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Surveillance of Dengue with Immune Enzematic Test UMELISA IgM Dengue Plus

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Abstract: *Introduction:* Dengue is an acute fever disease of sudden beginning, which is characterized by fever, cefalea, arthralgia, myalgia, rash, nausea, vomits and is caused by the Dengue virus that belongs to the *Flaviviridae* family, flavivirus genre and has four viral serotypes DEN -1, DEN - 2, DEN - 3, DEN – 4. It is transmitted by female mosquito bites from the *Aedes aegypti* genre and the *A. albopictus*. Medically, it constitutes the most important viral disease transmitted by anthropoid and the most important in terms of morbidity and mortality. Therefore, it is more important to assess the detection of antibodies IgM Dengue with immune enzymatic test UMELISA IgM Dengue plus in the surveillance of Dengue. *Material and Methods:* An observational study of transversal type was done from January to December 2017 in SUMA Laboratory of Advance Technology Hygiene, Epidemiology and Microbiology Provincial Center of Ciego de Ávila, Cuba to samples of specimen of serum that were collected from people with SFI from the 6th day of the beginning of symptoms to detect antibodies IgM against Dengue using immune enzymatic test UMELISA IgM Dengue plus. *Results:* The results are represented in graphs from January to December 2017. *Conclusions:* The month of greater reactivity was October with 25.99% and the municipalities more affected were Baraguá with 20%, Ciego de Ávila with 11.99%, Morón with 11.86%, and Ciro Redondo with 11.11% of reactivity which were municipalities with transmission. The positive and negative control serum of the test was under statistic control. The concordance between the tests was 86.60% and the prevalence for the UMELISA IgM DENGUE PLUS test was 10.32%.

Keywords: Dengue Survillance, UMELISA IgM PLUS DENGUE, ELISA IgM MAC, Unspecific Fever Symptoms

1. Introduction

Dengue is an acute fever disease with sudden outbrake [1-4], which is characterized by fever, headache, arthralgia, mialgia, rash, nausea, vomit and caused by the Dengue virus that belongs to the *Flaviviridae*family, flavivirus type which has four viral serotypes DEN -1, DEN - 2, DEN - 3, DEN – 4 [5-9]. It is transmitted by the female mosquito bite of the *Aedesaegypti*typeand the *A. albopictus* [1-9]. It constitutes a viral disease transmitted by anthropoids of major medical importance and the most important in terms of morbidity and mortality [10, 11]. In the last years, Dengue fever has reemerged accompanied by a wide geographical distribution of the virus as well as the mosquito, an increased epidemic activity, the development of hyper-endemicity, or co-circulation of different serotypes alike and the outbreak of the disease in new geographical zones [12]. Since 1998, it has become the most important tropical infectious disease, seconded by malaria, with an estimate of 2.5 billions of people and more than 100 countries in risk areas, 50-100 millions of cases annually, 500,000 hospitalized cases of hemorrhage fever with Dengue with 25,000 deaths every year [13, 14]. In the America region, Dengue has maintained a sustainable increase in the last 25 years, with epidemic outbreaks that are repeated in a cyclic way [13, 14]. During 2002, more than a million of cases has been reported, and in 2005, a discrete increase was estimated in respect to the two preceding years. Approximately, two fifth parts of the world population are in risk and more than 100 countries have suffered from Dengue outbreaks [14]. Nowadays,

