

## Original Research Article

# Clinical profile, diagnostic challenge and management of alveolar hydatid disease: a prospective study

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## ABSTRACT

**Background:** Although a rare entity, alveolar hydatid disease is associated with significant morbidity. This disease presents a diagnostic challenge because of its low prevalence, unfamiliarity and nonspecific presentation. Aim: To look about the clinical profile, diagnosis and management of these patients.

**Methods:** This prospective study was conducted in the department of surgery at SMHS (Shri Maharaja Harisingh) hospital. All patients with a diagnosis of alveolar hydatid disease of liver during this time period were enrolled in the study.

**Results:** Eight patients in our study were females and 5 patients were males. The age ranged from 21 to 56 years with mean age of 42.07±8.88 years (SD =8.88). The most common presentation in our study was pain abdomen (38%). The most common finding on physical examination was hepatomegaly (30.76%). CT (computerized tomography) scan abdomen gave an impression of alveolar hydatid disease in 5 patients, a suspicion of malignancy in 3 patients and tuberculosis in one patient, and a possibility of liver abscess in one patient. Results of tru cut biopsy were suggestive of alveolar hydatid disease in 4 out of 6 patients. Twelve patients were operated on elective basis (liver radical resection in 8 patients, while “laparotomy and only tumor biopsy” in 4 unresectable patients) and one patient on emergency basis, and all were subjected to histopathological examination. ABZ (albendazole) was given orally at a dosage of 10-15 mg/kg per day.

**Conclusions:** Alveolar hydatid is a rare disease with atypical (unfamiliar) and nonspecific clinical features and atypical radiological features. Also, the disease is associated with significant morbidity, hence a high index of suspicion is needed along with supplementary imaging studies for timely intervention to prevent further complications arising from the disease.

**Keywords:** Alveolar hydatid, Albendazole, Malignant, Rare

## INTRODUCTION

Alveolar echinococcosis is caused by the rodent cestode (*Echinococcus multilocularis*). Alveolar hydatid disease is a less common disease which is mostly seen in countries with larger reservoirs of hosts (foxes, dogs and wolves) such as antarctica and arctic region.<sup>1</sup> Increasing fox population, increased fox encroachment into urban areas and *E. multilocularis* spillover from wild carnivores

to domestic hosts, are all factors that may explain *E. multilocularis* spreading from endemic areas to previously non-endemic European countries.<sup>2,3</sup> Considering the parasite life cycle, exposure of humans to echinococcal eggs may be influenced by occupational and behavioral factors. Hunters, trappers and persons who work with fox fur should be more frequently exposed to *E. multilocularis* eggs, but there is no evidence that these groups are at increased risk.<sup>4,5</sup>

Biological behavior of larval *Echinococcus multilocularis* in human is similar to a malignant tumor that is determined by growth of damaging tissues and metastasis to distant organs. The disease has a high mortality rate (more than 90 % within 10 years and virtually 100% within 15 years of the onset of symptoms) in untreated cases.<sup>6</sup> This larva differs from *E. granulosus* in cystic echinococcosis of the liver. The growth and proliferation of this larva is similar to a slow-growing tumor of the liver and can damage liver function. Sometimes, it is difficult to differentiate it from liver cancer because of invasion to biliary and vascular tissue of the liver. Early diagnosis and radical surgery provide the best chance for definitive treatment and cure.<sup>7</sup> Although treatment of AE is less effective than treatment of cystic echinococcus, still the general approach to its treatment remains to be surgery with the purpose of complete resection of infected parts of involved organs. Also, liver transplantation can be a lifesaving approach in patients who are at risk of death.<sup>8</sup>

Although a rare entity, alveolar hydatid disease is associated with significant morbidity. This disease presents a diagnostic challenge because of its low prevalence and nonspecific presentation. In this setup authors have encountered few such patients with an unusual diagnosis of alveolar hydatid liver, hence we felt need to conduct a study regarding the clinical profile, diagnosis, and management of alveolar patients with hydatid disease of liver.

