# VISCERAL LEISHMANIASIS (KALA AZAR): PRESENTATION, DIAGNOSIS AND RESPONSE TO THERAPY (AN EXPERIENCE OF TEN CASES IN ADULTS)

**Muhammad Uzair,[1] Sheraz Jamal Khan[2], Syed Munib[2], Fazal Raheem[3] and Syed Humayun Shah[1]**

[1]THQ Hospital Samarbagh, [2]DHQ Hospital Timergera and [3]Gomal Medical College, D. I. Khan

## ABSTRACT

**Background:** Visceral Leishmaniasis is not uncommon in the NWFP and Afghanistan. Samarbagh and Timergera being the areas of NWFP adjoining Afghanistan has the distinction that both cutaneous and visceral leishmaniasis present early to the physicians. Cutaneous Leishmaniasis is usually easy to diagnose. Visceral Leishmaniasis on the other hand present usually with a diagnostic dilemma. Mostly the cases present in the paediatric age group but some present in adolescents and adults. We are presenting a study of ten such patients in the adult population.

**Objectives:** To study the different modes of presentation of Visceral Leishmaniasis in adult population, the methods of diagnosis and the response to therapy with Arsenic compounds.

**Setting:** Tehsil Headquarter Hospital, Samarbagh and District Headquarter Hospital, Timergera.

**Methods:** A prospective cases of ten cases of Visceral Leishmaniasis in the adult population. The age range varied between 15 years and 35 years. Six patients were males and four were females.

**Results:** The commonest presenting symptoms were fever, mass in the abdomen, anorexia, generalized fatigue and malaise. The common signs were organomegaly and fever. Laboratory diagnosis confirmed Leishman Danovan bodies in the bone marrow smear of all patients. There was also pancytopenia in eight patients. Two patients had anaemia without pancytopenia.

Meglumine antimonate (glucantime) is the only drug available for Visceral Leishmaniasis, is very effective and all of these patients responded to the standard therapy with no relapse at six month's followup.

**Conclusion:** The physician should have a high suspicion of Visceral Leishmaniasis in patients presenting with fever and organomegaly, usually of long standing, with no response to the conventional treatment, worsening of symptoms and mostly negative laboratory investigations or anaemia and pancytopenia which is gradually worsening from an endemic area. It is an easily treatable condition and once the sinister diagnosis of lymphoma and leukaemia are excluded by bone marrow smear examination and a positive diagnosis done, it is amenable to therapy with antimonials.

**Key words:** Visceral leishmaniasis, Kala azar.

## INTRODUCTION

Visceral leishmaniasis was first described in 1903, by Leishman and Donovan. Visceral leishmaniasis is endemic in over 60 countries. The incidence is estimated at 500 000 cases each year(1). It is the most severe form of leishmaniasis and it can be fatal in the absence of treatment. It is transmitted to man by phlebotomus (sandfly) in the Old world and Lutzomiyia in the New World Sergentomyia is another vector found in Baluchistan . The incubation period is 3-6 months, though 10-24 years is also reported .The disease is common in tropical and subtropical areas of the world The protozoon multiplies intracellularly in the reticuloendothelial system The different species may explain the local spread or dissemination. Massive splenomegaly may occur. Lymphadenopathy is also common. Bone marrow involvement vary from hyperplasia to severe hypoplasia resulting in bleeding and severe infections. Organomegaly may not be seen. Fever, usually is of sudden onset, high grade, remittent, intermittent or continuous with a double rise in twenty four hours, vomiting, cough, diarrhea, liver functions derangements, thin brittle hair, dry and scaly skin with ashen appearance and increased pigmentation around the mouth, malar region and temples (signifying the name Kala-Azar or black sickness), and hypergammaglobulinaemia. Sometimes spontaneous bleeding may occur. Both the new world and the old world forms of the disease display similar symptoms and are often complicated by secondary infections The

symptoms of VL vary between individuals and according to geographical foci. However, some of the common symptoms include high undulating fever often with two or even three peaks in 24 hours and drenching sweats which can easily be misdiagnosed as malaria, Chills, rigors, weight loss, fatigue, poor appetite, cough, burning feet, insomnia, abdominal pain, joint pain, anorexia, epistaxis and diarrhoea. Clinical sings include splenomegaly, hepatomegaly and lymphadenopathy. The incubation period is highly variable, the disease can appear anything between ten days to over one year[2,3]. Visceral Leishmaniasis may be completely asymptomatic and may be an incidental finding after investigation for splenomegaly[4].

