

## MEDICAL EDUCATION (ORIGINAL ARTICLES)

### RISK OF ACQUIRING CUTANEOUS LEISHMANIASIS IN TRIBAL AREAS OF PAKISTAN

Shaista Nayyar, Asif Niaz\*, Muhammad Farooq\*, Ehsan Zafar\*

Sahiwal Medical College, Sahiwal Pakistan, \*Combined Military Hospital Okara Pakistan

#### ABSTRACT

**Objective:** To assess the risk of acquiring cutaneous leishmaniasis (CL) in tribal areas of Pakistan.

**Study Design:** A cross sectional observational study.

**Place and duration of study:** Combined Military Hospital, Okara, from Oct 2014 to Mar 2015.

**Material and Methods:** A total of 4500 persons between the ages of 22 to 50 years, who were moved from central areas of Punjab to Waziristan on duty, were studied for the occurrence of CL. All cases developed cutaneous lesions and were confirmed as having CL were included in the study. During the same period, 4300 persons living at Okara, who did not have any exposure to the Federally Administered Tribal Area in same age group, were also observed and studied as control group.

**Results:** A total of 36 patients suffered from CL in the study population, while one case from the control group developed the disease ( $p < 0.05$ ). This patient was resident of Sindh and had repeated visits to his home station. The risk of developing CL was greater in Waziristan as compared to central Punjab as odds ratio (OR) was calculated as 30.79.

**Conclusion:** There is substantial risk of developing CL in persons exposed to tribal areas of Pakistan.

**Keywords:** Cutaneous Leishmaniasis, Odds ratio, Risk factors, Waziristan.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### INTRODUCTION

Cutaneous leishmaniasis (CL) is a major tropical infection of public health importance. It is caused by a protozoan, *Leishmania*, which is an intracellular parasite<sup>1</sup>. The vector involved is sandfly<sup>2</sup>. It is prevalent in 92 countries of the world<sup>3</sup>. In Pakistan, Balochistan and some parts of Khaiber Pakhtoon khwah are considered endemic for this disease<sup>4</sup>. The disease is at its increase after rapid move of people as refugees due to regional conflicts (Afghan war). There are many factors which contribute towards prevalence of this disease including lack of resistance of individual, presence and concentration of vector and temperature of that area. In general, the overall incidence of leishmaniasis is increasing worldwide<sup>5-7</sup>. It affects all the ages and considering the site of the bite, it may inflict heavy costs in terms of finances and cosmetic disfiguring, even when treated. *Leishmania* is a

protozoa and anthroponotic which spreads by the sandfly<sup>8</sup>. Desert rodents and some animals act as a reservoir in areas of endemic population. Outbreaks have been recorded in various parts of the world among refugees and areas of poor hygienic conditions. Now as per WHO perspectives countries like nepal and India are taking fast track measures to control this vector born disease<sup>9</sup>.

In Pakistan, increasingly more cases have been encountered in general medical practice<sup>10</sup> because of more exposure of army troops to the endemic areas and also wide movements in terms of travelers and internally displaced persons (IDPs). As these people are having low immunity and are liable to develop the disease more frequently, so the need to investigate this emerging problem cannot be overlooked. Although some studies are available on the prevalence of this disease among residents of endemic areas of Baluchistan, no significant study has yet been conducted in the newly explored tribal areas. In recent era we had large

**Correspondence:** Dr Shaista Nayyar, Sahiwal Medical Collage Sahiwal Pakistan (Email: [shaistanayyar@gmail.com](mailto:shaistanayyar@gmail.com))

Received: 27 Nov 2017; revised received: 01 Mar 2017; accepted: 16 Mar 2017

number of troops moved from interior Pakistan to the tribal zone, which provided us with the unique opportunity to study various diseases prevalent in the area. CL is among the top most prevalent diseases in this area.

The risk of developing CL in other wise a healthy, non- immunocompromised person when exposed to tribal areas of south Waziristan agency (SWA) is greater as compared to similar population residing in non- endemic parts of the country. The purpose of this study was to assess the risk of acquiring CL in tribal areas of Pakistan.

