A Retrospective Analysis Comparing Treatment Response for Visceral Leishmaniasis-HIV Co-Infected Patients from the New World

Igor T Queiroz1,4, Lisete L Cruz3, João Fred1, Geraldine Madaloso4 and Jose A L Lindoso*1

1Departamento de Doenças Infecciosas e Parasitárias da Universidade de São Paulo – São Paulo/SP, Brazil
2Hospital Giselda Trigueiro, SESAP-RN, Brazil
3Centro de Vigilância Epidemiológica "Prof. Alexandre Vranjac” – CVE, Coordenadoria de Controle de Doenças – CDC, Secretaria de Estado da Saúde – SES-SP, Brazil
4Instituto de Infectologia Emilio Ribas-SES-SP-Brazil
5Laboratório de Soroepidemiologia (LIM-38 HC-FMUSP), Brazil

Abstract

Background: Visceral Leishmaniasis and Human Immunodeficiency Virus co-infection (VL-HIV) occurs mainly in risk groups for HIV/AIDS (youth adult males). These co-infected individuals have greater mortality and relapse rates compared to VL, as they share similar immune pathogenic mechanisms. Interest in co-infection VL-HIV and the lack of data in the literature led the authors to a survey on the subject comparing outcomes in VL-HIV co-infected treated with different drugs anti-Leishmania used in Brazil, such that Pentavalent Antimoniate (MA), Amphotericin B deoxicolate (AmBd), and liposomal Amphotericin B (LAmB).

Methods: A retrospective descriptive study using routine program data was performed comparing drugs used for treatment of co-infected patients in Sao Paulo state, Brazil, among 1999-2010, observing their outcomes (cure, failure, relapse or death), and analyzing them by each drug used.

Results: In the period of twelve years were reported 1,614 VL cases in Sao Paulo state from whom 1,070 (66.30%) were HIV-negative, 117 (7.25%) were HIV-positive and in 427 patients (26.45%) HIV status was unknown. To compare treatment response according to drugs used, we included only the 117 VL/HIV co-infected patients. Related to demographic data we found 72.65% (85/117) of males and 80.34% (94/117) of young adults (21-50 years old). From 117 co-infected patients, 95 had complete data of the treatment performed and these were included in the analysis. The lethality of VL-HIV co-infected patients was 24.2% (23/95) and general relapse rate was 10.5% (10/95). Deaths in co-infected were more prevalent among 31-50 years. According to drug used, 35.64% (36/101) were treated with pentavalent antimoniate (20 mg/kg/day per 28 days), 12 (11%) received Amphotericin B deoxicolate (AmBd) (total dose: 20 to 24 mg/kg) and 47 were treated with Liposomal Amphotericin B (LAmB).

Conclusion: High lethality and relapses rates occur in VL-HIV co-infected patients. Poor outcome leading to death was observed in AmBd group. There is an urgent necessity to perform prospective clinical trials to evaluate the safety and efficacy of different schemes for treatment of co-infected patients, especially in New World.

Introduction

Visceral Leishmaniasis and Human Immunodeficiency Virus co-infection (VL-HIV) has emerged as an important public health problem worldwide. However it was observed a decreasing in the number of co-infected patients in Mediterranean area [1,2]. VL-HIV has increased in East Africa and Latina America [3,4] and the prevalence of VL-HIV is still low in Indian subcontinent which estimates ranges from 2-5.6% [5]. The impact of VL-HIV co-infection is directly related to unusual clinical manifestation, poor outcome and worst treatment response for VL. Remarkably, HIV increases the risk of Leishmania infection to disease progression to VL and Leishmania enhance HIV replication, depleting more CD4+ T Lymphocytes, leading the patient to AIDS more rapidly. As they share similar immune pathogenic mechanisms by attacking the same cellular immune compartment, there is an impairing in the immune response to opportunistic infections consequently [6,7]. By this way, atypical manifestation, high relapse and high lethality rates have been observed [3].