Visceral leishmaniasis can be complicated by serious secondary bacterial infections such as pneumonia, dysentery and pulmonary tuberculosis, which often contribute to the high fatality rate of VL patients. Other complications, though rare include haemolytic anemia, acute renal damage and sever mucosal haemorrhage.

Diagnosis is based on demonstration of L.D. bodies in smears obtained from bone marrow, lymph nodes, spleen and liver and skin snap smears . Looking for parasites in the spleen and liver is one of the most accurate methods available. Ninty percent of the active cases show parasites in splenic and liver aspirates .The smallest needle possible, preferably, 21-gauge (0.8 mm) should be used to minimise the risk of complications such as haemorrhage of the spleen. Part of the splenic aspirate can be used to make smears for direst microscopic examination and the rest should be cultured. *L. donovani* grows well on Novy- MacNeal- Nicolle (NNN) or Schneider's insect medium supplemented 10% v/v foetal calf serum, although other suitable growth media can be used just as well. Liver biopsy material is less likely to demonstrate parasites on direct examination or on culture, however histological examination will show amasatigotes in Kupffer cells in the portal system.

Other procedures include inoculation of infected tissues into specific culture media and susceptible animals, nasal and oral secretions, tonsillopharyngeal mucosa, urine centrifugates of V.L. patients, aldehyde test, complement fixation test, indirect haemagglutination test and counterimmunofluoresence, direct agglutination , polymerase chain reaction, immunoblot (western blotting), plasma c-reactive protein levels both for diagnosis and for monitoring the response to therapy, immunochromatographic test although it lacks sufficient sensitivity, and Montenegro skin test for the detection of previous infection with leishmania. Cytological clues in bone marrow other than L.D. bodies e.g. "granular stippling" and "basophilic bare cells" may increase the diagnostic value of histopathological methods for the detection of V.L.

Treatment consists of pentavalent antimony compounds, amphotericin B, pentamidine, allupurinol, stibogluconate with paromomycin or interferon gamma, miltefosine, and amphotericin B deoxycholate. The two pentavalent antimonial compounds, sodium stibogluconate and meglumine antimoniate were first introduced in the 1940's and have since been used as first-line chemotherapeutic agents against all forms of leishmaniasis including visceral leishmaniasis. The drugs are administered parenterally and are the safest currently available since they are rapidly excreted by the kidneys and there is virtually no accumulation in the body. Potential side effects include nausea, vomiting, diarrhoea, ECG changes and convulsions. Antimony resistant leishmania Donovani strains may be the cause of treatment failure. One of the methods employed is the use of interferon gamma (IFN-gamma) to treat visceral leishmanasis.

## MATERIALS AND METHODS

This study was conducted the Tehsil Headquarter Hospital Samarbagh and District Headquarter Hospital Timergera from 1st of January 2002 to 31st December 2002. It was a study about the different and varied presentations of Visceral Leishmaniasis. The signs and symptoms were noted in tubulated form on a proforma. The incidence was noted in the whole population who presented to the units during the one year of study. The data was noted down on a proforma and analyzed later and noted down according to the percentage presentation. All those patients were included in the study who had Leishmania Donovani in the bone marrow smears. Majority of them were referred for diagnosis and management from far flung areas of the province as well as Afghanistan. A thorough history was taken and physical examination conducted and recorded including age, sex and the symptoms and signs e.g. fever, nausea, vomiting anorexia, diarrhoea, abdominal distension, weight loss, cough, haemoptysis, temperature, lymphadenopathy, organomegaly, skin and hair changes.

Each patient was investigated and laboratory tests were done. These included complete blood count (CBC), erythrocyte sedimentation rate (E.S.R.), special blood smear, platelet count, smear for malarial parasites (M.P.), urinalysis and bone marrow examination. Neither lymph nodes nor spleen or liver aspiration was done in any case for diagnosis.

All patients were treated with sodium stibogluconate 15-30 mg/kg body weight daily for a total of four weeks each. The response of the treatment was assessed by observing improvement in the general condition of the patient, regression of

the size of the spleen, liver and lymph nodes, reversal of the blood picture to normal, correction of anemia and lastly the resolution of abdominal distension and weight gain. Patients were followed up for 6 months, to note any relapse and/or treatment failure.

## RESULTS

In this prospective study, extending from January 2000 to December 2003, a total of 10 patients, suffering from V.L. were enrolled. The ages ranged from 15 and 35 years. Six patients were male and only 4 patients were females. All patients had history of fever and weakness while other symptoms less frequent as shown in Table I, Table II shows the signs observed. Weight loss and organomegaly were found in all cases.

