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Profile of hemogram and transaminases in dengue-suspected patients at a first-aid health unit

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ABSTRACT. Current retrospective analysis describes the laboratorial profile of patients hypothetically diagnosed with dengue at a First-Aid Health Unit in Recife, Pernambuco State, Brazil. Results of hemograms were assessed by counting platelets and transaminase dosages, in the first half of 2012. Further, 394 patients (252 females or 64% and 142 males or 34%) were listed, mostly during March and April. Hemograms with platelet counting was undertaken with 210 patients (53.3%) and hemogram plus transaminases dosages with 184 patients (46.7%). Thrombocytopenia, neutropenia and atypical lymphocytes occurred in both genders. Hematocrits were highest in males and transaminases were more altered in females. Patients attended at the health unit with clinical symptoms of classical dengue had a laboratory profile of non-specific exams which is a feature of infection by the dengue virus. Diagnosis could not be confirmed and the need of a fast test in the health unit services was mandatory. The above avoids dengue cases not being notified and treated or overestimated.

Keywords: dengue, complete hemogram, thrombocytopenia, transaminases.

Perfil do hemograma e das transaminases em usuários com suspeita de dengue em serviço de pronto atendimento

RESUMO. Estudo retrospectivo que objetivou descrever o perfil laboratorial dos usuários com hipótese diagnóstica de dengue em um Serviço de Pronto Atendimento (SPA) do Recife (PE). Foram avaliados resultados do hemograma com contagem de plaquetas e dosagem de transaminases, no primeiro semestre de 2012. Registraram-se 394 usuários, sendo 252 do sexo feminino (64%) e 142 do sexo masculino (36%). Hemograma com contagem de plaquetas foi realizado em 210 usuários (53,3%) e hemograma junto com dosagem de transaminases em 184 (46,7%). Trombocitopenia, neutropenia e linfócitos atípicos ocorreram em ambos os sexos. O hematócrito mostrou maior elevação em pacientes do sexo masculino. As transaminases estavam mais alteradas nas mulheres. Os usuários atendidos no SPA com sintomas clínicos de dengue clássica apresentaram perfil laboratorial de exames inespecíficos, característico de infecção pelo vírus da dengue, porém, o diagnóstico não pôde ser confirmado. Isto mostra a necessidade de implantação do teste rápido para dengue nos serviços de pronto atendimento, o que irá evitar que casos de dengue não sejam notificados e tratados, assim como outros sejam superestimados.

Palavras-chave: dengue, hemograma completo, trombocitopenia, transaminases.

Introduction

Dengue, a public health problem worldwide (BHATT et al., 2013), is a virus-caused disease, with *Aedes aegypti* as its main vector (LIMKITTIKUL et al., 2014; FERNANDES et al., 2014) and with four serum types known (DENV 1-4). Dengue cases during the last decades have risen in all countries and between 50 and 100 million of infections by the dengue virus occur every year in some 125 countries (WHO, 2013; PAPA et al., 2015). Endemic regions comprise the American continent, Southeast Asia and the Western Pacific, with more than 2.3 million people in 2010 (MURUGANANTHAN et al., 2014).

The dengue epidemiology has greatly modified during the last score of years and global distribution expanded to other geographical areas. Transmission intensity and the seriousness of infections have increased in regions in which it was already endemic (WILSON, CHEN, 2014). Demographic and social changes, such as population growth, urbanization and modern transport have contributed towards an increase in the occurrence and geographical

extension of the disease (GUZMAN et al., 2010; SABA et al., 2014).

With its tropical climate, high temperatures, high humidity and seasonal rainfall variations, Brazil has the adequate conditions for the reproduction and survival of the *A. aegypti* mosquitoes (TEIXEIRA et al., 2013). After a quickly controlled dengue epidemic in Boa Vista, Roraima State, Brazil in 1982 (OSANI et al., 1983) and an epidemic and subsequent propagation in Rio de Janeiro in 1986 (RODRIGUEZ-ROCHE; GOULD, 2013), occurrences of the diseases increased and in 2000 dengue infection was reported in 22 out of the 27 Brazilian states (TEIXEIRA et al., 2013). Between 2000 and 2010 new dengue cases reached the count of 4,507,946 in Brazil. Further, 254,73 cases were notified in the first six months of 2011 (OLIVEIRA et al., 2012) with the northeastern region tallying approximately one third of dengue cases in the country (LEITE et al., 2014).

