Original Article

Products of adaptive host immune response to viral agents in hyperthermia pediatric patients receiving malaria treatment and the immunoserologic status of their mothers

Mathew Folaranmi Olaniyan, Musa Abidemi Muhibi, Tolulope Busayo Ojediran

Department of Medical Laboratory Science, Edo University, Iyamho, Edo State, Nigeria

Abstract

Study Background: Hyperthermia is a manifestation of disease condition, which may also be as a result of immune response to the presence of infectious agent in the body that can be expressed in the serum/plasma. At times, it is erroneously assumed for *Plasmodium* infection.

Aims and Objectives: This work was designed to express the products of adaptive host immune response to viral agents in hyperthermia pediatric patients receiving malaria treatment and the immunoserologic status of their mothers for effective management and diagnosis.

Materials and Methods: One hundred and four hyperthermia children aged 5–9 years receiving treatment in herbal homes were investigated as test, while one hundred age-matched children with normal body temperature were recruited from Owo and Ose local government areas as control subjects. Mothers of the hyperthermia children were also studied. Antihepatitis C virus (HCV), human immunodeficiency virus (HIV) P24 antigen/antibody, anti-HBe, and HBeAg were determined by enzyme-linked immunosorbent assay, *Plasmodium* by Geimsa thick blood film, and acid-fast bacilli by Ziehl–Neelsen techniques.

Results: R Results obtained showed that the frequency of anti-HBe in mothers of hyperthermia patients (10.6% [11]) and in children with normal body temperature (9% [9]) was higher than the frequency of anti-HBe obtained in the hyperthermia herbal home children (4.8% [5]) while the frequency of HBeAg found in hyperthermia herbal home children (14.4% [15]) and their mothers (14.4% [15]) was higher than the results obtained in children with normal body temperature (4% [4]). The frequency of anti-HCV in herbal home hyperthermia children (2.9% [3]) was higher than the results obtained in their mothers (1.9% [2]) and children with normal body temperature (1% [1]). The HIV P24 antigen/antibody expressed by the mothers of herbal home hyperthermia children (3.85% [4]) was higher the results obtained in their children (2.9% [3]), while none of the children with normal body temperature expressed HIV P24 antigen/antibody. The frequency of *Plasmodium* in mothers of herbal home hyperthermia children (19.2% [20]) was higher than the results obtained in their hyperthermia children (9.6% [10]) and children with normal body temperature (3% [3]). The frequency of HIV in hyperthermia was 2.9% (3), while that of active/replicating hepatitis B virus (HBV) and HCV was 14.4% (HBeAg) and 2.9% (anti-HCV), respectively. Only mothers of hyperthermia herbal home

Address for correspondence: Prof. Mathew Folaranmi Olaniyan, Department of Medical Laboratory Science, Edo University, Iyamho, Edo State, Nigeria.
E-mail: olaniyanmat@yahoo.com

Submitted: 03-Aug-2020 **Revised:** 8-Sep-2020 **Accepted:** 11-Sep-2020 **Published:** 27-Nov-2020

Access this article online	
Quick Response Code:	Website: www.ijcpc.org
	DOI: 10.4103/ijcpc.ijcpc_11_20

How to cite this article: Olaniyan MF, Muhibi MA, Ojediran TB. Products of adaptive host immune response to viral agents in hyperthermia pediatric patients receiving malaria treatment and the immunoserologic status of their mothers. Int J Clinicopathol Correl 2020;4:46-51.

children expressed 1.6% (2) HIV P24Ag/Ab + HBeAg + anti-HBe. None of the mothers of hyperthermia herbal home children expressed HIV P24 antigen/antibody and infected with *Plasmodium* as against 2.9% (3) and 9.6% (10) obtained in their children. 1.6% (2) of the mothers of hyperthermia herbal home children expressed anti-HCV as against 2.9% (3) of their children who expressed the immunoserologic marker, while the hyperthermia herbal home children and their mothers expressed anti-HBe (4.8%[5] vs. 4.8% [5]) and HBeAg (14.4%[15] vs. 14.4% [15]).