Dengue continues being the most important emergent and reemergent disease becoming a health problem [1-15]; at the same time, other diseases such as Zika, Chikungunya and Yellow fever have incorporated which are transmitted by the same vector. As well as in the whole country, in Ciego de Ávila province epidemic events of sporadic outbreaks have occurred [11, 13], evidencing this as a serious health problem that negatively affects economy, since it originates high hospitalization costs, sick patients' assistance and emerging campaigns to control the vector [1-12]. Therefore, better insecticides, safe vaccines, new medicines and quick diagnosis methods are needed. Currently, direct tests like viral isolation, PCR-TR, NS1 detection, indirect tests of specific IgM, IgG antibodies detection are used for lab surveillance [1]. It is known that the detection of the second confirms cases and by being detected the first against the Dengue virus, they indicate active or current infection. This type of antibodies appears early and generally at the sixth day of beginning the symptoms, and they decrease approximately by day 30; though they may be detected in a longer period of time, i.e. more than 90 days in some cases [15-25]. Therefore, UMELISA DENGUE IgM Plus, heterogeneous immunoenzematic clinic trial of capturing type is used in our country since 1990 [15], and has been introduced in our province since 2005, for the detection of specific IgM antibodies against the four Dengue serotypes in human serum specimens with Unspecific Febrile Syndromes (UFS), being lab and epidemiological surveillance of great importance with the use of UMELISA DENGUE IgM Plus which has a sensitivity and specificity over 97% and 94%, respectively [15]. This test is used for primary Dengue quest for it is a sensible, specific, fast and cheap method of vital importance to achieve an adequate surveillance to control the vector and stop viral transmission [26-31]; so this trial is very useful in the diagnosis of presumptive clinical cases of Dengue and as part of the epidemiological surveillance systems of this enterprise which operationalizes reactive trials as suspected cases of Dengue. That´s why it is important to consider the detection of Dengue IgM antibodies with UMELISA DENGUE IgM Plus immunoenzematic clinic trial during Dengue surveillance.

1.1. General Objective

Assess the detection of Dengue IgM antibodies with UMELISA DENGUE IgM Plus immunoenzematic clinic trial during Dengue surveillance.

1.2. Specific Objectives

Detection of reactivity with UMELISA DENGUE IgM Plus immunoenzematic clinic trial monthly.

Detection of reactivity with UMELISA DENGUE IgM Plus immunoenzematic clinic trial per municipality.

Report the behavior of positive internal control serum of the trial in the year as internal control of quality.

Assess the behavior of the parameter Repetitiveness of negative internal control serum of quality trial.

Determine the concordance between UMELISA DENGUE IgM Plus immunoenzematic clinic trial and ELISA MAC of the detection of Dengue IgM antibodies.

Determine the prevalence of the detection of Dengue IgM antibodies in the samples processed with UMELISA DENGUE IgM Plus trial.

2. Materials and Methods

An observational study of transverse type was done, from January to December of 2017 at Advance Technology SUMA Lab from Provincial Center of Hygiene, Epidemiology and Microbiology (PCHEM) in Ciego de Ávila, Cuba, of samples of serum specimens taken from people with UFS at the sixth day of the beginning of symptoms to detect IgM antibodies against Dengue using UMELISA DENGUE IgM Plus immunoenzematic clinic trial with the software for Strips Reader coupled with the shield/plate reader PR-521; intermediate washings were done with automatic plate washer of UMELISA MW-2001 Version 2.00. The total of processed MONOSUERO were 3218 patients and data were collected from the register of semi-automatized statistics of SUMA laboratory. The reactivity was calculated in percent with IC 95% per month and municipality. Concordance was calculated with kapp index between UMELISA DENGUE IgM Plus and ELISA MAC trial with 328 reactive samples and 160 samples as quality control of the 10% of sent negative samples at reference lab of Tropical Medicine Institute IPK in Havana city, Cuba.

These data were analyzed with the program for epidemiological analysis of tabulated data EPIDAT version 3.1 distributed by the Xunta de Galicia and the PHO. To report the behavior of positive internal control serum of the UMELISA IgM DENGUE Plus trial, the mean of 207 rounds, the standard deviation, the limits of inferior and superior control plus and minus two standard deviations were calculated with formula of calculus sheets Microsoft Office 2003, Excel.xls. The value of Repetitiveness of negative internal control serum was calculated at 95% of reliability which was of 2.7 and the results of the difference of the value of the maximum negative internal control serum minus minimum negative internal control serum were plottered in each round to observe if the trial is statistically under control. Data were processed with Intel Pentium Dual – Core – Incide^{TM}computer, Microsoft Windows^{XP} Operating System, and results were graphically represented.