Between 2010 and 2011, some 57,362 dengue cases were notified in 185 municipalities in the state of Pernambuco, Brazil, or rather, a 585.73% increase when compared with the number during the same period in 2009, with 8,365 cases in 49 municipalities (SILVA; NÓBREGA, 2012). The introduction of DENV in Recife, the capital city of the state of Pernambuco, was reported in the early 1980 (LEITE et al., 2014). In 2012 some 9,640 dengue cases were notified and during the same year DENV occurrences reached 487 cases per 100,000 inhabitants (BRASIL, 2014). At present, the four DENV serum types co-circulate in the region (LEITE et al., 2014).

DENV infection may cause a wide spectrum of symptoms even though some may remain asymptomatic or subclinical cases (GUZMAN; HARRIS, 2015). In its less severe form (classical dengue), the disease is characterized by fever, headache, fatigue, arthralgia, eye pain, nausea, skin rash and other symptoms. The most severe type of dengue is Hemorrhagic Dengue Fever (HDF) with bleeding, thrombocytopenia and plasma effusion which may develop into circulatory death, featuring the Dengue Shock Syndrome (DCS) and death (BRAGA et al., 2014; XAVIER et al., 2014).

Dengue is diagnosed by clinical-epidemiological (especially during epidemics) and laboratorial criteria. In the case of laboratory diagnosis, when confirmatory tests are not available, the hemogram is absolutely important especially in cases of hemorrhagic dengue where platelet ($< 100{,}000$ mm^{-3}) and hematocrit (a 20% increase or more for the reference rate) counts, coupled to other laboratory tests, such as Rumpel-Leede test and clinical exams, may confirm HDF (BRASIL, 2013).

A hemogram may show a characteristic profile and becomes a good ally not merely in diagnosis but also in the disease follow-up (OLIVEIRA et al., 2012, FUJIMORO; KOIFMAN, 2014). Other tests, such as hepatic enzyme dosage, are required when dengue with liver condition is suspected. Rise of aspartate aminotransferase hepatic (AST) and alanine aminotransferase (ALT) enzymes is common in acute infection cases by dengue and increases during the disease´s convalescence period (from the 7th to the 10th day) (LEE et al., 2012).

Hemogram with platelet counts is a great help in acknowledging the presence of hemorrhagic dengue since the decrease in lymphocytes and platelet counts are associated with this serious type of the disease (BRASIER et al., 2012). Current analysis describes the laboratory profile of patients with possible dengue diagnosis in a health service unit in Recife, Pernambuco State, Brazil.

Material and methods

Current retrospective study was undertaken in the First-Aid Health Unit of the Polyclinic and Maternity Professor Barros Lima (PMPBL) run by the Health Secretary of Recife PE Brazil. The polyclinic is a reference hospital for people suspected of dengue and attends about 7,200 people a month and 3,000 children in the children´s section.

All suspects with suggestive clinical syndromes for dengue were included, between February and July 2012. A suspected case of classical dengue may be defined as the patient with acute high fever, for a maximum 7-day period, with at least two of the following symptoms: headache, eye pain, myalgia, arthralgia, body weakness and exanthema. Besides the above symptoms, the patient must have been within the last fortnight in a region where dengue transmission has occurred or where *A. Aegypti* occurs (BRASIL, 2013).

Data were harvested from clinical files with the identification of the patients (name and number of register), the date when the laboratory tests were performed and their results within the study´s period. Inclusion criterion was the occurrence of dengue symptoms in people who frequented the health unit of the PMPBL. The diagnostic hypothesis had to be taken into account to request the hemogram with platelet counts and dosages of the ALT and AST hepatic enzymes.

The hemogram was performed in ABX Micros 60 (HORIBA ABX Diagnostic) with the following reference rates: global counts of leucocytes between 3.5 and 11.0x103 mm^{-3}; red globule counts between

3.8 and 6.5 x106 mm^{-3}; hematocrit 35 to 50%; hemoglobin between 11.0 and 16.5 g dL^{-1} and platelet counts between 150 and 450x103 mm^{-3}. For the differential counting of 100 cells, the equipment includes the following percentages within acceptable rates: segmented neutrophils between 43 and 76%; typical lymphocytes between 17 and 48%; monocytes between 4 and 10%. Counts were performed under an optic microscope to identify neutrophil rod cells, eosinophils and atypical lymphocytes and cells not counted by the ABX equipment, respectively at 4, 4 and 3% as normal limits. Hepatic enzyme dosage (AST and ALT) was undertaken by serum sample with BT 3000 plus device (Lab. Wiener) by the enzyme method and with reference rates between 0 and 38 U L^{-1} for ALT and between 0 and 42 U L^{-1} for AST.