## METHODS

This prospective study was conducted in the department of surgery at SMHS (Shri Maharaja Harisingh) hospital, an associated hospital of Government Medical College Srinagar over a period of 5.5 years from June 2012 to December 2017. Our aim was to look about the clinical profile, diagnosis and management of patients with alveolar hydatid disease of liver. In addition to physical examination, base line blood investigations (including LFT, i.e., liver function test), USG abdomen, CT (computed tomography) scan abdomen and pelvis (supplemented by MRI whenever feasible), radiograph chest and CT scan brain were done in all patients with suspicious liver lesions. All patients with a final diagnosis of alveolar hydatid disease of liver on histopathological examination were included in the study. All other patients in whom histopathological examination did not prove the diagnosis of alveolar hydatid disease were excluded from the study. A total of 13 patients with this rare diagnosis were included in our study.

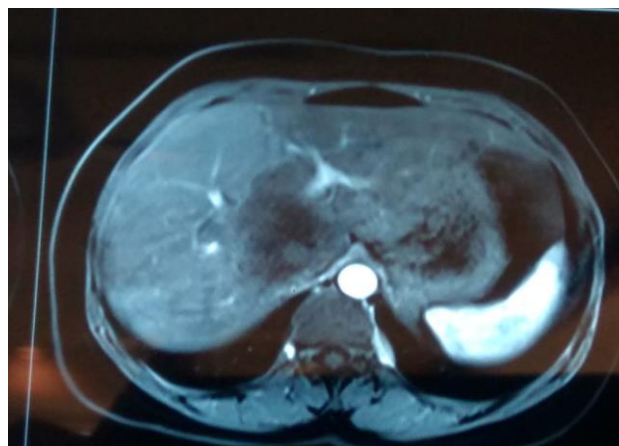
### Statistical analysis

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as

Mean  $\pm$ SD and categorical variables were summarized as frequencies and percentages.

## RESULTS

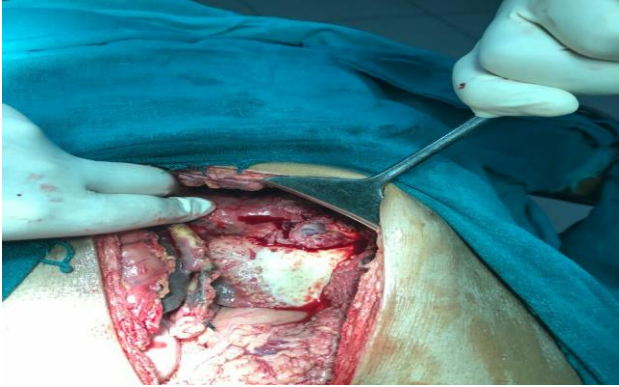
Total number of patients enrolled in this study was 13 over a study period of 5 years and 6 months. Majority of patients in our study were female (8 out of 13). The age of patients in our study ranged from 21 to 56 years with mean age of  $42.07 \pm 8.88$  years (SD =8.88). Out of 13 patients 10 were from rural areas and 3 were from urban areas. The most common presentation of patients in our study was pain abdomen. The most common finding on physical examination was hepatomegaly. The duration of symptoms prior to diagnosis ranged from 15 days to 2 years and 4 months with an average duration of 16 months. Total serum bilirubin level in our patients ranged from 0.9 to 5.3 mg/dl with a mean of 2.3mg/dl. Liver enzymes except ALP (alkaline phosphatase) were within normal range (or slightly raised) in most of the patients. Mean value of alkaline phosphatase was 563u/l ranging from 96 to 1378u/l. In our study USG (ultrasonography) abdomen showed liver space occupying lesion (SOL) in 10 patients, impression of alveolar hydatid in 2 patients, and was inconclusive in one patient. All patients were subjected to triple phase CT (computerized tomography) scan of abdomen and pelvis, and MRI (magnetic resonance imaging) was feasible in 2 patients only. CTscan abdomen (Figure 1) gave impression of alveolar hydatid disease in 5 patients, a suspicion of malignancy in 3 patients and tuberculosis in one patient, and a possibility of liver abscess in one patient. MRI supplemented the diagnosis of CT scan in two patients. CT scan was inconclusive in 3 patients.