Conclusion: Products of adaptive host immune response expressed in hyperthermia pediatric patients receiving malaria treatment and the immunoserologic status of their mothers include HIV P24Ag/Ab, HBeAg, anti-HBe, and anti-HCV, while the frequency of HIV in hyperthermia was 2.9% (3) and that of active/replicating HBV and HCV was 14.4% (HBeAg) and 2.9% (anti-HCV), respectively, with only HBV and HCV traceable to the mothers.

Keywords: Anti-HBe and antihepatitis C virus, HBeAg, human immunodeficiency virus P24Ag/Ab, hyperthermia, immune response, malaria, pediatric

INTRODUCTION

Host immune response is usually generated by the invasion or presence of pathogenic microbes such as virus, fungi, bacteria, and protozoa in the body system. Immune response can be grouped into innate and adaptive/acquired immunity.[1-3]

Innate immune response forms the first line of defense, which can be classified into mechanical/physical, which includes physical barriers such as the skin and mucous membranes; cellular which involves immune cells such as neutrophils, macrophages, and monocytes; and humoral which involves soluble substances including cytokines, transferrin, lactoferrin, and complement. Innate immune response is nonspecific.[1-3]

Adaptive or acquired immune response is a specific response to pathogens, which involves cells such as dendritic cells, T-cell, and B-cells (cellular immune response) and soluble substances such as antibodies known as immunoglobulins (humoral).[1-3] Antibodies such as IgG and IgM are produced upon antigenic stimulation as a result of the presence of pathogen in the body. This is a specific immune response that occurs when the pathogen has overcome the innate immune defense of the host.[4-6]

Primary immune response occurs on the first contact of the pathogen with the body leading to the production and activation of effector T and B cells against the microbe. It also involves production of memory T and memory B cells in case of re-exposure for secondary response. Thymus-derived lymphocyte (T-lymphocyte) is responsible for cell-mediated immunity, while bone marrow-derived lymphocyte is responsible for humoral immunity which involves production of antibodies.[4-6]

Immune responses may bring about hyperthermia through inflammatory processes as immune cells within the blood upon activation by inflammatory cytokines will release pyrogens which have a direct effect on the anterior hypothalamus resulting into increase in body temperature.[7]

Antibodies are produced against their corresponding/specific pathogens (antigens). The antibody can act against their specific pathogen (neutralizing antibodies) or produced as a result of the presence of pathogen in the body without any neutralizing effect (nonneutralizing antibodies). Immune response against viral invasion of human immunodeficiency virus will lead to the production of non-protective antibody to HIV (antiHIV), in hepatitis C virus infection antibody to HCV (antiHCV) is produced while antiHBe is produced to clear HBeAg in the host in HBV infection.[46]

This work therefore investigated products of adaptive host immune response to viral agents in hyperthermia pediatric patients receiving malaria treatment and the immunoserologic status of their mothers to provide useful guidelines in the diagnosis of diseases and management of hyperthermia in herbal homes.

MATERIALS AND METHODS

Study area

This work was carried out in 11 herbal homes in Owo/Ose federal constituency in Ondo State. It consists of Owo and Ose local government areas located in Owo and Ifon, respectively, in Ondo State.

Study population

One hundred and four hyperthermia children aged 5–9 years receiving treatment in 11 herbal homes in

Owo/Ose federal constituency in Ondo State were investigated as test, while one hundred age matched children with normal body temperature were recruited from Owo and Ose local government areas as control subjects. Mothers of the hyperthermia children were also studied.

Inclusion criteria

1. Only hyperthermia pediatrics receiving malaria treatment in herbal homes were included
2. Only mothers of the children undergoing malaria treatment in herbal home were included.

Exclusion criteria

1. Hyperthermia pediatrics receiving malaria treatment in hospitals
2. Hyperthermia pediatrics receiving treatment for diseases other than malaria were excluded.

Study duration

September, 2019–January, 2020.