Since suspects with altered hemogram and hepatic enzyme dosage could not confirm diagnosis for dengue at the PMPBL, they were invited to continue laboratory investigation with the specific test ELISA for dengue at the Municipal Laboratory Julião Paulo in Recife, Pernambuco State, Brazil. Current assay was approved by the Ethics Committee of the Faculdade Paula Frassinetti (CAAE 30544514.9.0000.5586).

Results

Three hundred and ninety-four people suspected of dengue were attended to. Females were higher than the number of males (252 females and 142 males, respectively). Laboratory tests comprised hemogram by 210 patients (53.3%) and hemogram plus transaminase dosage by 184 patients (46.7%). Thrombocytopenia, neutropenia and atypical lymphocytes occurred in both genders at similar percentages. Hematocrit increased in eight patients (2%) (Table 1). In the case of transaminases, ALT was altered in 20 patients (5%) and AST in 15 patients (3.8%) (Table 2).

Table 1. Main alterations in patients´ hemogram suspected of classical dengue attended to at the health unit in Recife, Pernambuco State, Brazil, 2012.

Changes in the hemogram	Total	
	n	%
Plateletopenia (< 150X10^3 L^{-1})		
Yes	27	6.8
No	367	93.2
Leucopenia (< 5.45x10^3 L^{-1})		
Yes	106	27
No	288	73
Neutropenia (< 3.5X10^3 L^{-1})		
Yes	62	16
No	332	84
Atypical lymphocytes		
Yes	29	7.4
No	365	92.6
Increase in hematocrit (≥ 50%)		
Yes	2	0.5
No	392	99.5

Table 2. Alteration of transaminase in patients suspected of dengue attended to at the health unit in Recife, Pernambuco State, Brazil, 2012.

Alterations in hepatic enzymes	Total	
	n	%
Alt (≥ 38 U)		
Yes	20	5
No	374	95
AST (≥ 42 U)		
Yes	15	3.8
No	379	96.2
AST/ALT (≥ 42 U and ≥ 38 U)		
Yes	38	9.7
No	356	90.3

Discussion

Alterations in the hemogram such as platelet counts and dosage of the hepatic enzymes ALT and AST are taken into account, plus the initial clinical symptoms of dengue. In fact, they are related to DENV pathogenic stance and the response of the human host to the virus. DENV may cause suppression in the bone marrow and leucopenia and link to platelet antigens causing the immunological destruction of platelets through antibodies (JAIN et al., 2013). The virus also causes the release of cytokines by monocytes and lymphocytes T, coupled to alterations in the vascular permeability and plasma overflowing. Results occur in hemoconcentration verified by an increase in hematocrits (DURÁN et al., 2010).

The infection´s acute immunological response may cause lesions to the liver with the consequent alterations of hepatic enzymes (NASCIMENTO et al., 2011). A moderate rise in transaminases (two to five times the normal limit) is a common factor in classical dengue, contrastingly to the hemorrhage dengue. Transaminases in the latter are higher as studies by Fujimoto and Koifman (2014) have shown. In the state of Acre, Brazil, 95% of the 267 patients suffering from hemorrhage had a variation of AST between 40.7 and 478.7 UI L^{-1} and a variation of ALT between 105.6 and 229.7 UI L^{-1}. Current assay demonstrates that hepatic enzymes mostly changed in females. One study showed higher rates of transaminases in males than in females although it was underscored that AST increase may be associated with alcohol consumption mostly associated to males (OLIVEIRA et al., 2012).

The alterations in the hemogram had only a slight percentage variation in males and females when the total count of leucocytes, number of platelets, counts of segmented neutrophils and

atypical lymphocytes and determination of hematocrits were taken into account, excepting total counts of leucocytes where leucopenia was higher in females. Several authors report that leucopenia is a common factor in dengue, albeit with great variations. The World Health Organization still considers it as one of the main bases in cases of dengue fever (NASCIMENTO et al., 2011; OLIVEIRA et al., 2012; PRAMILADEVI et al., 2013).