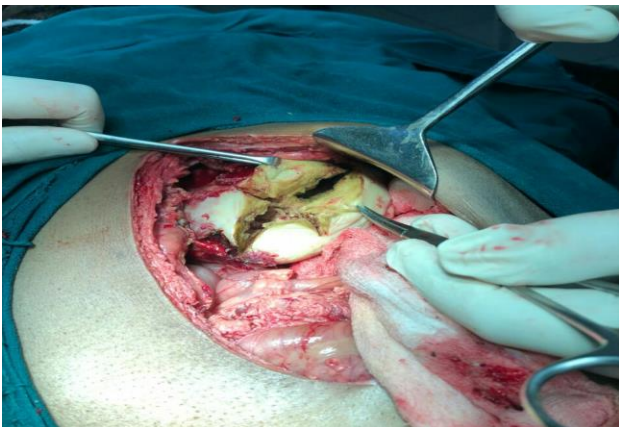
**Figure 1: CT scan of a patient showing alveolar hydatid liver.**

Tru cut biopsy was done in 3 patients with suspicion of malignancy and in another 3 patients in whom CT scan was inconclusive. Results of tru cut biopsy were suggestive of alveolar hydatid disease in 4 of these 6 patients. Clinical condition of the patient, in whom we were suspecting liver abscess, started deteriorating and was hence operated on emergency basis. Intra-operatively

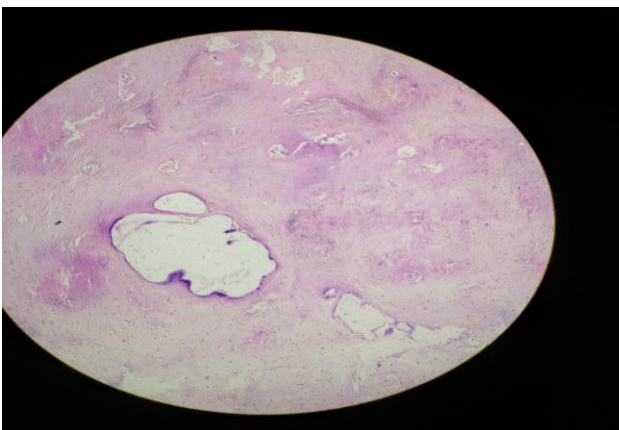
he was found to have yellowish white lesion in the liver for which near radical resection was done. The lesion proved to be echinococcus multilocularis on histopathological examination. The remaining 12 patients were operated (Figure 2 and Figure 3) on elective basis (liver radical resection in 8 patients, while “laparotomy and only tumor biopsy” in 4 unresectable patients) and subjected to histopathological examination.



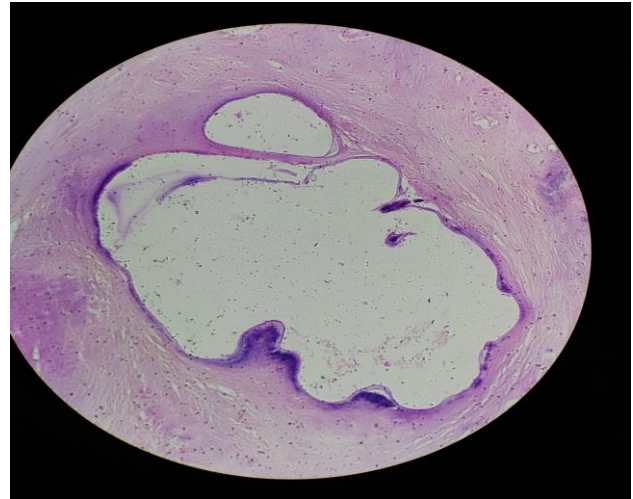
**Figure 2: Intra-operative view of alveolar hydatid liver.**



**Figure 3: Intra-operative view of alveolar hydatid liver.**



**Figure 4: Low power microscopic view of alveolar hydatid liver.**



**Figure 5: High power microscopic view of alveolar hydatid liver.**

The right lobe of liver was involved in 2 patients, left lobe of liver was involved in 2 patients and in 9 patients both lobes were involved. Histopathological examination (Figure 4 and 5) showed features of echinococcosis multilocularis. Some of the reports also showed dense fibrosis, necrosis, calcifications and mild to moderate granulomatous inflammation in the surrounding tissue of the lesion.

