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Short Communication

Determining the Frequency of Cystic Echinococcosis among Suspected Cases Referred to Health Centers Southwest Iran, and Post-Treatment Serologic Follow-Up

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Abstract

Background: This study was designed to determine the frequency of hydatidosis in Khuzestan Province, Iran and to evaluate the antibody changes in infected individuals after treatment.

Methods: Overall, 454 sera were collected from health centers of Khuzestan Province, southern Iran (from 2013 to 2018). Demographic data such as age, gender and history of disease were recorded. Serum samples were investigated for antibody against CE by ELISA using antigen B. Thirty six of cases were followed up after treatment.

Results: Among the 454 evaluated cases, antibody against CE was detected in 184 (40.52%) including 115 (62.5%) females and 69 (37.5%) males. Age distribution was from 8-97 yr, the highest prevalence of hydatid cyst was observed in age group 40-49 years. Liver was the most infected organ (76.63%). Relapse of CE occurred in 23 of patients. In the majority of patients the antibody decreased, whereas in some cases increased CE antibody observed during post-treatment follow up.

Conclusion: Current study indicated the high prevalence of hydatidosis and rate of relapse after treatment among suspected patients. Therefore, long periods and regular follow-up of patients after treatment is necessary and for these monitoring, antibody assay can be an appropriate method.



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Introduction

Cystic echinococcosis is a zoonotic disease caused by the larval stage of *Echinococcus granulosus*. In the life cycle of this parasite, dogs and other canids are the definitive host and herbivores acts as intermediate host. Humans acquire infection by accidental ingestion of parasite embryonated eggs excreted in the feces of definitive host (1-3).

Diagnosis of hydatid cyst is performed using serological methods along with radiological examination (4). Relapses CE may occur between 2%-25% of cases after therapy (5). Therefore, long periods and regular follow-up of patients after treatment is necessary.

CE has a cosmopolitan distribution, but the highest prevalence's of CE in Animal and human are observed in the Mediterranean region, southern and central Russia, Central Asia, China, Australia, some regions of South America, and northern and eastern regions of Africa (6, 7). Iran is country of endemic situation for CE, the disease is prevalent in different part of the country. Prevalence rate of CE in Iran is reported from 0.6 to 1.2 in 100000 populations (8). In a study Rafiei et al. reported prevalence rate of seropositivity, 13.8% among the nomadic people in Khuzestan Province (6). The overall annual economic loss caused by hydatidosis in humans and animals in Iran is estimated at US\$ 232.3 million. This disease is one of the major public health priority (9).

The present study aimed to determine the importance of post-treatment follow up in patients with CE and awareness of the prevalence of the disease in the region.

Materials and Methods

Ethic statement

The study protocol was reviewed and approved by the Ethics Committee of Ahvaz

Jundishapur University of Medical Sciences (Approval No IR.AJUMS.REC 1397.128).

Serum samples

Four hundred fifty four sera (292 females and 162 males) were collected from individuals with clinical signs and CE suspected cases referred to health centers during 5 years (from 2013 to 2018). This research was conducted on patients with clinical symptoms such as abdominal pain, liver dysfunction signs, hemoptysis, and respiratory disorder. Demographic data such as age, gender and history of disease were recorded. Antibody against CE was evaluated by ELISA assay. The present study ELISA used the same method developed previously (6) The imaging technique was used to determine the location of the cysts.

Preparation of Antigen B

Hydatid cyst fluid (HCF) was obtained from livers of sheep slaughtered at the Ahvaz abattoirs. Antigen B (AgB) was purified and prepared from HCF (10).

ELISA

Antibody against CE was evaluated by ELISA using antigen B. The present study ELISA used the same method which was developed previously (11). In each run the positive CE and negative sera were used as positive and negative control. Cut-off was determined using normal human serum obtained from healthy people in the region and mean ± 2 SD was used as cut-off value.