In the case of hematocrit increase, since hemoconcentration and plasma overflowing are symptoms of HDF and not determining factors of classical dengue, the hematocrit did not seem altered in the females under analysis. A slight alteration was detected in males. Increase occurred in only two cases (0.5%) and corroborates a study in the state of Minas Gerais, Brazil, in which only four (0.38%) out of 1,061 patients assessed in 2005-2006 experienced a rise in hematocrits (OLIVEIRA et al., 2012).

Although laboratory tests used in first-aid health units, such as hemogram and transaminase dosages, give a laboratory profile of the patient suspected of dengue, probably in its more acute phase, they do not provide a safe and differential diagnosis with other viroses. More specific tests, such as the ELISA test for the detection of NS1Ag, present in four DENV serum types and detected during the first days of the disease, are more useful in this case. In fact, it was one hundred per cent positive in a research in Rio de Janeiro in 2012 (ALLONSO et al., 2014).

The detection of NS1Ag by IgM ELISA was specific and sensitive in the early stage of the disease (from the 6^{th} to the 10^{th} day) in a study during a dengue epidemic in the district of Angul, Odisha, India, in 2011 (MAHAPATRA et al., 2014). However NSI research is not recommended in places with endemic dengue where late clinical manifestations may occur. The test is effective in such places when combined with IgM research (BLACKSELL, 2012). A low-cost alternative with an easy installation in emergency services is the fast immunochromatography dengue test. Studies undertaken in Cambodia with kit SD Bioline Dengue Duo kit (fast tests for dengue) have shown that it is unable to exclude dengue when the results are negative, although the test fulfills the requirements of a field diagnostic test, it is easy to use and interpret, it has stability at room temperature and it is capable of providing results highly suggestive of dengue when positive for IgM and/or IgG (ANDRIES et al., 2012).

Conclusion

Laboratory changes in dengue are relevant, especially in endemic cases, since many health units do not have diagnostic kits or they have them in insufficient amounts to meet the demands of flavivirus-caused infection cases. Abnormalities in the hemogram and in transaminases, albeit not specific, may be of great help to the health agent in the diagnosis of dengue, when associated with clinical symptoms and epidemiological data. This is due to their characteristic profile. The need to confirm suspect dengue cases is evident in health units so that the diagnosis may be correctly concluded. The immediate start of treatment and the notification of cases are highly important and contribute towards more poignant epidemiological surveys which are a great help as a strategy against the dengue disease.

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References

ALLONSO, D. Assessing positivity and circulating levels of NS1 in samples from a 2012 dengue outbreak in Rio de Janeiro, Brazil. **Plos One**, v. 9, n. 11, p. 113634-113641, 2014.

ANDRIES, A. -C., DUONG, V.; NGAN, C.; ONG, S.; HUY, R.; SROIN, K. K. Y. B.;TRY, P. L.; BUCHY, P. Field evaluation and impact on clinical management of a rapid diagnostic kit that detects dengue NS1, IgM and IgG. **PLOS Neglected Tropical Diseases**, v. 6, n. 12, p. 1-9, 2012.

BHATT, S.; GETHING, P. W.; BRADY, O. J.; MESSINA, J. P.; FARLOW, A. W.; MOYES, C. L.; DRAKE, J. M.; BROWNSTEIN, J. S.; HOEN, A. G.; SANKOH, O.; MYERS, M. F.; GEORGE, D. B.; JAENISCH, T.; WINT, G. R. W.; SIMMONS, C. P.; SCOTT, T. W.; FARRAR, J. J.; HAY, S. I. The global distribution and burden of dengue. **Nature**, v. 496, n. 7446, p. 504-507, 2013.

BLACKSELL, S. D. Commercial dengue rapid diagnostic tests for point off-care application: recent evolutions and future needs? **Journal of Biomedicine and Biotechnology**, v. 2012, p. 1-12, 2012.