### **MATERIAL AND METHODS**

This was a case-control study conducted at Combined Military Hospital (CMH), Okara, from October 2014 to March 2015. A total of 4500 male individuals between the ages of 22 to 50 years were observed for at least six months after their first movement in the subject area of SWA. These were labeled as group 1. An almost similar number of individuals were studied who had no history of travel towards the subject area or other endemic areas of Pakistan and were included as the control group (group 2). Individuals with history of travel to Baluchistan, having diseases like diabetes mellitus, pulmonary tuberculosis, chronic hepatitis or any other disease affecting immune system, were excluded from the study.

All the cases that developed non-healing cutaneous ulcers with strong suspicion of CL were studied at CMH, Okara. The lesions, were studied clinically and confirmed by isolation of protozoa in skin scrapping examination<sup>11</sup>. The patients were then followed- up during their treatment for response.

The data was analyzed with a web-based statistics analyzer Open Epi V 3.03a.5 Frequencies along with percentages were calculated for the sub-groups of sampled individuals. The unadjusted association between the independent variable and the outcome variable were evaluated using odds ratios (ORs) and tested for the statistical significance using Fisher's, exact test. A *p*-value <0.05 was considered significant.

### **RESULTS**

A total of 36 individuals suffered from CL among the study population at SWA while one case in the control group, was diagnosed with the disease (table-I). This exposure was found statistically significant (*p*<0.001). OR was calculated as 30.79 with 95% confidence limits of 4.206-225.4.

The mean age of the patients was  $32 \pm 8$  years in group 1 and  $36 \pm 6$ , years in group 2. Four patients among the study group showed relatively low total leucocyte count (TLC), while hemoglobin, platelets, liver and renal function tests, were within normal limits. Average time of exposure in the area before the presentation of the disease was  $5 \pm 2$  months in group 1 while in group 2, it was  $6 \pm 1$  months. Family history of CL in the only case of group 2 was positive. Two of his family members had developed CL in recent past. Other clinical features observed in patients of CL are highlighted in table-II.

### **DISCUSSION**

Leishmaniasis is a major health problem worldwide. It is also a particular problem in the rural areas of Pakistan. The disease occurs in varying presentations, from the self-limited and even self-healing cutaneous forms to fatal systemic disease<sup>12</sup>. Although it is endemic in over 80 countries of the world and some parts of Pakistan, the overall prevalence is estimated at about 12 million cases worldwide<sup>13</sup>. Almost 2 million new cases have been estimated worldwide<sup>14</sup>. In Pakistan, Baluchistan<sup>15</sup>, some parts of southern Punjab and Sindh<sup>16</sup> have been considered as endemic areas. One positive case among control group of our study acquired leishmaniasis during his repeated visits to his home town in Sindh. There is no study available on the subject of incidence, prevalence or risk of acquiring infection in newly explored area of Waziristan agency which is neighbored by Afghanistan on the west and Baluchistan on the south. It has been declared as an emerging worldwide infection lately<sup>17</sup>. So the need was to study the risk in persons who were exposed to

this area for the first time. This has also been over stressed since the United States (US) troops were exposed to the areas of Afghanistan<sup>18,19</sup>. Although leishmaniasis occurs predominantly in individuals living in endemic regions, travelers to these areas can also be infected, even after less than one week of exposure.

The commencement of operations in tribal areas of Pakistan by Pakistan army provided us with the unique opportunity to study the various

no vaccine to prevent the acquisition of infection, although attempts are in progress. Contradictory reports are available that show that there is evidence of cellular immune response associated with at least partial acquired immunity<sup>21</sup>. Although the vector of CL has not so far been incriminated in Pakistan; and the situation of prevalence of leishmaniasis is much alarming and needs to be readdressed by the health authorities.