Statistical analysis

All statistical analyses were performed using SPSS software ver. 24 (Chicago, IL, USA). Statistical evaluation was carried out Chi square test and $P < 0.05$ was considered significant.

Results

Among the 454 evaluated cases, antibody against CE was detected in 184 (40.52%) including 115 (62.5%) females and 69 (37.5%) males. Seropositivity was more prevalent in females than in males. Age distribution was from 8-97 yr (mean 49.1 ± 16.1 yr), the highest

prevalence of hydatid cyst was observed in age group 40-49 years. There was a significant association between the prevalence of hydatid cyst and the age group ($P=0.000$).

Liver was the most infected organ and the second most frequent infected organ was lung (Table 1).

Table 1: Organs involved among CE serpositivity of suspected patients referred to primary health care in Southwest, Iran

<i>Cyst location</i>	<i>Male (%)</i>	<i>Female (%)</i>	<i>Total (%)</i>
Liver	38(20.65)	80(43.47)	118(64.13)
Lung	6(3.26)	10(5.43)	16(8.69)
Kidney	4(2.17)	5(2.71)	9(4.89)
Spleen	1(0.54)	3(1.63)	4 (2.19)
Abdomen	-	3(1.63)	3(1.63)
Bone	3(1.63)	1(0.54)	4(2.17)
Brain	1(0.54)	-	1(0.54)
Liver+ Other organs	49(26.63)	92(50)	141(76.63)
Lung+ Other organs	15(8.15)	18(9.78)	33(17.93)
More than one organ	5(2.71)	1(0.54)	6(3.26)

Twenty nine patients simultaneously had two or more organs infected with hydatid cyst and most of them were hepatopulmonary.

Follow up of patients after treatment

One hundred and twenty-one of cases were surgically treated. Of these, 36 patients were followed up for 12-66 months (Because there was evidence of relapse in them), Relapse occurred in 23 patients. In fact, the rate of relapse among surgical patients was approximately 19%. The liver was primary infected organ with 18 cases, followed by lung with 3 cases, two cases in bone. Liver was the most involved organ after relapse, infected alone or along with other organs. Most cases of relapse were occurred within 1-4 yr after the initial disease.

Discussion

In this study, antibody against CE was detected in the sera of 454 CE suspected sub-

jects and the results indicated that 40% of cases had antibody against CE. In Behan et al. study 15.03% of CE suspected subjects had (12) and in Netherland it was detected in sera 26% of CE suspected subjects (13).

Although seropositive rate in CE suspected subjects depends on various factors, nevertheless, the high percentage of positive cases in this study may indicate a higher prevalence of disease in the region than the above mentioned cases. In some cases, 30%-40% of patients with hydatid cyst are negative for antibody detection, and this possibility could be due to the ability of *Echinococcus granulosus* antigens to inhibit B cell activity and proliferation (14). Antibody response in patients with CE depends on factors such as type of cyst, size and number of cyst, the stage of disease and involved organ, therefore false negative results are seen in cases of calcified cysts, extra hepatic cysts and small cysts (15).

Although most organs of the body could be involved with hydatid cyst, but in this study

liver was the most infected organ (76.63%) and the second most frequent infected organ was lung (17.93%). This finding was in accordance with the results obtained in other studies in Iran (16-19).

Findings of the current study revealed that the prevalence of hydatid cyst in female (62.5%) was greater than male (37.5%). This result is in accordance with most previous researches. Although gender is not a risk factor for CE and there is no clear explanation for this higher prevalence rate, but it seems more contacts with suspicious materials such as vegetables could increase risk of infection (20-22).

In current study the highest prevalence of hydatid cyst was observed in age group 40-49 years. Considering the slow growth of hydatid cyst, clinical signs appear several years after initial infection. Therefore original infection might be occurred in early ages but clinical signs have appeared in older ages.