BRAGA, J. C. D.; SILVA, L. C.; TIBÚRCIO, J. D.; SILVA, M. A.; PEREIRA, L. H. S.; DUTRA, K. R.; FERREIRA, J. M. S.; LOPES, D. O.; SANTOS, L. L. Clinical, molecular and epidemiological analysis of dengue cases during a major outbreak in the midwest region of

Minas Gerais, Brazil. **Journal of Tropical Medicine**, p. 1-6, 2014. Available from: <http://www.hindawi.com/journals/jtm/2014/276912>. Access on: Mar. 30, 2015.

BRASIER, A. R.; JU, H.; GARCIA, J.; SPRATT, H. M.; VICTOR, S. S.; FORSHEY, B. M; ROCHA, C.; MORRISON, A. C.; SCOTT, T. W.; BAZAN, I.; KOCHEL, T. J. A three components biomarker panel for prediction of dengue hemorrhagic fever. **American Journal of Tropical Medicine and Hygiene**, v. 86, n. 2, p. 341-348, 2012.

BRASIL. Ministério da Saúde. **Dengue**: diagnóstico e manejo clínico. 4. ed. Brasília Ministério da Saúde, 2013.

BRASIL. Ministério da Saúde. Secretaria Executiva. **Informações de saúde**. Dengue-notificações registradas no sistemas de informações de agravos de notificação-Sinan. Brasília, Ministério da Saúde, 2014.

DURÁN, C. A.; LANZA, T. M.; PLATA, J. A. Fisiopatología y diagnóstico del dengue. **Revista Médica Hondurena**, v. 18, n. 3, p. 136-141, 2010.

FERNANDES, M. A. B.; NATAL, D.; DOMINGOS, M. F. Aspectos epidemiológicos da transmissão de dengue em Santos, São Paulo, no período de 1997 a 2012. **Journal Health Biologic Science**, v. 1, n. 2, p. 5-12, 2014.

FUJIMORO, D. E.; KOIFMAN, S. Clinical and laboratory characteristics of patients with dengue hemorrhagic fever manifestations and their prolife. **Revista Brasileira de Hematologia e Hemoterapia**, v. 2, n. 16, p. 115-120, 2014.

GUZMAN, M. G.; HALSTEAD, S. B.; ARTSOB, H.; BUCHY, P.; FARRAR, J.; GUBLER, D.; HUNSPERGER, E.; KROEGER, A.; MARGOLIS, H. S.; MARTINEZ, E.; NATHAN, M. B.; PELEGRINO, J. L.; SIMMONS, C.; YOKSAN, S.; PEELING, R. W. Dengue: a continuing global threat. **Nature Review Microbiology**, v. 8, suppl. 12, p. 7-16, 2010.

GUZMAN, M. G.; HARRIS, E. Dengue. **The Lancet**, v. 386, n. 9966, p. 453-465, 2015.

JAIN, A.; SHAH, A. N.; PATE, P.; DESAI, M.; SOMANI, S.; PARIKH, P.; SINGHAL, R.; JOSHI, D. A clinic-hematological profile of dengue outbreak among healthcare professionals in a tertiary care hospital of Ahmedabad with analysis on economic impact. **National Journal of Community Medicine**, v. 4, n. 2, p. 286-290, 2013.

LEE, K. L.; GAN, V. C.; LEE, V. J.; TAN, A. G.; LEO, Y. S.; LYE, D. C. Clinical relevance and discriminatory value of elevated liver aminotransferases levels for dengue severity. **PLOS Neglected Tropical Diseases**, v. 6, n. 6, p. 1-8, 2012.

LEITE, R. C.; SOUZA, A. I.; CASTANHA, P. M. S.; CORDEIRO, M. T.; MARTELLI, C. T.; FERREIRA, A. L. G.; KATZ, L.; BRAGA, C. Dengue infection in pregnancy and transplacental transfer of anti-dengue antibodies in Northeast, Brazil. **Journal of Clinical Virology**, v. 60, n. 1, p. 16-21, 2014.

LIMKITTIKUL, K.; BRETT, J. L'. A. M. Epidemiological trends of dengue disease in thailand (2000–2011): A systematic literature review. **PLOS Neglected Tropical Diseases**, v. 8, n. 11, e3241, 2014. Doi: 10.1371/journal.pntd.0003241.

MAHAPATRA, D.; SARANGI, G.; MAHAPATRA, S.; PATY, B. P.; DAS, P.; CHAYANI, N. NS1 antigen capture ELISA an effective method for diagnosis of early dengue infection - report of an outbreak at angul district, Odisha, India. **Journal of Clinical and Diagnostic Research**, v. 8, n. 8, p. 8-10, 2014.