In our study, there was a high risk of

**Table-I: Comparison of the study and the control groups.**

	Group 1	Group 2	*OR (**CL)	<i>p</i> -value
Total number of individuals	4500	4300	-	<0.001
Patients who developed Cutaneous Leishmaniasis	36	1	30.79 (4.206, 225.4)	

\*Odds ratio, \*\*Confidence limits

**Table-II: Other clinical features of the cases in the study group.**

Symptoms/ signs	Number (n=36)	Percentage (%)
Constitutional symptoms	19	52.7
Fever	2	5.5
<i>Number of lesions</i>		
Single lesion	35	97.2
Multiple lesions	1	2.8
<i>Size of lesion</i>		
>1 cm	23	
<1 cm	13	
Induration at the site	19	52.8
Discharge from the lesion	7	19.4
<i>Site of the lesion</i>		
Upper limb	23	63.8
Lower limb	10	27.8
Face	2	5.5
Others	1	2.8
<i>Response to treatment</i>		
Responders	36	100
Non-responders	-	-

diseases prevalent in the newly exposed area<sup>20</sup>. Leishmaniasis was one of the major health hazards, prevailing in this region and we studied the young healthy population which was exposed to the Waziristan agency. As the typical incubation period is one week to several months, so we included the cases at presentation and also followed them for more than 4 months. There is

developing CL in young population when first time exposed to endemic area. Local studies on this subject only provide vague data with no significant statistical analysis. A survey conducted in a hospital of Baluchistan, the incidence of CL was 1% and similarly, the prevalence of skin lesion was also 1% in school children<sup>22</sup>. In refugee camps of Khyber province,

the prevalence of CL lesions was 2.7%, and the prevalence of scars was 4.2%<sup>23</sup>. The prevalence of lesions was lower in Pakistanis than in the Afghan refugee population. All these studies do not give idea of risk assessment in newly exposed population. In our study, the useful information regarding the risk assessment was calculated for the visitors and travelers who were visiting these endemic areas for the first time.

Increasing re-emergence of leishmania, due to IDPs movement, travelers and induction of troops in the endemic areas, makes CL a growing public health concern in many countries<sup>24</sup>. In our study, we tried to address the problem by assessing the risk while entering into the endemic area which has pointed the need for further studies to be conducted for this emergent problem. The study also guides the new visitors as well as the health authorities to take extra measures of prevention and vector control when dealing with refugees, IDPs and new population groups moving to endemic areas<sup>25</sup>. So this study can go a long way to help planning a comprehensive health program<sup>26</sup>.

## CONCLUSION

In conclusion, young, healthy individuals exposed for the first time to tribal areas have a much higher risk of developing CL. More studies are needed to identify specific risk factors leading to the development of CL in vulnerable population.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any authors.