3. Results

Figure 1 shows the reactivity percent with UMELISA DENGUE IgM Plus immunoenzematic clinic trial from January to December. It can be seen a reactivity of 18.34% with an IC95% (13.70 – 22.97) in the month of January, i.e. trailing a Dengue outbreak epidemiological event from the end of 2016 which was later controlled with sustainability actions from February to August 2017. It began in September with a reactivity of 12.86% with an IC95% (8.09 – 17.62), October with 25.99% with an IC95% (21.73 – 30.24) and November with a reactivity of 23.19% with an IC95% (18.59

-27.79). This second epidemiological even began to decrease by December with 9.92% of reactivity and an IC95% (4.42 – 15.43). Reactivity has significant difference among all months with a $p < 0.05$.

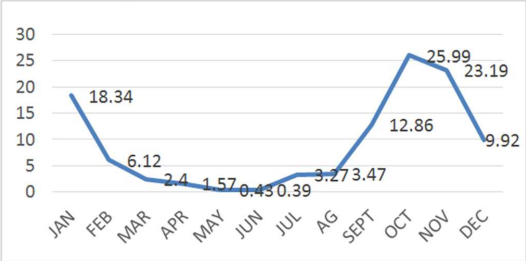

Figure 1. *Percent of Reactivity with UMELISA DENGUE IgM Plus Immunoenzematic Clinic Trial.*

Source: Semi-automatized Statistics Register of SUMA Laboratory from Hygiene, Epimediology and Microbiology Provincial Center.

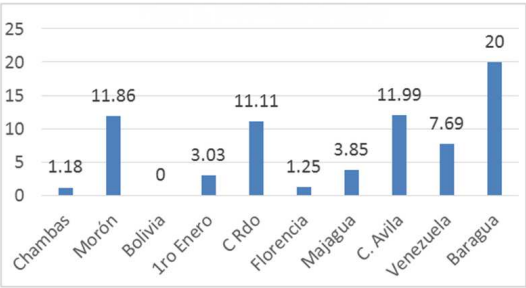

Figure 2. *Percent of Reactivity with UMELISA DENGUE IgM Plus Immunoenzematic Clinic Trial PER Municipalities from Ciego de Ávila province.*

Source: Semi-automatized Statistics Register of SUMA Laboratory from Hygiene, Epimediology and Microbiology Provincial Center.

Figure 2 shows the reactivity results per municipalities. It can be observed that four municipalities are more affected with significant difference $p < 0.05$ among all municipalities. The most affected are Baraguá with 20% and an IC95% (4.33 – 48.01); secondly, Ciego de Ávila municipality with a reactivity of 11.99% and an IC95% (10.58 – 13.41); later Morón with 11.86% and an IC95% (9.10 -14.60), and finally Ciro Redondo with 11.11% and an IC95% (0.28 – 48.25). It is important to highlight that Chambas municipality, 1ro de Enero, Florencia and Majagua municipalities had low reactivity and had no transmission; nevertheless, Bolivia municipality with 0% of reactivity is one of the municipalities that has never had any transmission and remains the same during the current year 2017 as in previous years because in there are no vectors in its ecology. [11]

Figure 3 shows the behavior of positive internal control serum with UMELISA DENGUE IgM Plus immunoenzematic clinic trial. It can be stated that with a level of reliability of 95%, the trial was statistically under control and that only 9 from 207 rounds executed in the whole year were out of the control limits (9/207) for a 35%, which is considered far below the 20% permissible to verify that the process is statistically under control.

