

Review Article

Hydatid Disease — An Overview

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Human Hydatid Disease is a growing menace, a parasitic disease present in many countries all over the globe (more than 1 million people are affected throughout the World annually). Tape-worm is the main causative organism. In humans it is prevalent in two forms – Cystic Echinococcosis (CE) [caused by *Echinococcus granulosus*] and Alveolar Echinococcosis (AE) [caused by *Echinococcus multilocularis*]. Humans are the accidental intermediate host; they are being affected by drinking water or eating food contaminated with parasite eggs or by direct contact with infected animal hosts like dogs. In humans, the most commonly affected organ is Liver followed by the Lungs. The main investigational tool is Ultrasonography but Computed Tomography (CT) and serological tests are also helpful in the diagnosis of Liver Hydatid Cysts (LHC).

Although PAIR technique is the most important modality of therapy along with medical treatment, surgery has got a great role in the management of the entire spectrum of the disease. Nowadays, various Laparoscopic techniques have been safely used to improve the morbidity and mortality associated with the surgical management of the disease, and is the only other therapeutic option used all over the World.

Prevention programme includes, public awareness and Education, dog deworming and slaughterhouse hygiene.

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Key words : Hydatid, Echinococcus, Dog tapeworm, PAIR, Albendazole.

Hydatic disease is a gradually progressive parasitic disease caused by a tape-worm having 2 species- *Echinococcus granulosus* and *Echinococcus multilocularis*. The number of cases has been gradually increasing for last couple of decades, especially in the sheep rearing areas of USA and also in the Indian subcontinent¹ due to intercontinental migration of people. So now, physicians have to be more aware and careful about the clinical profile of hydatid disease and its management strategies.

About the Parasite :

There are four known species of echinococcus¹, out of which three species affect humans. They are –

1. E Granulosus causing cystic Echinococcosis (CE), also known as Hydatid disease or Hydatidosis and is the most common amongst all the members. cDNA encoding calmodulin³, a calcium sensor protein (r Egcam)² which has got a direct role in the life cycle of *E. granulosus*.

2. E Multilocularis- It causes alveolar echinococcosis. Most virulent but rare.

3. Other two forms of Echinococcosis:

a) Polycystic- caused by **E vogeli**

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Editor's Comment :

■ Hydatid disease is a parasitic disease which is showing increasing incidence all over the world. It is therefore prudent to have a thorough grasp of the pathophysiology, the life cycle of the parasite, the imaging and classification systems, as well as the various management options available. It is also important for physicians to know about alveolar echinococcosis which can be a great mimicker of various other disseminated infectious/malignant diseases.

b) Uncystic – caused by **E Oligoarthrus** are also detected.

Hydatid disease, with its twin phenotypes of cystic and alveolar echinococcosis, is therefore a major public health as well as medical problem.

Mode of Transmission :

Larval cestodes of the phylum Platyhelminthes (tape worms) cause Echinococcosis.

Their life cycle involves two hosts –

1. One Definitive Host– Dogs and other carnivores act as a definitive host.⁴ They become infected by consuming the viscera of intermediate hosts, thereby harbouring the mature tapeworm in their intestine.

2. One Intermediate Host– Few herbivorous and Omnivorous animals which act as intermediate hosts, gets the infection by ingesting parasite eggs found in contaminated food and water and parasite grows into larval stages in their viscera.

The life cycle has three developmental stages –

a) The adult tape-worm in the definitive host,

b) Eggs in the environment

c) The metacestode in the intermediate host.

LIFE CYCLE — After ingestion by the definitive host, the metacestode matures into an Adult Tape-worm in the intestine of definitive host like dogs, which release eggs in their stool which are taken up by the intermediate hosts, sometimes accidentally, who subsequently hatch eggs, which ultimately infest the Liver, Lungs, Muscles and other organs of the intermediate host. The metacestodes are ingested by the definitive host.

Humans act as an accidental intermediate hosts⁴, in the sense that they acquire infection in the same way as other intermediate host but are not involved in transmitting the infection to the definitive host.

Several distinct genotype of *E Granulosus*, are recognised, some having distinct host preferences. Some Genotypes are considered species distinct from *E Granulosus*. Not all genotypes cause infections in humans. In humans, the majority of cystic echinococcosis infection is maintained by dog – sheep – dog cycle.

Alveolar Echinococcosis (*E multilocularis*) usually occurs in a wild life cycle between foxes and other carnivores with small mammals (mostly rodents) acting as intermediate hosts. Domestic dogs and cats can also as definitive hosts.