Reports evaluating drug response of VL in HIV co-infected patient are scarce [8]. Treatment failure has been observed in VL-HIV co-infected patients treated with Liposomal Amphotericin B (LAmB), pentavalent antimoniate (SbV) or drug associations [9-14]. In Ethiopia, the reported risk of relapse at six months varied between 25.4% and 11.4%, as the drug used for treatment of co-infected were miltefosine or sodium stibogluconate, respectively [9]. After one-year of follow up,
the relapse risk is close to 20% for individuals with primary VL and having a CD4+ T cell counts of around 200 cells/mL and for those with multiple previous VL episodes and CD4+ T cell counts below 100 cells/mL is around 60% [10]. In Europe (Mediterranean area specifically), pentavalent antimonials have been compared with Amphotericin B deoxicolate (AmBd) and Amphotericin B Lipid Complex (AmBLC) showing similar cure rates, but with more severe toxicity [15-17]. In Brazil, some reports have evaluated the overall therapy response in co-infected patients showing relapses rates of 56.5% and 52.9% [18-19], and an increasing lethality ranging from 4.8 to 22.0%, depending on the drug used for VL treatment [9-14,20]. Indeed, these reports do not compare relapse and lethality rates among anti-
*Leishmania* drugs used. Here we show the lethality and relapse rates in a cohort of VL-HIV co-infected patients from Sao Paulo state, Brazil, comparing the drugs response used to treat VL.

**Methods**

**Study design**

A retrospective descriptive study was performed to analyze the outcome (cure, failure, relapse or death) according to the drug used for treatment of VL, in HIV-coinfected patients.

**Studied area and population**

In this study, we included only patients whom presented VL confirmed by parasitological method and a positive result to anti-
*Leishmania* serology from Sao Paulo state.

**Diagnostic of VL and HIV**

**VL diagnostic**: Patients presenting clinical signals suggestive of VL (fever, splenomegaly or hepatomegaly) from VL endemic area were submitted to bone marrow aspirate to detect *Leishmania* amastigotes by direct search, according to laboratorial routine (Guideline to Treatment and Diagnostic of Visceral Leishmaniasis from Health Ministry from Brazil).

**HIV infection**: All patients included in this study were submitted to serology from HIV, using ELISA method, according to laboratorial routine (Guideline to Treatment and Diagnostic of HIV/AIDS from Ministry of Health from Brazil).

**Data source of VL and HIV/AIDS patients**

VL data (clinical features, epidemiology and treatment) was carried out by searching databases from the Epidemiological Surveillance Center “Prof. Alexandre Vranjac” from Sao Paulo Health Department (CVE-SES-SP) and database from SINAN (National System from Ministry of Health of Brazil). Notification forms provided all information and it was not necessary to do a search in the medical records.

Regarding to data on HIV infection (CD4+ and CD8+ T cells count and viral load of HIV from HIV/AIDS patients), they were collected by active search in the database of STD/AIDS from Sao Paulo state in addition to the databases of CVE-SES-SP and SINAN.

**Diagnostic criteria**

**VL cases**: VL cases included were those with parasitological confirmation, i.e., presence of *Leishmania spp* in aspirate of bone marrow by direct search or culture.

**HIV/AIDS cases**: Patients considered to be HIV-positive were those with laboratory confirmation according to the Brazilian Ministry of Health, i.e., two screening tests (ELISA or immunocromatography) and a confirmatory test (Western blot, immunoblot, IFI) or by the presence of HIV viral load.

**Outcome definitions**

**Cure**: Absence of fever, reduced viscera (liver and/or spleen), weight gain and return of appetite, and the patient remained without symptoms and active signal of VL for twelve months at the end of treatment.

**Failure**: Regular treatment that does not meet criteria for clinical cure after a series of treatment.

**Relapse**: Recrudescence of symptoms within twelve months after the end of treatment.

**Death**: Information about death by VL or other causes (when not specified) until the closing of the case.

**Data collection and statistical analysis**

The Microsoft Excel 2007 program was used to produce comparative tables for analysis of the results and interpretation, after crossing information of data obtained from the CVE-SES-SP, SINAN and STD/AIDS databases, one complementing another. Individuals who were notified between 30 days after the start of treatment until one year of that were considered recurrence. Those with the same date of notification were considered duplicates and were excluded. Using the GraphPad Prism 3.0 (Chi-square and Fisher’s exact test for categorical variables and Kruskal-Wallis One Way Analysis of Variance on Ranks for continuous variables) it was performed statistical analysis of demographic data. P values <0.05 were considered significant in this study. After performing the descriptive analysis and pointing out the frequencies of the independent variables studied they were characterized in two distinct groups: cure and death. Thus, a bivariate analysis of treatment and death was developed using the EpInfo 3.5.4 program whose basic database was developed in Microsoft Excel 2007. It was performed chi-square test or Fisher’s exact test for qualitative variables, which those with p <0.05 were considered to make the completion of the multivariate logistic regression model, using the “stepwise forward”, from the lower value of p to the largest. The existence of an association between death by VL and drugs used for treatment was investigated by unadjusted and adjusted estimates of Odds Ratios (OR) with confidence intervals of 95%, using unconditional logistic regression. The statistical significance of the variables in the models was assessed by likelihood ratio test.

