported. Colombia, 2013.

resuscitation, transfusions, inotropic and respiratory support, or specific treatment for organ failure.[2]

This severity definition represents a small proportion of patients with dengue fever. This implies a restriction of its applicability, given that the majority of dengue fever infections do not require hospitalization or such interventions.[1,14] Consequently, the category for severe dengue fever seems a little insensitive in the characterization of disease damage in terms of total hospitalizations and socioeconomic losses caused by the disability.

Case definitions, with or without WS, define all febrile events as dengue fever suspects, with symptoms that are very unspecific, as they are common in other prevailing tropical diseases. Therefore, the case definitions have been widely criticized for their inability to discriminate between dengue fever and other SFA cases.[11] These public health surveillance tools have important limitations that can negatively affect their acceptance by health professionals who must apply them.

There are other obstacles to disease reporting, including difficulties in clinical diagnosis, administrative factors, and possible negative expectations regarding the reports. Previous studies have reported difficulties in identifying dengue fever in the first appointment, usually when complications have not yet arised.[11,12]

Furthermore, there are factors within the institutions that limit the access to health services and increase condition of social exclusion in populations without medical insurance. This happens regardless of the regulatory effects, for they favor their assistance within the General Health Social Security System (GHSSS). Because inequality is evidently caused by bureaucratic procedures, there is limited inter- and intrasectorial coordination, lack of resources to health service providers, and the excess of formalities for the assistance.[13]

The administrative factors, including the lack of time of professionals to fill-in forms, can reduce case reporting. Furthermore, it is plausible that health professionals have poor expectations regarding the reports. This is caused by the fact that only a small proportion of reported patients undergo laboratory tests and the incidence of serious complications is relatively small considering the volume of SFA patients that should be reported.

Reporting could be focused to the more serious patients who spend more time in inner hospital environment assessed by a greater number of health professionals, and who develop manifestations typically attributed to dengue fever. This could lead to the delayed identification of cases with potentially fatal complications, thus preventing the implementation of preventive measures at the early febrile stage.

The main limitation of this study is the retrospective collection of information. Therefore, it could possibly not identify relevant information for the classification of patients. In addition, this research does not include laboratory studies that allow the estimation of consensus between the corroborative evidence and the clinical perception represented by the clinical histories and in the ultimate report.

However, the identification of additional clinical data would probably evidence more unreported dengue fever-compatible patients. In addition, the absence of laboratory evidence does not invalidate the findings of poor consensus found between reporting and the systematic application of internationally suggested clinical definitions. This finding reveals an important barrier for the estimation of disease damage and the assessment of interventions, individual and community based, directed at reducing the damage caused by this priority disease.

The results of this study, which had a considerable number of fever cases from different regions of an endemic country, evidenced the lack of consensus between the reporting of dengue cases and the systematic application of the definitions proposed by the WHO. This could be associated with the low acceptance of these reference definitions, with difficulty in the diagnosis or with negative reactions toward public health surveillance processes. It is necessary to develop easily applicable strategies to identify and notify dengue fever cases, as well as to improve the surveillance system and support the enhancement of prevention and control measures.

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