E Vogeli is a rare species found in the bush dogs. It can easily infect other mammals that are exposed to its faeces.

Epidemiology :

Cystic Echinococcosis (CE) is found all over the World except Antarctica. It is mostly found in Mediterranean countries, the Middle East, South America (Southern part), Australia, New Zealand and parts of Africa (mainly southern); Central Asia^{5,6} particularly China is also endemic for this disease. It is uncommon in Northern Europe.

The incidence of Cystic Echinococcosis (CE) in endemic areas varies from 1-220 cases per 100000 population while the incidence of AE ranges from 0.03-1.2 cases per 100000 population⁶. Infestation with *E Vogeli* is quite a rare form of Echinococcosis and is reported mainly in the Southern Parts of South America.

Age, Sex and Racial Distribution :

There is no sexual predilection for Human Hydatid disease.

Though the parasite affects all races equally, it has been seen that persons belonging to certain races in a specific geographical area are more affected; young adults in the age group between 30 to 40 years are mainly affected by CE whereas older debilitated age group (above 50 years) is mainly affected by AE.

Economic Burden due to Disease :

All over the Globe, more than 1 million people are suffering from CE and AE of which many people are suffering severe clinical symptoms which are sometimes life threatening, affecting their quality of life.

For CE, postoperative death rate is about 2.2% and relapse rate after treatment is about 6.5%.

Annually, around US \$ 3 billion is being spent to cover losses incurred by the livestock industry.

Presentation of Human Hydatid Disease :

Human infection with *E Granulosus* most commonly affects the Liver (50% to 93%) and Lungs (25%); relatively uncommon sites are in the Bones (3%), Kidneys (2%), Spleen (1%), Muscles (5%), CNS (1%) or Eyes (1%). Cardiac hydatid cyst is a very rare presentation⁷.

If Liver Hydatid Cysts (LHC) are not treated properly, they may have the following fates –

- May develop fistulae with surrounding organs, intra/extrahepatic biliary apparatus.
- Rupture into the peritoneal cavity with seeding of daughter cysts
- Develop Daughter cysts inside itself or rarely die⁸.

The disease can remain undetected for several years until Hydatid Cysts grow to an extent that gives rise to pressure effects especially in the brain or eyes.

Abdominal pain and pressure effects are initially vague; fullness, low grade fever, flatulence, nausea and vomiting are the cardinal symptoms of Liver Hydatid cyst. Sometimes pain in the epigastrium or right hypochondrium is also a presenting feature.

In Liver Hydatid Cyst, the cyst can produce Obstructive Jaundice symptoms by pressure effect, which can often lead to a misdiagnosis of metastatic deposits. With biliary rupture, the classic triad of biliary Colic, Jaundice and Urticaria is often observed. Bits and pieces of Hydatid membranes may be passed during emesis (hydatid emesia) and in the stool (Hydatid Enterica), rarely.

If the lung is affected, symptoms include chronic cough with expectoration (sometimes cyst membranes may be found with sputum), chest pain and shortness of breath. Other constitutional symptoms like malaise, weight loss, weakness, mild fever or pain in the extremities may also be present.

Alveolar Echinococcosis may be asymptomatic, with incubation period of 5-15 years. It develops slowly usually in the Liver, like a primary tumor, and therefore often mimics Cirrhosis of Liver or Hepatic Carcinoma, and may ultimately lead to hepatocellular failure.

When the parasite is disseminated in the bloodstream or via the lymphatic system, it may affect the Lungs, Brain or spleen, Causing specific symptoms; if left untreated, it is definitely fatal.

Diagnostic Approach :

Even though Human Hydatid disease may be asymptomatic for a long time or have non-specific symptoms, about 33% of the patients with Liver Hydatid Cyst (LHC) may present with pressure effects or complications.

The total diagnostic workup⁹ includes.

(1) Routine Laboratory Haematological Examination which may Show – Leucocytosis (suggesting infection in the cyst), Eosinophilia is present in 25% of cases, there may be elevated bilirubin level along with raised Alkaline Phosphatase level, Hypogammaglobulinemia is present in 30% of cases.

(2) Casoni's Test – The test was first described by an Italian physician Tomaso Casoni in 1912.

It is a hypersensitivity based Intradermal Skin Test used to detect Hydatid Disease. Although once a major test in diagnosing Hydatid disease, it has largely been superseded by newer more sensitive, specific and safer serologic tests. Casoni's test is only 63.8% sensitive and 47% specific for diagnosing Hydatid disease.