**Ethics**

The data included in this retrospective analysis were constituted from routine data and was approved by the Ethical Committee of Department of Health of Sao Paulo state, respecting the National Counseling of Health for Scientific Research in Human Beings from Brazilian Ministry of Health.

**Results**

**Demographic data**

_Citation:_ Queiroz IT, Cruz LL, Fred J, Madaloso G and Lindoso JAL. A Retrospective Analysis Comparing Treatment Response for Visceral Leishmaniasis-HIV Co-Infected Patients from the New World. _SM Trop Med J._ 2017; 2(1): 1014. https://dx.doi.org/10.36876/smtmj.1014
Leishmania 00.00 (0) Anti- (N=23)
26.1 (6)
11.11 (4)
41.66 (5)
8.2(88/1078) 
16.66 (6)
10.5(10/95)
43,5 (10)
100
Leishmania + PA 0.08
AmBd 0.40
LAmB 35
0.48-3.99
Response to treatment from anti-
14.89 (7)
+ 63.16
0.034
36.84
24.2(23/95)
40,3 (29)
0.223
0
1.8(19/1078)
21.27 (10)
16.66 (2)
100% (12)
100% (36)
0,03
30,4(7)
0.192
69.44 (25)
0.076
No
63.82 (30)
VL
100% (23/95)
Liposomal Amphotericin B.
PA= Pentavalent Antimoniate, AmBd = Amphotericin B deoxicolate, LAmB = Liposomal Amphotericin B.
* Chi-square; * Comparing each one to others.

Citation: Queiroz IT, Cruz LL, Fred J, Madaloso G and Lindoso JAL. A Retrospective Analysis Comparing Treatment Response for Visceral Leishmaniasis-HIV Co-Infected Patients from the New World. SM Trop Med J. 2017; 2(1): 1014. https://dx.doi.org/10.36876/smtmj.1014
Discussion

VL-HIV co-infection has impacted directly in the epidemiology and clinical outcome of VL, mainly in relapse and lethality rates. Furthermore, HIV has contributed to the re-emergence of VL in some Mediterranean areas [3] and others regions as Ethiopia, where an increasing prevalence from 13.3% to 38.2% has been observed [11-21]. In Brazil VL/HIV prevalence is at about 8.5%, and the number of VL affected individuals and the number of co-infected patients is increasing yearly nationwide [2]. Data from treatment of co-infected patients have been shown an increasing in lethality and relapse rates, although the introduction of Antiretroviral Therapy (ART) promoted a decreasing in the incidence of VL in HIV-infected, as occurred in patients in Mediterranean area [3,4,22]. In our study we also observed that co-infected patients had higher lethality than VL alone (almost three-fold), and relapses rates of co-infected was fivefold higher compared to VL alone, independent on the drug used. Regarding to lethality, our data are similar to others presented by others authors [3,18,19,23,24]. A possible risk factor related with high lethality of co-infected patients is the low CD4+ T cell count since Cota et al. (2011) observed in a systematic review that CD4+ T count less than 100 cells/mm3 is an important factor related to relapse in VL-HIV co-infected patients [25]. Also, HIV infection further suppresses CD4+ T cell levels by direct attack. Therefore, HIV and VL reinforce each other, allowing the development of the latter (100-2320-fold higher risk), contributing to an increased spread of the Leishmania infection, and causing a negative response to ART [3,26]. On the other hand, infection by Leishmania increases the replication of HIV due to chronic activation of the immune system, favoring the entry of HIV into the reticuloendothelial system cells, integration and release of new viruses [3,22,27-29].