Laboratory identification of *Plasmodium spp.*, and acid-fast bacilli

Laboratory of *Plasmodium spp., Wuchereria bancrofti* was carried out by microscopy using Geimsa thick film method while acid-fast bacilli (AFB) was demonstrated in the sputum as described by Cheesbrough.[8]

Hepatitis C antibody (anti-HCV) Enzyme-Linked Immunosorbent Assay

Hepatitis C antibody (anti-HCV) detection in the plasma was carried out using the reagent kit of DIA. PRO, Diagnostic Bioprobes Srl Via Columella, No. 31, 20128 Milano, Italy. E-mail: diapro@tin.it.

Human immunodeficiency virus Enzyme-Linked Immunosorbent Assay

HIV test was carried out using Genscreen™ ULTRA HIV Ag-Ab Biorad Kit.

The Genscreen™ ULTRA HIV Ag-Ab is an enzyme immunoassay based on the principle of the sandwich technique for the detection of HIV antigen and of the various antibodies associated with HIV-1 and/or HIV-2 virus in human serum or plasma.

HBeAg and anti-HBe Enzyme-Linked Immunosorbent Assay

Detection of HBeAg (envelope antigen) and hepatitis B "e" (envelope) antibody in the plasma was carried out using the reagent kit of DIA. PRO, Diagnostic Bioprobes Srl via Columella no 31, 20128 Milano, Italy. E-mail: diapro@tin.it.

Temperature measurement

This was determined in subjects using an infrared thermometer.

Ethical consideration

The proposal of this work was presented to the Research and Ethical Committee of the Department of Medical Laboratory Science, Achievers University, Owo, Nigeria. The proposal was reviewed and approved before the commencement of the work.

Method of data analysis

The results of this work were subjected to statistical analysis to determine mean, standard deviation, frequency and probability at 0.05 level of significance using IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY, USA: IBM Corp.

RESULTS

The results obtained showed a frequency of 2.9% (3) antiHCV; 2.9% (3) HIV P24 antigen/antibody; 4.8% (5) antiHBe; 14.4% (15) HBeAg; 9.6% (10) Plasmodium; 0% (0) AFB in Herbal home hyperthermia children and none of them expressed more than one viral marker while their mothers expressed: 1.9% (2) AntiHCV; 3.85% (4) HIV P24 antigen/antibody; 10.6% (11) AntiHBe; 14.4% (15) HBeAg; 19.2% (20) Plasmodium and 1.6% (2) HIV P24Ag/ Ab + HBeAg + AntiHBe [Tables 1 and 2; Figures 1 and 2].

However, the results obtained in the children with normal body temperature showed 1% (1) anti-HCV; 0% (0) HIV P24 antigen/antibody; 9% (9) anti-HBe; 4% (4) HBeAg; 3% (3) *Plasmodium*; 0% (0) AFB, and none of them expressed two or more of anti-HCV, HIV P24 antigen/antibody, HBeAg, and anti-HBe [Tables 1 and 2; Figures 1 and 2].

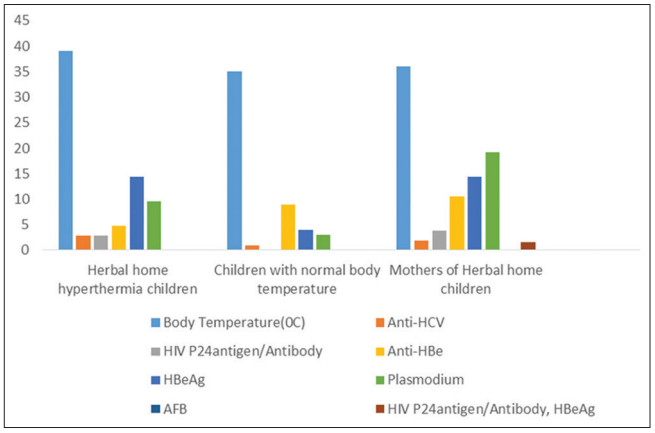

Figure 1: Comparative description of the frequency of products of immune response/infectious agents and values of body temperature obtained in the subjects

Table 1: Frequency of products of immune response/infectious agents and values of body temperature obtained in the subjects