In our study, different patterns of total IgG antibody changes were observed in post-treatment follow up, in most patients, antibody level decreased after treatment. Considering that, antibody assay is easy in these patient and the existence of antibody can indicate cyst in all organs of the body, therefore this test can be appropriate method for patients follow up.

However, in some patients, antibody changes were irregular and in some cases, antibody was increased after treatment. Various factors affect antibody changes in patients with hydatid cyst such as, sensitivity of serologic test, possibility post-treatment relapse in patients, as well as the release of antigenic material in the presence of the remains of the dead cysts (23).

Total IgG alone was not effective for post-treatment follow up and probably the measurement of the IgG subclasses especially IgG2 can help to diagnosis active disease, therefore IgG2 assay can be helpful in post-treatment follow up or relapse diagnosis. In addition,

IgG3 and IgG4 was not suitable subclass for post-treatment follow up (24). Conversely, in other studies, the researchers showed relationship between the IgG4 with the presence of an active disease and IgG4 was proposed as a suitable subclass for post-treatment follow up (5).

In this study relapse of CE occurred in 23 of patients. Despite advance in surgical techniques and the use of chemotherapy, relapse is one of the main complication in patients with hydatid cyst (25). It is difficult to detect the exact time of relapse in CE patients. In this study, the approximate time of relapse in patients was considered after initial surgery.

Disease relapse we determined by surgery and confirmed by pathology. However, it is not clear that these secondary cases are resulted as new exposure to the infectious resources or spillage of cyst materials during surgery.

As regards, lack of information about the exact time of relapse of the disease, occurrence of persistently relapse in the majority of followed-up patients, impossibility of following up the patients in regular times it makes hard achieving a proper perspective on the antibody fluctuation after relapse.

Conclusion

Despite advances in therapeutic techniques of Cystic echinococcosis, recurrence of the disease is one of the main problems in patients. Current study indicated the high prevalence of hydatidosis and rate of relapse after treatment among suspected patients. Therefore, long periods and regular follow-up of patients after treatment is necessary and for this monitoring, antibody assay can be an appropriate method.

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Conflict of interest

The authors declare that there is no conflict of interest.