MURUGANANTHAN, K; KANDASAMY, M.; RAJESHKANNA, N.; NOORDEEN, F. Demographic and clinical features of suspected dengue and dengue haemorrhagic fever in the northern province of Sri Lanka, a region afflicted by an internal conflict for more than 30 years- a retrospective analysis. **International Journal Infectious Diseases**, v. 27, p. 32-36, 2014.

NASCIMENTO, D.; CASTRO, A. R. C. M.; FROES, I. B.; BIGATON, G.; OLIVEIRA, E. C. L.; FABBRO, M. F. J. D. F.; CUNHA, R. N.; COSTA, P. Clinical and laboratory findings in patients with dengue associated with hepathopaty. **Revista da Sociedade Brasileira de Medicina Tropical**, v. 6, n. 44, p. 674-677, 2011.

OLIVEIRA, A. C. S.; TERRA, A. P. S; SILVA-TEIXEIRA, D. N.; DULGHEROFF, A. C. B.; FERREIRA, D. A.; ABREU, M. T. C. L.; MARTINS, P. R. J. Alterações do hemograma no diagnóstico da dengue: Um estudo de 1. 269 casos na cidade de Uberaba, Minas Gerais. **Revista do Instituto de Patologia Tropical**, v. 41, n. 4, p. 401-408, 2012.

OSANI, C. H.; ROSA, A. A. P.; TANG, A. T.; AMARAL, R. S.; PASSOS, A. D.; TAUIL, P. L. Surto de dengue em Boa Vista, Roraima. Nota prévia. **Revista do Instituto de Medicina Tropical**, v. 25, n. 1, p. 53-54, 1983.

PAPA, A.; GAVANA, E.; DETSIS, M.; TERZAKI, E.; VENETI, L.; PERVANIDOU, D.; GEORGAKOPOUULOU, T.; MARANGOS, M.; KOLIOPOULOS, G.; BAKA, A.; TSIODRAS, S.; TSAKRIS, A.; HADJICHRISTOODOULOU, C. Laboratory and surveillance studies following a suspected dengue case in Greece, 2012. **International Journal of Infectious Diseases**, v. 30, p. 150-153, 2015.

PRAMILADEVI, R.; KAIVALYA, ; KORA, S. Study of serological test for diagnosis of dengue. **Scholars Journal of Applied Medical Sciences**, v. 1, n. 5, p. 548-551, 2013.

RODRIGUEZ-ROCHE, R.; GOULD, E. A. Understanding the dengue viruses and progress towards their control. **Biomed Research International**, p. 1-20, 2013. Available from: <http://www.hindawi.com/journals/bmri/2013/690835/>. Access on: Mar. 25, 2015.

SABA, H.; VALE, V. C.; MORET, M. A.; MIRANDA, J. G. V. Spatio-temporal correlation networks of dengue in the state of Bahia. 2014. **BMC Public Health**, v. 14, n. 1085, p. 1-6, 2014.

SILVA, E. B.; NÓBREGA, P. R. C. Dengue: reflexões sobre a incidência da doença no município de Palmares, Pernambuco no pós-enchente (2010, 2011). **Journal Management and Primary Health Care**, v. 3, n. 2, p. 106-113, 2012.

TEIXEIRA, M. G.; SIQUEIRA JÚNIOR, J. B.; FERREIRA, G. L. C.; BRICKS, L.; JOINT, G. Epidemiological trends of dengue disease in Brazil (2000-2010): a systematic literature search and analysis. **PLOS Neglected Tropical Diseases**, v. 7, n. 12, p. 1-13, 2013.p. 240-256, 2013.

WHO-World Health Organization. **Dengue and severe dengue**. Fact sheet. N8117. Geneva, Who, 2013.

WILSON, M. E.; CHEN, L. H. Dengue: update on epidemiology. **Current Infectious Diseases Reports**, v. 17, n. 457, 2014.

XAVIER, A. R.; FREITAS, M. S.; BORGHI, D. P.; KAVAAN, S. Manifestações clínicas na dengue diagnóstico laboratorial. **Jornal Brasileiro de Medicina**, v. 102, n. 2, p. 7-14, 2014.

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