Figure 1 belongs to one patient while figures 2 to 5 belong to another patient. Chest radiograph and CT brain was done in all patients after the diagnosis of alveolar hydatid disease reached. Metastasis of lesion was not present in any of these patients. ABZ is given orally at a dosage of 10-15mg/kg per day. All patients were advised to receive post-operative chemotherapy for two years after radical surgery and are still under close follow-up. A long-term chemotherapy with benzimidazole derivative was advised for unresectable cases.

## DISCUSSION

Human infection can happen through direct contact with the definitive host or it can be indirect, through contamination of food or water with parasite eggs.<sup>9,10</sup> The echinococcal metacestode develops in the liver and is characterized by an alveolar structure, made up by several vesicles whose diameter varies from <1mm up to 15-20cm.<sup>11,10</sup> Each vesicle has a wall structure similar to that of the *E. granulosus* cyst, consisting of a germinal and a laminated layer.<sup>12</sup> Brood capsules or protoscolices are only occasionally seen and lesions may be complicated by central necrosis, producing a cavity or pseudocyst after liquidization. Small cysts are surrounded by a dense connective tissue and they usually do not contain fluid but instead a semisolid matrix.<sup>13</sup> WHO classification of AE is based on imaging findings and it is useful to have an internationally recognized, uniform standard for disease diagnosis and treatment strategies. The WHO-IWGE PNM classification system is similar to tumor



TNM classification: “P” refers to the extent of parasite localization inside the liver, “N” establishes the involvement of neighboring organs, “M” evaluates the absence (M0) or presence (M1) of distant metastasis, after having performed a chest X-ray and a cerebral CT.<sup>10,14</sup> As in CE, immunodiagnosis has a complementary role to other procedures, not only in primary diagnosis but also for follow-up of patients after surgical treatment or chemotherapy and for the specific differential diagnosis between AE and CE in those regions where the diseases are co-endemic.<sup>15-18</sup> Immunodiagnosis (with indirect hemoagglutination test or ELISA) is more reliable for the diagnosis of AE than for CE, because more specific antigens are available. For example, the Em2plus-ELISA, which is a mixture of affinity purified *E. multilocularis* metacestode antigens (Em2-antigen) and a recombinant antigen (Em II/3-10), has shown a great sensitivity and specificity, but it is not able to discriminate between active and inactive lesions; in fact, Em2- ELISA may be positive for years after spontaneous or pharmacological-induced dying out of the metacestode in patients with calcified lesions, because the Em2 antigen main source is the laminated layer of the parasite which obviously persists in these inactive lesions.<sup>19</sup> Surgical removal of the dried-out lesion results in an immediate seroconversion to negative anti-Em2 antibodies.<sup>20,21</sup>

Alveolar echinococcosis was first reported in the mid 19<sup>th</sup> century. Based on the studies of Vougle (1955) in Germany; *Echinococcus granulosus* and *Echinococcus multilocularis* were considered as two distinct species.<sup>22</sup> Total number of patients enrolled in this study was 13 over a study period of 5 years and 6 months. Majority of patients in our study were female (8 out of 13). The age of patients in our study ranged from 21 to 56 years with mean age of 42.07±8.88 years (SD =8.88).

Clinical diagnosis includes epidemiological data, characteristics of lesions in imaging studies (ultrasound, CT scan, etc.) and serologic markers. Alveolar echinococcosis is characterized by calcification in or around the liver lesions (seen in 70% of cases). In the evaluation of 70 patients with unresectable alveolar echinococcosis, the primary clinical symptoms were epigastric pain (one-third) or obstructive jaundice (one-third) and in other cases the disease was diagnosed accidentally.<sup>23</sup> In our study, out of 13 patients 10 were from rural areas and 3 were from urban areas. The most common presentation of patients in our study was pain abdomen. The most common finding on physical examination was hepatomegaly. Human alveolar echinococcosis is a progressive and potentially fatal parasitic infection. Early diagnosis of alveolar echinococcosis is difficult because the disease has an asymptomatic period which can last up to 20 years.<sup>24</sup> First symptoms are usually vague: patients may complain of fatigue, weight loss or may have hepatomegaly. One third of them have cholestatic jaundice; one third present with abdominal pain.<sup>25,12,26</sup> Total serum bilirubin level in our

