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Short Commentary

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Diagnostic value of 15 days fever history for screening of kala-azar with rK39 test kit: A hospital-based observational study

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Abstract

Visceral Leishmaniasis (VL), also known as kala-azar (KA), is a neglected vector-borne disease and a major public health problem in Bihar, India. The disease is targeted for elimination (reducing incidence to less than one per 10,000 populations at the PHC level) by 2020. Despite the main strategy, early detection of kala-azar (KA) cases is still posing a greater challenge to KA elimination from the Indian subcontinent. To document this problem, a hospital-based study was conducted at primary-level health facilities (Paroo PHC & Patepur PHC; hot spot). A total of 585 patients with a fever history ≥ one day attended these two primary-level health facilities. We observed a statistically significant difference ($p<0.001$) for the age group 21-30 years (51.8%) when compared to another age group. Only 6.7% (39) were found rK39 positive with mean ± SD as 21.6 ± 20.0 years. There was no statistically significant difference ($p>0.05$) between sex and age group among the positive patients. However, a highly significant difference ($p<0.0001$) was observed for rK-39 strip test positivity with a fever history of more than 15 days (97.4%) when compared to a fever history of lower than 15 days (2.6%). The study concluded that a fever history of ≥15 days (as adopted under National guidelines in India), is hold appropriate for detecting VL infection.

Keywords: Visceral leishmaniasis (VL); Fever history; Indian sub-continent; Health facilities.

Introduction

VL is a complex vector-borne protozoan infection that greatly influences public health if left untreated. In India, this fatal disease is also popularly known as Kala-azar. Bihar and Jharkhand are the two states in the eastern region of the country that confined too many hot spots [1]. The causal organism *Leishmania donovani* complex which is widely distributed in the Indian subcontinent is transmitted by infected female *Phlebotomus argentipes* sand flies [2,3]. The pathogen primarily persists in humans but in some instant may circulate in animals. The clinical syndrome of this disease is well characterized by prolonged history of fever, loss of appetite, weight loss, progressive anemia, hepatomegaly, splenomegaly, pancytopenia, and hypergammaglobulinemia [4,5]. In these clinical features, fever is one of the major features of chronic infectious disease. It is mainly is a febrile response by the central nervous system, which leads to many metabolic and physiological changes in the body. It also causes alterations in immune responses during the incubation period [6,7]. For the validation of the incubation period of VL, we conducted our study on the patients who come with fever without any previous VL history, in Paroo, Primary Health Center (PHC) in Muzaffarpur and Patepur, PHC in Vaishali district. These two districts are highly VL endemic regions of Bihar state. The evaluations were conducted by using a rapid diagnostic rK39 strip test.

Methodology & results

We enrolled a total of 585 patients who have reported clinical evidence of fever history ≥ one day. Among them, 406 (69.4%) and 179 (30.6%) patients were from Muzaffarpur district (Paroo, PHC) and Vaishali district (Patepur, PHC) respectively. We observed a statistically significant difference ($p<0.05$) among males (26.8%) and females (73.2%). Similarly, statistically significant difference was observed ($p<0.001$) for age group 21-30 years (51.8%) when compared to other age group respectively viz 0-10 (9.9%), 11-20 (13.0%), 31-40 (10.1%), 41-50 (5.8%) and >50 years (9.4%) as mentioned in Table 1.

Table 1: Age and sex distribution

Age Group ↓	Male		Female		Total	
	N	%	N	%	N	%
0-10	28	48.3	30	51.7	58	9.9
11-20	25	32.9	51	67.1	76	13.0
21-30	40	13.2	263	86.8	303	51.8
31-40	22	37.3	37	62.7	59	10.1
41-50	16	47.1	18	52.9	34	5.8
>50	26	47.3	29	52.7	55	9.4
Total	**157**	**26.8**	**428**	**73.2**	**585**	**100.0**

The structured questionnaire details including history of fever, history of visceral leishmaniasis, family history of visceral leishmaniasis, etc along with informed consent, blood samples were collected for the performance of rK39 strip test (InBios International, Inc. Seattle, USA), for VL screening. In the 585 screened patients, we diagnosed 39 (6.7%) positive, whereas the rest 546 (93.3%) rK39 strip test negative. The mean age ± standard deviation (SD) for rK39 strip positive patients was as 21.6 ± 20.0 years. Among rK39 strip positive 18 (46.2%) male and 21 (46.2%) female patients, the mean age ± SD showed 21.4 ± 20.5 years and (21.7 ± 20.0 years), respectively. There is no statistically significant difference ($p>0.05$) observed between sex and age group among the positive patients. The majority (38, 97.4%) of the rK-39 strip test results positive were with the fever history of more than 15 days, while only one (2.6%) had shown the rK39 strip test positive in less than 15 days fever history, and this difference was found highly significant ($p<0.0001$) (Table 2).

Table 2: Fever history of patients.

History of fever (Days)	Positive		Negative		Total	
	N	%	N	%	N	%
0-5	0	0.0	142	100.0	142	24.3
6-10	1	0.5	183	99.5	184	31.5
11-15	0	0.0	130	100.0	130	22.2
>15	38	29.5	91	70.5	129	22.1
Total	**39**	**6.7**	**546**	**93.3**	**585**	**100.0**

Discussion

The VL diagnosis is a complex procedure as it shows some similar clinical features of many other diseases such as malaria, typhoid, and tuberculosis. Although the rK39 strip test is easy, reliable, rapid, cost-effective with high sensitivity and specificity, it shows cross-reactivity with malaria, tuberculosis, and toxoplasmosis [8]. As anti-rK 39-IgG is present in the serum of previously VL treated patients, the rK39 strip test shouldn't be used to diagnose relapse case of Visceral leishmaniasis [9,10]. There is a need to be careful in those patients who had a history of VL, not to treat them without confirming the L.D (Leishman donovan) bodies identification through gold standard technique either bone marrow aspiration or splenic aspiration. The occurrence of false-rK39 positive strip or positive rK39 strip test for up to 2 years in successfully VL treated patients which cannot well-differentiated active and past VL infection [11-13]. These limitations were considered during the study of fever history in all the patients [14-16]. Being a natural reservoir host of Leishmania parasites, humans need alert as the disease may be transmitted to healthy people and it may be lethal if not treated at right time.

Conclusion

As per our study objectives, early detection of VL and its treatment would be very helpful to check out the disease transmission dynamics and later its elimination. With this approach, we targeted all patients who have had at least one-day fever history. We observed that the patients who had come with less than 15 days history of fever, showed rK39 strip test negative except one who was positive (with no previous history of VL in that particular patient). Therefore, the recommendation made by the National Vector Borne Disease Control Programme (NBVDCP), India guideline for prediction of VL cases by using of rK39 strip diagnosis test kit is found positive with a fever history of 15 days. This appropriately fulfills the criteria laid down in the Kala-azar elimination program.

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