Laboratory data showed that all the patients had anaemia (Hb < 7 gm%), thrombocytopenia (platelet count < 60,000/cmm), leukopenia (WBC < 4X10 $^{9}$/L) and neutropenia (Neutrophils count < 2.5 X 10 $^{9}$/L). Almost all patients had normal lymphocytic count. Bone marrow smears of all the patients were having L.D. bodies present. Formal gel test was positive in all the cases. Liver enzymes were raised in 24% of the cases. The data is shown in Table III.

Response was good to sodium stiboglunconate therapy. Fever was the first to subside in the initial 7-10 days period followed by the regression of the hepatosplenomegaly and the reversal of the laboratory data.

No relapse was observed during the 6 months follow up period, by which time the patients were declared cured.

Only two patients died because of the very late presentation/referral, having hepatic failure and profound thrombocytopenia (platelet count < 10000/cmm).

**Table I: Presenting symptoms of V.L. observed.**

| Symptoms | Percentage (%) |
|---|---|
| Fever | 100 % |
| Weakness | 100 % |
| Anorexia | 80 % |
| Abdominal distension | 80 % |
| Yellow discoloration of sclera | 20 % |
| Nausea/vomiting | 20 % |
| Cough | 20 % |
| Diarrhea | 20 % |
| Bleeding | 08 % |

**Table II: Presenting Signs.**

| Signs | Percentage (%) |
|---|---|
| Weight loss | 100 % |
| Splenomegaly | 100 % |
| Hepatomegaly | 100 % |
| Jaundice | 40 % |
| Purpuric spots | 40 % |
| Epistaxis | 20 % |
| Lymphadenopathy | 20 % |
| Hepatic failure | 08 % |

**Table III: Laboratory Data.**

| Test | Percentage (%) |
|---|---|
| Anaemia | 100 % |
| Thrombocytopenia | 100 % |
| Leukopenia | 100 % |
| Neutropenia | 100 % |
| L.D. bodies in bone marrow | 100 % |
| Formal Gel test | 100 % |
| Raised liver enzymes | 24 % |

## DISCUSSION

V. L. mainly affects infants and young children as is evident from this study and others[1,2,3,4,5,6]. We observed a male sex predominance. Similar male sex predominance is reported by Rahim F. et al[7,8]. However, this may be merely due to male sex predominant society. Rahim F. et al describes a similar picture in Cutaneous Leishmaniasis as well.

The main clinical features were fever, weakness, weight loss, hepatosplenomegaly, anorexia and abdominal distension. Other features like purpuric spots, epistaxis, lymphadenopathy, jaundice, nausea, vomiting, cough, diarrhea and bleeding were less frequent. Hepatic failure was observed in two patients and both of them died. Rahim F. et al[8] has almost similar clinical presentations. Lymphadenopathy is rare in this part of the world but is common in African type of the disease[9,10,11].

Laboratory data revealed anaemia in all the cases. This is also reported by others[8] and is caused

by haemolysis, ineffective erythroporesis and hypersplenism Thrombocytopenia, leukopenia and neutropenia were also observed in all the patients. These are well-documented findings. L.D. bodies were present in bone marrow smears of all the patients and in fact this was the main diagnostic test in this study. We did not try splenic aspirate because of its impending complications though it is considered to be more sensitive than bone marrow aspirate examination provided that the procedure is performed with proper precautions . Formal gel test was also positive in all cases. Rahim F. et al had also 100% result. Raised liver enzymes were seen in 6 cases (24%), of whom 2 cases (8%) died. Hepatic damage is a late complication[8] and combined with thrombocytopenia, leads to intractable hemorrhage as did occur in our two dying patients.

All of our patients except the two who died due to late presentation, responded well to Meglumine antimonate (glucantime), which is the only available drug here at Peshawar for the treatment of Leishmaniasis. These results correlate with other studies[8] although the African variety of V.L. is reported to be less responsive to sodium stibogluconate[12,13,14]. Resistant cases have been reported from other places of the world especially India[15,16,17].

## CONCLUSIONS

V.L., a treatable disease which may prove fatal if not detected and treated early enough, is not uncommon in our country and physicians should have high index of suspicion when confronted with a case of pyrexia, anemia, leucopenia and unexplained organomegaly.

Prevention can be achieved by using mosquito nets, insecticide sprays, destruction of animal reservoirs and early detection and treatment of infected persons.