(3) Serodiagnostic Techniques – Can be either antibody detection or antigen detection:

a) **Antibody Detection** : The indirect Haemagglutination test and Enzyme Linked Immunosorbent Assay (ELISA) have a sensitivity of 90% overall and are the initial screening tests of choice.

b) **Antigen Detection** : Double diffusion and Counter-immunoelectrophoresis methods were used, however they are not in vogue in these days.

Most Sensitive and Specific immunological test is IgG ELISA; and the sensitivity of ELISA for detection of Hepatic Cysts is more than that of Pulmonary cysts.

(4) Ultrasonography – USG is an indispensable tool in the diagnosis, treatment and follow up of Liver Hydatid Cysts. WHO informal working group on Echinococcus (IWGE)¹⁰ classification of LHCs is presently accepted globally (Fig 1).

Hepatic Hydatid Cyst - ultrasound water lily sign (Radiopedia)

USG Classification of Echinococcal cyst

CE1 – Active Unilocular Anechoic cyst with double line sign- Active Cyst

CE2 – Multiseptate Honeycomb cyst- Active cyst

CE3a – Cyst having Transitional biologic activity, showing detached membrane

CE3b – Cyst having Transitional biologic activity with presence of Daughter cysts in the solid matrix

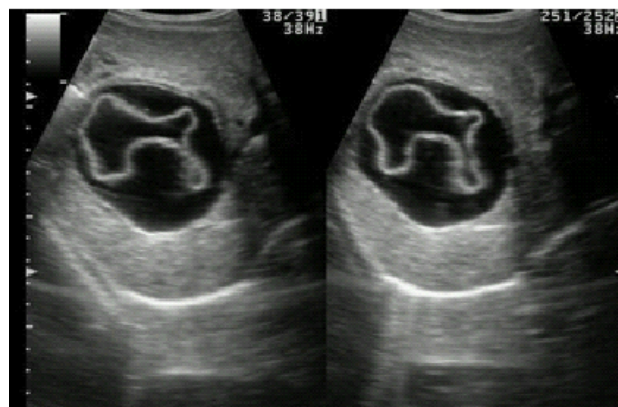


Fig 1 — Hepatic hydatid cyst - ultrasound water lily sign (Radiopedia)

CE4 – Heterogenous Hypoechoic / Hyperechoic cyst contents with no Daughter cysts- Inactive cyst

CE5 – Solid and calcified wall cysts- inactive cyst.

(5) Computed Tomography (CT scan) – CT scan is very accurate (98%) in diagnosing Hydatid Disease and its sensitivity in diagnosing Daughter cysts is very good in conditions¹¹ where USG fails as in obesity, excessive intestinal gas, abdominal wall deformities or previous surgical procedures (Fig 2).

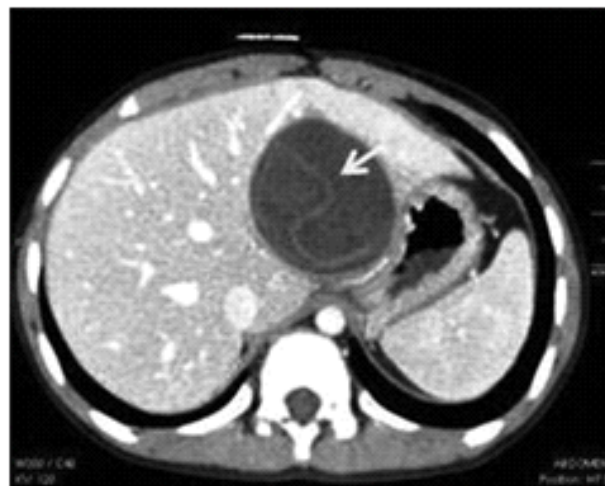


Fig 2 — CT Scan image (News-Medical.Net)

It is very effective in differentiating Hydatid Disease from amebic or pyogenic Liver abscess. Intravenous contrast is only used during CT scan when a communication with the biliary apparatus is suspected.

In AE, the CT Scan findings are sometimes indistinguishable from those of Hepatocellular Carcinoma.

In patients in whom an intrabiliary rupture is suspected, a perioperative ERCP is a good modality to establish cystobiliary communication, providing a therapeutic option at the same time.

(6) Magnetic Resonance Imaging (MRI)
MRI offers no real advantage over CT Scanning
(Fig 3).