Products of adaptive immune response	Herbal home hyperthermia children (*n*=104; 5-8 years)	Children with normal body temperature (*n*=100; 5-8 years)	Mothers of Herbal home hyperthermia children (*n*=104; 24-38 years)
Body temperature (°C)	39±0.5	35±1.0	36±1.0
Anti-HCV	3 (2.9)	1 (1)	2 (1.9)
HIV P24 antigen/antibody	3 (2.9)	0	4 (3.85)
Anti-HBe	5 (4.8)	9 (9)	11 (10.6)
HBeAg	15 (14.4)	4 (4)	15 (14.4)
Plasmodium	10 (9.6)	3 (3)	20 (19.2)
AFB	0	0	0
Expression of two or more of anti-HCV, HIV P24 antigen/antibody and anti-HBe	0	0	2 (1.6) HIV P24 antigen/antibody, HBeAg and anti-HBe

HCV: Hepatitis C virus, AFB: Acid-fast bacillus

Table 2: Results of herbal home hyperthermia mothers and their children who expressed products of adaptive immune response

Products of adaptive immune response	Herbal home hyperthermia children (*n*=104; 5-8 years)	Herbal home hyperthermia mothers and their children who expressed products of adaptive immune response
Anti-HCV	3 (2.9)	2 (1.6)
HIV P24 antigen/antibody	3 (2.9)	0
Anti-HBe	5 (4.8)	5 (4.8)
HBeAg	15 (14.4)	15 (14.4)
Plasmodium	10 (9.6)	0
AFB	0	0
Expression of two or more of anti-HCV, HIV P24 antigen/antibody and anti-HBe	0	2 (1.6) HIV P24Ag/Ab+HBeAg+anti-HBe

HCV: Hepatitis C virus, AFB: Acid-fast bacillus

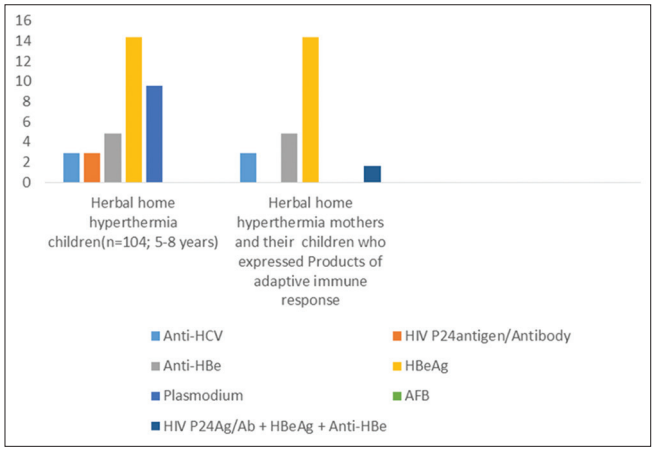

Figure 2: Frequency of herbal home hyperthermia mothers and their children who expressed Products of adaptive immune response

Frequency of anti-HBe expressed in mothers of hyperthermia patients (10.6% [11]) and children with normal body temperature (9% [9]) was higher than in the hyperthermia herbal home children (4.8% [5]), while higher frequency of HBeAg was found in hyperthermia herbal home children (14.4% [15]) and their mothers (14.4% [15]) compared with the results obtained in children with normal body temperature (4% [4]) [Tables 1 and 2; Figures 1 and 2].

The frequency of anti-HCV in herbal home hyperthermia children (2.9% [3]) was higher than the results obtained in their mothers (1.9% [2]) and children with normal body temperature (1% [1]) [Tables 1 and 2; Figures 1 and 2].

The HIV P24 antigen/antibody expressed by the mothers of herbal home hyperthermia children (3.85% [4]) was higher than the results obtained in their children (2.9% [3]), while none of the children with normal body temperature expressed HIV P24 antigen/antibody [Tables 1 and 2; Figures 1 and 2].

The frequency of *Plasmodium* in mothers of herbal home hyperthermia children (19.2% [20]) was higher than the results obtained in their hyperthermia children (9.6% [10]) and children with normal body temperature (3% [3]).