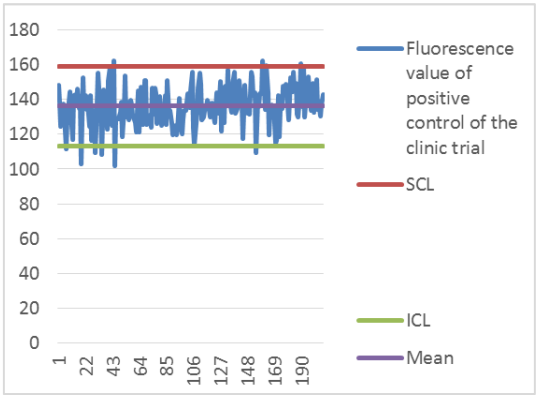

Figure 3. *Behavior of Positive Internal Control Serum with UMELISA DENGUE IgM Plus Immunoenzematic Clinic Trial.*

Source: Semi-automatized Statistics Register of SUMA Laboratory from Hygiene, Epimediology and Microbiology Provincial Center.

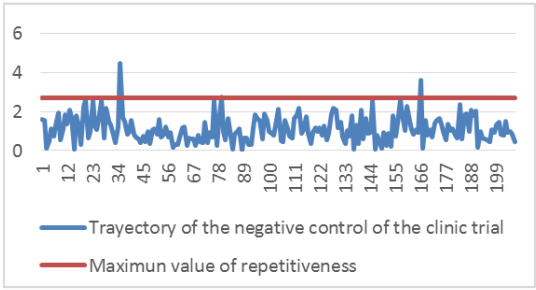

Figure 4. *Repetitiveness of Negative Internal Control Serum of UMELISA DENGUE IgM Plus Immunoenzematic Clinic Trial.*

Source: Semi-automatized Statistics Register of SUMA Laboratory from Hygiene, Epimediology and Microbiology Provincial Center.

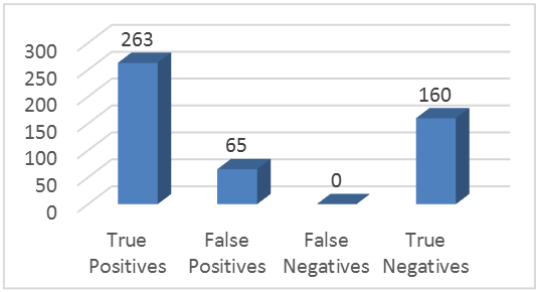

Figure 5. *Concordance Values between UMELISA IgM DENGUE PLUS Clinic Trial and and ELISA IgM Dengue MAC Trial.*

Source: Semi-automatized Statistics Register of SUMA Laboratory from Hygiene, Epimediology and Microbiology Provincial Center.

Figure 4 shows the repetitiveness of negative internal control serum trial, showing very good repeatability and that the process is statistically under control with a 95% reliability level and that it was only observed in the 207 executed rounds (2/207) for a 1.45% of points out of control.

Figure 5 shows the values for the calculus of concordance in the statistics program EPIDAT which was of 86.60% with Kappa index of 0.7252 and a standard error of 0.0305 with an IC95% of kappa index (0.6654 – 0.7858) and a $p < 0.05\%$. [15]

Calculated prevalence for UMELISA DENGUE IgM Plus clinic trial was of 10.32% with an IC95% (9.250 – 11.383); i.e. 332 reactive samples with the trial out of the 3218 processed samples in the year. [15]

4. Conclusions

October was the month with more reactivity in the year with 25.99% with an IC95% (21.73 -30.24) and the control actions began to be observed in December with reactivity decrease. The municipalities with higher reactivity were Baragúa (20%), Ciego de Ávila (11.99%), Morón (11.86%) and Ciro Redondo with (11.11%). In Bolivia municipality there was no transmission as in previous years.

It can be stayed that the 207 rounds with UMELISA DENGUE IgM Plus clinic trial for the assessment of positive and negative internal control serum trial were statistically under control with a reliability level of 95%. Concordance between UMELISA IgM DENGUE PLUS trial and ELISA IgM MAC trial for detection of IgM antibodies against Dengue was of 86.60%. Prevalence of UMELISA DENGUE IgM Plus trial was of 10.32%.

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