Analyzing drugs used for the treatment of VL in co-infected patients and their outcomes, it was observed that: (1) patients treated with PA had similar cure rates compared to those who received LAmB; (2) there were no failures when co-infected were treated with LAmB; (3) lethality was higher when AmBd was used comparing to other ones; and (4) higher relapse rates was detected when LAmB were used comparing to PA and AmBd. In exception to failures, all results did not show significant difference. Possibly, there were selection biases when more severe cases were preferably treated with LAmB. As data about secondary prophylaxis was not available, we could not conclude that these co-infected patients had not received that, which would imply in a higher chance of relapse. As we use secondary data (retrospective study) some limitations of the study hinder a more accurate interpretation of the data obtained, since the lack of some information on the CD4 + lymphocyte count does not allow us to define which group is most vulnerable to therapeutic failure or to have an unfavorable outcome. Other factor to take into account is that a total dosage of 20mg/Kg of LAmB (as recommended by Ministry of Health of Brazil by 2000’s) might be insufficient for treatment of L. infantum in the New World as described for L. donovani in Ethiopia [14]. Furthermore, this same study in Ethiopia presents disappointing efficacy of LAmB monotherapy because high lethality and high relapse rate were observed in co-infected patients when compared to VL cases in HIV-negative ones (lethality 6.7% ± 6.4% respectively), suggesting a reduced sensitivity of L. donovani in East Africa for LAmB [14]. Comparing the three drugs used in the treatment of VL-HIV co-infected in Sao Paulo, AmBd has presented worst outcomes than the two others drugs. As a greater number of negative outcomes in co-infected patients treated with AmBd compared to PA and LAmB was observed, it is assumed that treatment interruptions due to renal failure (high nephrotoxicity of AmBd) could had been responsible for the high rate of deaths and failures, given that this formulation was potentially causing serious side effects and require hospitalization for about 30 days [3]. However, this hypothesis could not be confirmed because it was not possible to obtain further information on the treatment due to the limitations of this study. The initial cure was achieved in 69.44% of co-infected patients treated with PA and some treatments have failed (11.11%) which required change in therapy for retreatment. Clinical improvement after treatment with PA in co-infected patients does not mean parasite cure and recurrence rate in 12 months is estimated to be approximately 70% in the absence of secondary prophylaxis [16]. Because PA is a drug known by presenting lower efficacy and by being more toxic to co-infected patients (in a dose-dependent manner), cardio, renal and pancreatic toxicity are responsible for the interruption of 11 to 28% of treatments [12,18,22,26,30,31]. As described elsewhere antimonials have a reasonable cure rate (85-95%) in HIV-negative patients, except in Bihar, India, where there are reports of resistance of L. donovani, in about 60% of cases [26,32,33]. The efficacy of PA depends on various factors (eg: the stage of the disease, pregnancy, poor nutrition, immunosuppression, drug toxicity). In a study in Ethiopia, between 92.9 to 100% of HIV-negative patients were cured when treated with pentavalent antimoniate, whereas among VL-HIV co-infected treated with the same drug, only 58.3% were cured at the end treatment and only 33.3% remained cured at six months follow-up after treatment [12]. A systematic review, which compared the use of pentavalent antimoniate against amphotericin B (deoxycholate or lipid formulation) in 920 episodes of VL-HIV co-infected patients showed superiority favorable to those treated with amphotericin B in relation to lethality, clinical improvement and presence of lower amount of adverse events, suggesting to be due to the lower toxicity of amphotericin B than pentavalent antimoniate, with greater effectiveness of lipid formulations of amphotericin B [30].

Regarding antiretroviral therapy, most of the patients had no data available, perhaps due to no tests have been ordered or to system failure. ART was not in use when VL was diagnosed in some patients. Of the 21 deaths and 68 cures observed, approximately 25% (both death and cure) had their data recorded regarding to ART. Concerning relapses, data from only one patient were available that included CD4+/CD8+ T cells count. This attracts attention to the necessity of training programs directed to physicians that focus on VL-HIV co-infection and emphasize the necessity of HIV testing for patients with a recent VL diagnosis, with respect to the difficulty that Leishmania-HIV co-infection brings to treatment, besides the overlap of epidemiological areas between these infections worldwide. In our study we noted that there was no significant difference between the outcomes (cure, death or relapse), when analyzing CD4+ and CD8+ T cells count and HIV viral load, mainly because of limitations imposed by few data available.

Some limitations of the study do not allow us to have more robust conclusions, mainly because we did not have data related to the adverse effects during the treatment, as well as we did not obtain data of CD4+ and TCD8+ lymphocyte counts, viral load and ART use of all patients involved.
In conclusion, our study confirms high lethality and relapse in VL-HIV co-infected patients, independent of the drugs used to treat VL. The lack of well-designed clinical trials leaves an important gap in the knowledge of therapeutic response in this population, since this co-morbidity is increasing in many regions worldwide, with direct impact on the clinical course of both diseases.