patients ranged from 0.9-5.3mg/dl with mean of 2.3mg/dl. Liver enzymes except ALP (alkaline phosphatase) were within normal range (or slightly raised) in most of the patients. Mean value of alkaline phosphatase was 563u/l, ranging from 96 to 1378 u/l. Among the imaging techniques, ultrasonography is the method of choice to identify hydatid lesions: ultrasound (US) typical aspect shows a pseudotumoral mass, with irregular limits and scattered calcification, where hypoechogenic and hyperechogenic areas are juxtaposed; central necrosis may give to the mass the appearance of a cysticlike structure, surrounded by a hyperechogenic ring.<sup>27,28</sup> Color doppler may be useful to evaluate biliary and vascular infiltration. Abdominal CT gives further anatomical details and information about the lesion pattern of calcification.<sup>10</sup> Early diagnosis is needed to prevent the complications and proper management of patients.<sup>29</sup> CT scan is one of the basic diagnostic methods for the diagnosis of AE.<sup>30</sup> Although surgical resection or organ sparing interventions in the early stages of the disease can be considered the best treatment modalities, these surgeries can be done only in 40% of cases).<sup>29</sup> Alveolar hydatid disease is characterized by calcification in about 70% patients.<sup>31</sup> In our study 7 out of 13 patients were having CT evidence of calcifications. MR imaging is the best standard to study the invasion of adjacent structures and may help in unclear cases.<sup>32</sup> In our study USG abdomen showed liver space occupying lesion (SOL) in 10 patients, impression of alveolar hydatid in 2 patients, and was inconclusive in one patient. All patients were subjected to triple phase CT scan of abdomen and pelvis, and MRI was available in 2 patients only. CTscan abdomen gave impression of alveolar hydatid disease in 5 patients, a suspicion of malignancy in 3 patients and tuberculosis in one patient, and a possibility of liver abscess in one patient. MRI supplemented the diagnosis of CT scan in two patients. CT scan was inconclusive in 3 patients. True cut biopsy was done in 3 patients with suspicion of malignancy and in another 3 patients in whom CT scan was inconclusive. Results of true cut biopsy were suggestive of alveolar hydatid disease in 4 of these 6 patients. The key concept of AE treatment is to adopt a multidisciplinary approach to disease. Surgery and chemotherapy are the cornerstones of AE treatment and, as for CE, a stage-specific approach is recommended.<sup>33</sup> Surgery is the first-choice option in all operable patients. Radical resection of the entire hepatic parasitic lesions is the only curative procedure, even though it is often difficult to achieve because of echinococcal dissemination into host tissues. Palliative liver surgery is almost always contraindicated, because it does not offer advantages when compared with conservative treatment.<sup>34,35</sup> Preoperative evaluation is important to establish lesions full resectability; WHO-IWGE PNM classification estimates quite well the likelihood to achieve radical resection.<sup>14</sup> Liver transplant (LT) has been employed in otherwise terminal cases.<sup>36</sup> Clinical condition of the patients, in whom we were suspecting liver abscess, started deteriorating and was hence operated on emergency basis. Intra-operatively he

was found to have whitish lesion in the liver for which near radical resection was done. The lesion proved to be echinococcus multilocularis on histopathological examination. The remaining 12 patients were operated on elective basis (liver radical resection 8 patients and laparotomy and tumor biopsy in 4 patients-inoperable) and subjected to histopathological examination. Inoperable AE patients should receive continuous BMZ treatment for life; moreover, long-term BMZ administration (at least 2 years) is mandatory after surgical treatment. Pre-surgical BMZ therapy is advised only in the case of LT. ABZ is given orally at a dosage of 10-15mg/kg per day, in two divided doses; if it is not tolerated, MBZ may be given at daily doses of 40-50mg/kg per day, split into three divided doses with fat-rich meals.<sup>33</sup> All patients in our study were advised to receive post-operative chemotherapy for two years after radical surgery and are still under close follow-up. A long term chemotherapy with benzimidazole derivative was advised for nonresectable cases.

## CONCLUSION

Alveolar hydatid is a rare disease with atypical (unfamiliar) and nonspecific clinical features and atypical radiological features. Also, the disease is associated with significant morbidity, hence a high index of suspicion is needed along with supplementary imaging studies for timely intervention to prevent further complications arising from the disease. Because of the difficulty in the eradication of the disease, patients with alveolar hydatid should be strictly followed after surgery along with medical management.

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