## REFERENCES


1. WHO Recommended Surveillance Standards, Second edition, October 1999, WHO/CDS/CSR/ISR/99.2
2. Al-Jurayyan, N. A., Al-Nasser, M. N., Al-Fawaz, I. M., Al-Ayed, I. H., Al-Herbish, A. S., Al-Mazrou, A. M., Al-Sohaibani, M. O., (1995), The haematological manifestations of visceral leishmaniasis in infancy and childhood. J. Trop. Pediatr. 41(3): 143-8.
3. Benjamin, B., Annobil, S. H., Bassuni, W. A., (1994), Diagnostic and management problems in childhood visceral leishmaniasis in south-western Saudi Arabia. Ann. Trop. Paediatr. 14(1): 7-13.3.
4. Ephros, M., Paz, A., Jaffe, C. L., (1994), Asymptomatic visceral leishmaniasis in Israel. Trans. R. Soc. Trop. Med. Hyg. 88(6): 651-2.
5. Hohenschild, S., Feldmeier, H., (1995), Imported Kala Azar in children and adults: Comparison of medical history, clinical, and diagnostic findings. J. Trop. Pediatrics. 41(6): 378-379.
6. Sacks, D. L., Kenney, R. T., Kreutzer, R. D., Jaffe, C.L., Gupta, A. K., Sharma, M. C., Sinha. S. P., Neva, F. A., Saran, R., (1995), Indian kala-azar caused by *Leishmania tropica*. Lancet.345(8955): 959-61.
7. WHO expert committee report, (1991). Control of the leishmaniasis. Technical report series 793.
8. Fazal Rahim, Shiraz Jamal, Fazal Raziq, Muhammad Uzair, Bakht Sarwar, Hazrat Ali, Mohammad Sherin. An outbreak of Cutaneous Leishmaniasis in a village of district Dir, JPMI 2003 Vol 17 No 1.
9. F. Rahim F, Rehman F, Ahmad S, Zada B. Visceral leishmaniasis in district Dir NWFP. J Pak Med Assoc 1998; 48: 162.
10. Ali, A., Ashford, R. W., (1994), Visceral leishmaniasis in Ethiopia. III. The magnitude and annual incidence of infection, as measured by serology in an endemic area. Ann. Trop. Med. Parasitol. 88(1): 43-7.
11. Ali, A., Ashford, R. W., (1994), Visceral leishmaniasis in Ethiopia. IV. Prevalence, incidence and relation of infection to disease in an endemic area. Ann. Trop. Med. Parasitol. 88(3): 289-93.
12. Shiddo, S. A., Aden-Mohamed, A., Akuffo, H. O., Mohamud, K. A., Herzi., A. A., Herzi-Mohamed, H., Huldt, G., Nilsson, L. A., Ouchterlony, O., Thorstensson, R., (1995), Visceral leishmaniasis in Somalia: prevalence of markers of infection and disease manifestations in a village in an endemic area. Trans. R. Soc. Trop. Med. Hyg. 89(4): 361-5.
13. Berhe, N., Ali, A., Hailu, A., Yeneneh, H., (1994), Relapse in Ethiopian visceral leishmaniasis (VL) patients after therapy with pentavalent antimonials: a ten year observation. Acta. Trop. 57(1): 83-90.
14. Baily, G. G., Nandy, A., (1994), Visceral leishmaniasis: more prevalent and more problematic. J. Infect. 29(3): 241-7.
15. Chance, M. L., (1995), New developments in the chemotherapy of leishmaniasis. Ann. Trop. Med. Parasitology. 89(1): 37-43.
16. Chatterjee, S., Chatterjee, R., (1994), Visceral leishmaniasis treated with rifampicin and co-trimoxazole. J. Indian. Med. Assoc. 92(9): 307.
17. Giri, O. P., (1994), Treatment of visceral Leishmaniasis unresponsive to pentamidine with amphotericin B. J. Assoc. Physicians. India. 42(9): 688-9.
18. Giri, O. P., Singh, A. N., (1994), Experience with amphotericin B in sodium stibogluconate- unresponsive cases of visceral Leishmaniasis in north Bihar. J. Assoc. Physicians. India. 42(9): 690-1.



**Address for correspondence:**
Dr Sheraz Jamal Khan,
Assistant Professor of Medicine,
Department of Medicine,
Gomal Medical College,
Dera Ismail Khan.
E-mail: shiraz.jamal@gmail.com
Phone: 0961-720366; 0333-9963164