References

1. Alvar J, Aparicio P, Aseffa A, Den Boer M, Canavate C, Dedet JP, et al. The relationship between leishmaniasis and AIDS: the second 10 years. Clin Microbiol Rev. 2008; 21: 334-359.
2. Monge-Maito B, Norman FF, Cruz I, Alvar J, Lopez-Velez R. Visceral leishmaniasis and HIV coinfection in the Mediterranean region. PLoS Negl Trop Dis. 2014; 8: 3021.
3. Diro E, Lynen L, Ritmeijer K, Boelaert M, Hallu A, van Grensven J. Visceral Leishmaniasis and HIV coinfection in East Africa. PLoS Negl Trop Dis. 2014; 8: 2869.
4. Lindoso JA, Cota GF, da Cruz AM, Goto H, Maia-Eikhoury AN, Romero GA, et al. Visceral leishmaniasis and HIV coinfection in Latin America. PLoS Negl Trop Dis. 2014; 8: 3136.
5. Burza S, Mahajan R, Sinha PK, van Grensven J, Pandey K, Lima MA, et al. Visceral leishmaniasis and HIV co-infection in Bihar, India: long-term effectiveness and treatment outcomes with liposomal amphotericin B (AmBisome). PLoS Negl Trop Dis. 2014; 8: 3053.
6. Bernier R, Turco SJ, Olivier M, Tremblay M. Activation of human immunodeficiency virus type 1 in monocyteid cells by the protozoan parasite Leishmania donovani. J Virol. 1995; 69: 7282-7285.
7. Garg R, Barat C, Ouellet M, Lodge R, Tremblay MJ. Leishmania infantum amastigotes enhance HIV-1 production in cocultures of human dendritic cells and CD4 T cells by inducing secretion of IL-6 and TNF-alpha. PLoS Negl Trop Dis 2009; 3: 441.
8. Jarvis JN, Lockwood DN. Clinical aspects of visceral leishmaniasis in HIV infection. Curr Opin Infect Dis. 2013; 26: 1-9.
9. Ritmeijer K, Dejenie A, Assefa Y, Hundle TB, Mesure J, Boots G, et al. A comparison of miltefosine and sodium stibogluconate for treatment of visceral leishmaniasis in an Ethiopian population with high prevalence of HIV infection. Clin Infect Dis. 2006; 43: 357-364.
10. ter Horst R, Collin SM, Ritmeijer K, Bogale A, Davidson RN. Concordant HIV infection and visceral leishmaniasis in Ethiopia: the influence of antiretroviral treatment and other factors on outcome. Clin Infect Dis. 2008; 46: 1702-1709.
11. Hurissa Z, Gebre-Silassie S, Hallu W, Teferra T, Laloo DG, Cuebas LE, et al. Clinical characteristics and treatment outcome of patients with visceral leishmaniasis and HIV co-infection in northwest Ethiopia. Trop Med Int Health. 2010; 15: 848-855.
12. Hallu W, Weldegebrael T, Hurissa Z, Tafes H, Omollo R, Yifu S, et al. Safety and effectiveness of meglumine antimoniate in the treatment of Ethiopian visceral leishmaniasis patients with and without HIV co-infection. Trans R Soc Trop Med Hyg. 2010; 104: 706-712.
13. Sinha PK, van Grensven J, Pandey K, Kumar N, Verma N, Mahajan R, et al. Liposomal amphotericin B for visceral leishmaniasis in humans with human immunodeficiency virus-infected patients: 2-year treatment outcomes in Bihar, India. Clin Infect Dis. 2011; 53: 91-98.
14. Ritmeijer K, ter Horst R, Chane S, Aderie EM, Pieuning T, Collin SM, et al. Limited effectiveness of high-dose liposomal amphotericin B (AmBisome) for treatment of visceral leishmaniasis in an Ethiopian population with high HIV prevalence. Clin Infect Dis. 2011; 53: 152-158.
15. Laguna F, Lopez-Velez R, Pulido F, Salas A, Torre-Cisneros J, Torres E, et al. Treatment of visceral leishmaniasis in HIV-infected patients: a randomized trial comparing meglumine antimoniate with amphotericin B. Spanish HIV-Leishmania Study Group. AIDS. 1999; 13: 1063-1069.
16. Laguna F, Videla S, Jimenez-Mejias ME, Sirera G, Torre-Cisneros J, Ribera E, et al. Amphotericin B lipid complex versus meglumine antimoniate in the treatment of visceral leishmaniasis in patients infected with HIV: a randomized pilot study. J Antimicrob Chemther. 2003; 52: 454-458.