The frequency of HIV in hyperthermia was 2.9% (3), while that of active/replicating hepatitis B virus (HBV) and HCV was 14.4% (HBeAg) and 2.9% (anti-HCV) [Tables 1 and 2; Figures 1 and 2].

Only mothers of hyperthermia herbal home children expressed 1.6% (2) HIV P24Ag/Ab + HBeAg + anti-HBe [Tables 1 and 2; Figures 1 and 2].

None of the mothers of hyperthermia herbal home children expressed HIV P24 antigen/antibody and infected with *Plasmodium* as against 2.9% (3) and (9.6% [10]) obtained in their children. 1.6% (2) of the mothers of hyperthermia herbal home children expressed anti-HCV as against 2.9% (3) of their children who expressed the immunoserologic marker, while the hyperthermia herbal home children and their mothers expressed

anti-HBe (4.8%[5] vs. 4.8% [5]) and HBeAg (14.4%[15] vs. 14.4% [15]) [Tables 1 and 2; Figures 1 and 2].

DISCUSSION

The results obtained showed products of adaptive host immune response to viral agents in hyperthermic pediatric patients receiving malaria treatment and the immunoserologic status of their mothers as: 2.9% (3) anti-HCV; 2.9% (3) HIV P24 antigen/antibody; 4.8% (5) anti-HBe; 14.4% (15) HBeAg; 9.6% (10) *Plasmodium*; 0% (0) AFB in herbal home hyperthermia children, and none of them expressed two or more of anti-HCV, HIV P24 antigen/antibody, HBeAg, and anti-HBe, while their mothers expressed: 1.9% (2) anti-HCV; 3.85% (4) HIV P24 antigen/antibody; 10.6% (11) anti-HBe; 14.4% (15) HBeAg; 19.2% (20) *Plasmodium;* and 1.6% (2) HIV P24Ag/Ab + HBeAg + anti-HBe.

Expression of anti-HCV indicates HCV infection, HIV P24 antigen/antibody indicates HIV infection, anti-HBe indicates antibody to envelope antibody of HBV, which is a sign of HBeAg clearance after 6 months of HBV infection, while HBeAg indicates active or replicating HBV. These viral infections are associated with hyperthermia in addition to *Plasmodium* infection. These infectious agent indices were also found in mothers and children with normal body temperatures, which can be associated with the explanation that some infection could be asymptomatic.[9-13]

However, the results obtained in the children with normal body temperature showed 1% (1) anti-HCV; 0% (0) HIV P24 antigen/antibody; 9% (9) Anti-HBe; 4% (4) HBeAg; 3% (3) *Plasmodium*; and 0% (0) AFB, and none of them expressed two or more of anti-HCV, HIV P24 antigen/antibody, HBeAg, and anti-HBe.

Frequency of anti-HBe expressed in mothers of hyperthermia patients (10.6% [11]) and children with normal body temperature (9% [9]) was higher than in the hyperthermia herbal home children (4.8% [5]), while higher frequency of HBeAg was found in hyperthermia herbal home children (14.4% [15]) and their mothers (14.4% [15]) compared with the results obtained in children with normal body temperature (4% [4]). Expression of anti-HBe indicates clearance of HBeAg in HBV infection, while HBeAg indicates active HBV infection, which also indicates that the HBV is replicating which can generate increase in body temperature.[9-13]

The frequency of anti-HCV in herbal home hyperthermia children (2.9% [3]) was higher than the results obtained in their mothers (1.9% [2]) and children with normal body temperature (1% [1]). This can be associated with the fact that one of the manifestations of active HCV infection is hyperthermia.