## REFERENCES

1. Fakhar M, Pazoki Ghohe H, Rasooli SA, Karamian M, Mohib AS, Ziaei Hezarjaribi H, et al. Genetic diversity of Leishmania tropica strains isolated from clinical forms of cutaneous leishmaniasis in rural districts of Herat province, Western Afghanistan, based on ITS1-rDNA. *Infect Genet Evol* 2016; 41: 120-7.
2. Rogers ME, Ilg T, Nikolaev AV, Ferguson MA, Bates PA. Transmission of cutaneous leishmaniasis by sand flies is enhanced by regurgitation of fPPG. *Nature* 2004; 430: 463-7.
3. World Health Organization: Weekly Epidemiological Record (WER) 2016; 91(22): 285-96.
4. Ahmad IP. Cutaneous leishmaniasis in southern Balochistan: Observations on a zoonosis. *Pak J Med Res* 1988; 27: 12-5.
5. Alvar J, Vélez ID, Bern C, Herrero M, Desjeux P, Cano J, et al. Leishmaniasis Worldwide and Global Estimates of its Incidence. *PLoS ONE* 2012; 10: 1371.
6. Khezzani B, Bouchemal S. Demographic and spatio-temporal distribution of cutaneous leishmaniasis in the Souf oasis (Eastern South of Algeria): Results of 13 years. *Acta Trop* 2017; 166: 74-80.
7. Hoyos CL, Cajal SP, Juarez M. Epidemiology of American Tegumentary Leishmaniasis and Trypanosoma cruzi Infection in the Northwestern Argentina. *Biomed Res Int* 2016; 6456031.
8. Aneela ZD, Haroon ZD. Prevalence of Leishmania in Sand Fly in Pakistan. *Pak J Zool* 2012; 44: 61-5.
9. Visceral leishmaniasis: WHO publishes validation document as countries approach elimination. [http://www.who.int/neglected\\_diseases/news/Visceral\\_leishmaniasis\\_WHO\\_publishes\\_validation\\_document](http://www.who.int/neglected_diseases/news/Visceral_leishmaniasis_WHO_publishes_validation_document).
10. Ashford RW. The Leishmaniasis as emerging and re-emerging globally. *Int J Parasitol* 2000; 30: 1269-81.
11. Herwaldt BL. Leishmaniasis. *Lancet* 1999; 354: 1191-9.
12. Khan SJ, Muneeb S. Cutaneous leishmaniasis in Pakistan. *Dermatol Online J* 2005; 11(1): 4.
13. Oryan A, Akbari M. Worldwide risk factors in leishmaniasis. *Asian Pac J Trop Med* 2016; 9(10): 925-32.
14. Choi CM, Lerner EA. Leishmaniasis as an emerging infection. *J Investig Dermatol Symp Proc* 2001; 6: 175-82.
15. Jan SN, Burney MI, Lari FA, Rab MA, Shafiq M. Cutaneous leishmaniasis in Balochistan. *Pakistan J Med Res* 1984; 23: 64-9.
16. Bhutto AM, Soomro FR, Katakura K. Leishmaniasis in Sindh, Pakistan: Outbreak and review of literature. *J Pakistan Assoc Dermatol* 2008; 18: 212-9.
17. Lawn D, Whetham J, Chiodini P. New world mucosal and cutaneous leishmaniasis: an emerging health problem among British travelers. *Q J Med* 2004; 97: 781-8.
18. Aronson NE, Sanders JW, Moran KA. In harm's way: infections in deployed American military forces. *Clin Infect Dis* 2006; 43: 1045-51.
19. Khosravani M, Moemenbellah-Fard MD, Sharafi M, et al. Epidemiologic profile of oriental sore caused by Leishmania parasites in a new endemic focus of cutaneous leishmaniasis, southern Iran. *J Parasit Dis* 2016; 40(3): 1077-81.
20. Ozkeklikci A, Karakus M, Ozbel Y. The new situation of cutaneous leishmaniasis after Syrian civil war in Gaziantep city, Southeastern region of Turkey. *Acta Trop* 2017; 166: 35-8.
21. Prati F, Goldman PA, Lizzi F, Belluti F, Koren R, Zilberstein D, Bolognesi ML. Quinone-amino acid conjugates targeting Leishmania amino acid transporters. *PLoS One* 2014; 9: e107994.
22. Rab MA, Azmi FA, Iqbal J. Cutaneous leishmaniasis in Baluchistan: reservoir host and sandfly vector in uthal, lasbella. *JPMA* 1986; 6: 134-8.
23. Brooker S, Mohammed N, Adil K, Agha S, Reithinger R, Rowland M, et al. Leishmaniasis in Refugee and Local Pakistani Populations. *Emerg infect Dis* 2004; 10: 1681-4.
24. Seidelin H. Leishmaniasis and Babesiosis in Yucatan. *Ann Trop Med Parasit* 2016; 6(2): 295-300.
25. Thies SF, Bronzoni RV, Espinosa MM. Frequency and diversity of phlebotomine sand flies (Diptera: Psychodidae) in Sinop, State of Mato Grosso, Brazil. *Rev Soc Bras Med Trop* 2016; 49(5): 544-52.
26. Peña S, Scarone L, Serra G. Macrocytes as potential therapeutic agents in neglected diseases. *Future Med Chem* 2015; 4: 1-28.