17. Montalban C, Calleja JL, Erice A, Laguna F, Ciolet B, Podzamczer D, et al. Visceral leishmaniasis in patients infected with human immunodeficiency virus. Co-operative Group for the Study of Leishmaniasis in AIDS. J Infect. 1990; 21: 261-270.
18. Alexandrino-de-Oliveira P, Santos-Oliveira JR, Dorval ME, Da-Costa F, Pereira GR, da Cunha RV, et al. HIV/AIDS-associated visceral leishmaniasis in patients from an endemic area in Central-west Brazil. Mem Inst Oswaldo Cruz. 2010; 105: 692-697.
19. Nascimento ET, Moura ML, Queiroz JW, Barroso AW, Araujo AF, Rego EF, et al. The emergence of concurrent HIV-1/AIDS and visceral leishmaniasis in Northeast Brazil. Trans R Soc Trop Med Hyg. 2011; 105: 298-300.
20. Herrero M, Orfanes G, Argaw D, Mulugeta A, Aparicio P, Parreno F, et al. Natural history of a visceral leishmaniasis outbreak in highland Ethiopia. Amer J Trop Med Hyg. 2009; 81: 373-377.
21. Ritmeijer K, Veeken H, Melaku Y, Leal G, Amsalu R, Seaman J, et al. Ethiopian visceral leishmaniasis: generic and proprietary sodium stibogluconate are equivalent; HIV co-infected patients have a poor outcome. Trans R Soc Trop Med Hyg. 2001; 95: 668-672.
22. Cruz I, Nieto J, Moreno J, Canavate C, Desjeux P, Alvar J. Leishmania/HIV co-infections in the second decade. Indian J Med Res. 2006; 123: 357-388.
23. Lima IP, Muller MC, Holanda TA, Harhay M, Costa CH, Costa DL. Human immunodeficiency virus/Leishmania infantum in the first foci of urban American visceral leishmaniasis: clinical presentation from 1994 to 2010. Rev Soc Bras Med Trop. 2013; 46: 156-160.
24. Daher EF, Evangelista LF, Silva Junior GB, Lima RS, Aragao EB, Aruda GA, et al. Clinical presentation and renal evaluation of human visceral leishmaniasis (kala-azar): a retrospective study of 57 patients in Brazil. Braz J Infect Dis. 2008; 12: 329-332.
25. Cota GF, de Sousa MR, Rabello A. Predictors of visceral leishmaniasis relapse in HIV-infected patients: a systematic review. PLoS Negl Trop Dis. 2011; 5: 1153.
26. den Boer ML, Alvar J, Davidson RN, Ritmeijer K, Balasegaram M. Developments in the treatment of visceral leishmaniasis. Expert Opin Emerg Drugs. 2009; 14: 395-410.
27. Santos-Oliveira JR, Gaiocia-Gripp CB, Alexandrino de Oliveira P, Amato VS, Lindoso JA, Goto H, et al. High levels of T lymphocyte activation in Leishmania-HIV-1 co-infected individuals despite low HIV viral load. BMC Infect Dis. 2010; 10: 358.
28. Pintado V, Martin-Rabadan P, Rivera ML, Moreno S, Bouza E. Visceral leishmaniasis in Patients from an Endemic Area in Brazil. PLoS Negl Trop Dis. 2014; 8: 3021.
29. Saporito L, Giannamanco GM, De Grazia S, Colonna C. Visceral leishmaniasis: host-parasite interactions and clinical presentation in the immunocompetent and in the immunocompromised host. Int J Infect Dis. 2013; 17: 572-576.
30. Cota GF, de Sousa MR, Fereguello TO, Rabello A. Efficacy of anti-leishmania therapy in visceral leishmaniasis among HIV infected patients: a systematic review with indirect comparison. PLoS Negl Trop Dis. 2013; 7: 2195.
31. Cota GF, de Sousa MR, de Mendonca AL, Patrocino A, Assuncao LS, de Faria SR, et al. Leishmania-HIV co-infection: clinical presentation and outcomes in an urban area in Brazil. PLoS Negl Trop Dis. 2014; 8: 2816.
32. Le Pape P. Development of new anti-leishmania drugs—current knowledge and future prospects. J Enzyme Inhib Med Chem. 2008; 23: 708-718.
33. Sundar S. Drug resistance in Indian visceral leishmaniasis. Trop Med Int Health. 2001; 6: 849-854.

Citation: Queiroz IT, Cruz LL, Fred J, Madaloso G and Lindoso JAL. A Retrospective Analysis Comparing Treatment Response for Visceral Leishmaniasis-HIV Co-Infected Patients from the New World. SM Trop Med J. 2017; 2(1): 1014. https://dx.doi.org/10.36876/smtmj.1014