References

1. Agudelo NH, Brunetti E, McCloskey C. Cystic Echinococcosis. *J Clin Microbiol.* 2016; 54(3):518-23.
2. Neumayr A, Tamarozzi F, Goblirsch S, et al. Spinal cystic echinococcosis—a systematic analysis and review of the literature: part 1. Epidemiology and anatomy. *PLoS Negl Trop Dis.* 2013; 7(9):e2458.
3. Brunetti E, Garcia HH, Junghanss T. Cystic echinococcosis: chronic, complex, and still neglected. *PLoS Negl Trop Dis.* 2011; 5(7):e1146.
4. Sarkari B, Rezaei Z. Immunodiagnosis of human hydatid disease: where do we stand? *World J Methodol.* 2015; 5(4):185-95.
5. Tenguria RK, Naik MI. Evaluation of human cystic echinococcosis before and after surgery and chemotherapy by demonstration of antibodies in serum. *Ann Parasitol.* 2014; 60(4):297-303.
6. Rafiei A, Hemadi A, Maraghi S, et al. Human cystic echinococcosis in nomads of south-west Islamic Republic of Iran. *East Mediterr Health J.* 2007; 13(1):41-8
7. Sadjjadi SM. Present situation of echinococcosis in the Middle East and Arabic North Africa. *Parasitol Int.* 2006;55:S197-202.
8. Rokni M. Echinococcosis/hydatidosis in Iran. *Iran J Parasitol.* 2009; 4(2):1-16.
9. Harandi MF, Budke CM, Rostami S. The monetary burden of cystic echinococcosis in Iran. *PLoS Negl Trop Dis.* 2012; 6(11):e1915.
10. Sadjjadi SM, Sedaghat F, Hosseini SV, et al. Serum antigen and antibody detection in echinococcosis: application in serodiagnosis of human hydatidosis. *Korean J Parasitol.* 2009; 47(2):153-157.
11. Karami MF, Maraghi S, Rafiei A, et al. Comparison of Sensitivity and Specificity of Native ELISA Test (Prepared in Khuzestan, Iran) and Commercial ELISA Kit in the Diagnosis of Human Hydatidosis. *Zahedan Journal of Research in Medical.* 2019; 21(4): e91416.
12. Beyhan YE, Babür C, Mungan M, et al. Evaluation of cystic echinococcosis suspected patients applied to national parasitology reference laboratory of public health institution of Turkey between 2009-2013. *Turkiye Parazitol Derg.* 2015; 39(1):17-21.
13. Madiyal M, Banerjee B, George AK, et al. Role of Serology in Diagnosis of Human Hydatidosis: Experience from a Tertiary Care Hospital. *International Journal of Current Microbiology and Applied Sciences.* 2016; 5(12):195-202.
14. Griffin DO, Donaghy HJ, Edwards B. Management of serology negative human hepatic hydatidosis (caused by *Echinococcus granulosus*) in a young woman from Bangladesh in a resource-rich setting: A case report. *IDCases.* 2014; 1(2):17-21.
15. Manzano-Román R, Sánchez-Ovejero C, Hernández-González A, et al. Serological diagnosis and follow-up of human cystic echinococcosis: a new hope for the future? *Biomed Res Int.* 2015;2015:428205.
16. Kamali M, Yousefi F, Mohammadi MJ, et al. Hydatid cyst epidemiology in Khuzestan, Iran: A 15-year evaluation. *Archives of Clinical Infectious Diseases.* 2018; 13(1):e13765.
17. Fallah N, Rahmati K, Fallah M. Prevalence of Human Hydatidosis Based on Hospital Records in Hamadan West of Iran from 2006 to 2013. *Iran J Parasitol.* 2017; 12(3):453-460.
18. Rezaei F, Saghafipour A, Sheikholeslami NZ, et al. Investigation of demographic and clinical status of sufferers of hydatid cysts referred to hospitals affiliated to Qom University of Medical Sciences during a 12-year period (2002-2013), Iran. *Qom Univ Med Sci J.* 2014; 8(5):63-67.
19. Hajjipirloo HM, Bozorgomid A, Alinia T, et al. Human cystic echinococcosis in west azerbaijan, northwest Iran: a retrospective hospital based survey from 2000 to 2009. *Iran J Parasitol.* 2013; 8(2):323-6.
20. Sarkari B, Hosseini F, Khabisi SA, et al. Seroprevalence of cystic echinococcosis in blood donors in Fars province, southern

- Iran. *Parasite Epidemiol Control*. 2016; 2(1):8-12.
21. Heidari Z, Mohebbali M, Zarei Z, et al. Seroepidemiological study of human hydatidosis in Meshkinshahr district, Ardabil province, Iran. *Iran J Parasitol*. 2011; 6(3):19-25.
22. Asghari M, Mohebbali M, Eshrat Beigom K, et al. Seroepidemiology of human hydatidosis using AgB-ELISA test in Arak, central Iran. *Iran J Public Health*. 2011; 44(9): 1219–1224.
23. Rafiei A, Jahanshahi A, Talaeizadeh A. Evaluation of specific IgG antibody detection in diagnosis and post surgical monitoring of cystic echinococcosis. *Iran J Parasitol*. 2008; 3(2):10-14.
24. Lawn SD, Bligh J, Craig PS, et al. Human cystic echinococcosis: evaluation of post-treatment serologic follow-up by IgG subclass antibody detection. *Am J Trop Med Hyg*. 2004; 70(3):329-35.
25. Piccoli L, Tamarozzi F, Cattaneo F, et al. Long-term sonographic and serological follow-up of inactive echinococcal cysts of the liver: hints for a “watch-and-wait” approach. *PLoS Negl Trop Dis*. 2014; 8(8):e3057.