The HIV P24 antigen/antibody expressed by the mothers of herbal home hyperthermia children (3.85% [4]) was higher than the results obtained in their children (2.9% [3]), while none of the children with normal body temperature expressed HIV P24 antigen/antibody. This may account for differences in the level of exposure to HIV infection and that not all cases of HIV infections are associated with hyperthermia.[9-13]

The frequency of *Plasmodium* in mothers of herbal home hyperthermia children (19.2% [20]) was higher than the results obtained in their hyperthermia children (9.6% [10]) and children with normal body temperature (3% [3]). This is because some *Plasmodium* infection may be asymptomatic because hyperthermia is a major manifestation of the infection.[9,10]

The frequency of HIV in hyperthermia was 2.9% (3), while that of active/replicating HBV and HCV was 14.4% (HBeAg) and 2.9% (anti-HCV), respectively. This affirms hyperthermia as a major symptom of active viral infection.[9-13]

Only mothers of hyperthermia herbal home children expressed 1.6% (2) HIV P24Ag/Ab + HBeAg + anti-HBe. This can be linked with the possibility of viral coinfections as they share common route of transmission.

None of the mothers of hyperthermia herbal home children expressed HIV P24 antigen/antibody and infected with *Plasmodium* as against 2.9% (3) and (9.6% [10]) obtained in their children. 1.6% (2) of the mothers of hyperthermia herbal home children expressed anti-HCV as against 2.9% (3) of their children who expressed the immunoserologic marker, while the hyperthermia herbal home children and their mothers expressed anti-HBe (4.8%[5] vs. 4.8% [5]) and HBeAg (14.4%[15] vs. 14.4% [15]). This can be explained as there is a possibility of maternal transmission of viral infection, which notwithstanding can also be contracted through other means.[11-13]

CONCLUSION

Adaptive immune response to viral infection in hyperthermia has been demonstrated through the expression of anti-HBe, HBeAg, anti-HCV, and HIV P24 antigen/

antibody associated with hyperthermia including HBeAg and anti-HCV traceable to maternal transmission.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sompayrac L. How the immune system works. In: Hoboken NJ, editor. ISBN 978-1-119-54219-3. OCLC 1083704429. 6th ed. 2019: Wiley-Blackwell; Hoboken, New Jersey, United States.
2. Sompayrac LM. How the Immune System Works. 6th ed. Newark: John Wiley & Sons, Incorporated; 2019.
3. Rich, Robert R. Clinical immunology: Principles and practice 2018: 5th ed. Elsevier, Amsterdam, Netherlands.
4. Punt J, Stranford SA, Jones PP, Owen JA. Kuby immunology 2018: 8th ed. New York: William H. Freeman, United States.
5. Bonilla FA, Oettgen HC. Adaptive immunity. J Allergy Clin Immunol 2010:125 Suppl 2:S33-40.
6. Janeway CA, Travers P, Walport M, Shlomchik MJ. Immunobiology. 5th ed. New York and London: Garland Science; 2001.
7. Marx J. Rosen's Emergency Medicine: Concepts and Clinical Practice. 6th ed. Philadelphia: Mosby/Elsevier; 2006. p. 2239.
8. Monica Cheesbrough District Laboratory Practice in Tropical Countries: Part 2 s Edition. New York: Cambridge University Press The Edinburgh Building, Cambridge CB2 8RU, UK Published in the United States of America by Cambridge University Press; 2006. http://www.cambridge.org 8 July, 2020.
9. Gao X, Chen H. Hyperthermia on skin immune system and its application in the treatment of human papillomavirus-infected skin diseases. Front Med 2014;8:1-5.
10. Mackowiak PA. Direct effects of hyperthermia on pathogenic microorganisms: Teleologic implications with regard to fever. Rev Infect Dis 1981;3:508-20.
11. Prabina P, Jayanthi S, Murthy CK, Kumar SB, Banu AS, Sakunthala SR, *et al*. A study on hepatitis B viral seromarkers and associated risk factors among the patients suffering from acute and chronic hepatitis B infection. Int J Appl Basic Med Res 2019;9:206-11.
12. Olowe OA, Mabayoje VO, Akanbi O, Adefioye OJ, Olowe RA, Fadeni EK, *et al*. HIV P24 antigen among HIV antibody seronegative blood donors in Osogbo Osun State, South Western Nigeria. Pathog Glob Health 2016;110:205-8.
13. Bonino F, Brunetto MR. Chronic hepatitis B e antigen (HBeAg) negative, anti-HBe positive hepatitis B: An overview. J Hepatol 2003;39:S160-3.