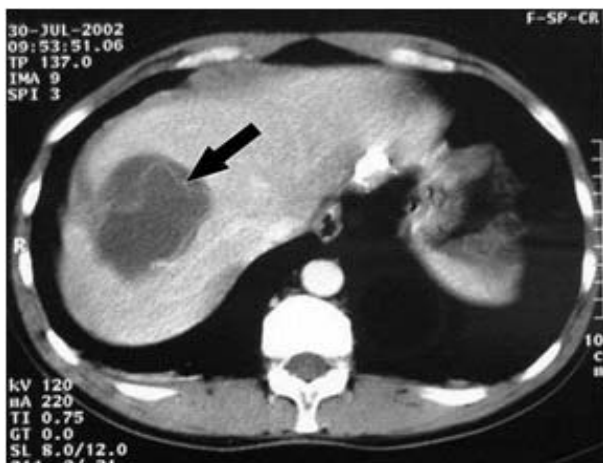


Fig 3 — The picture above is an image of the upper abdominal region, with a large cyst on the liver (arrow). Courtesy of Medline Plus

Different Diagnosis :

Many diseases simulate Hepatic Hydatid disease.
They are –

- Amoebic or Pyogenic Liver Abscess
- Benign Hepatic Cysts (haemangioma)
- Hepatocellular Carcinoma
- Cysticercosis
- Liver Metastasis
- Budd Chiari Syndrome
- Lung abscess in case of AE

Management Protocol :

There are various modalities for the treatment of Echinococcosis. They are –

- Watch and wait
- Percutaneous treatment (PT)
- Medical treatment
- Surgical treatment including Laparoscopic management.
- Adjunctive treatment
- Image oriented, stage specific treatment approach

(1) Watch and Wait :

As Hydatid Cyst is a slow growing disease, certain cyst types¹² are best left untreated and closely monitored over time. The consequences may be –

- A large number of cysts eventually calcify without any treatment and without any symptoms.
- Some cysts remain dormant, i.e. do not cause organ dysfunction or cause any symptoms for the patient; they need long term Ultrasonographic follow up for a period up to 10 years.

(2) Percutaneous Treatment (PT) :

Percutaneous treatment of LHC was introduced in 1980 and has become an attractive alternative to surgery and medical management¹³.

The first PT that was used was PAIR¹⁴ which includes USG or CT guided puncture of the cyst then aspiration of the cystic fluid, injection of a scolicidal agent (eg, hypertonic saline, 95% ethanol, albendazole or betadine) and then reaspirate the cystic content.

For unilocular cysts PAIR is a very safe and effective option. Great care is to be taken to avoid spillage and residual empty cavities are sterilised with 0.5% silver nitrate or 2.7% NaCl. PAIR therapy is contraindicated if cysts communicate with the biliary tract. PAIR includes a small risk of anaphylaxis in about 2% of cases but death due to anaphylaxis is very rare. Other percutaneous techniques are generally kept reserved for multivesiculated cysts or cysts with predominantly solid content which are very difficult to drain by PAIR method. Techniques are –

- Percutaneous Evacuation (PEVAC);
- Modified catheterisation technique (MoCAT);
- Dilatable multifunction trocar (DMFT);
- Radiofrequency thermal ablation (rarely used)

(3) Medical Treatment :

Drug therapy for Echinococcus is limited. The antihelminthic Benzimidazoles, namely Albendazole and mebendazole, are used for treatment and prophylaxis. Albendazole (10 -15 mg/kg/day orally) is used in the dose of 400mg twice daily orally for 3 to 6 months, in some cases it is used with alternating cycles of treatment and rest. Mebendazole (40-50 mg/kg/day orally) can also be used. Praziquantel, an isoquinoline derivative, is used in the dose of 20mg/kg twice daily for 14 days, as an adjunct for therapy.

Common side effects of the drugs are Alopecia and GI symptoms occurring in 1-5% of cases along with elevation of Liver enzymes. Benzimidazoles may suppress bone marrow functions may cause aplastic anaemia and also carry a risk to the foetus in the first trimester of pregnancy.

(4) Surgical Treatment

Previously, surgery was the only available therapeutic modality for LHC, for all different varieties of the disease¹⁵.

Surgical techniques can be conservative or radical. Among **Conservative Procedures**, Hydatidectomy and partial cyst removal are done, along with evacuation of the cyst contents; however there is considerable risk of anaphylactic shock and chemical Cholangitis. Also, the relapse rate is around 10-20%, with the residual cavity being the ideal seat for a secondary infection.

Radical Procedures target complete cyst removal sometimes along with a chunk of Liver tissue. Radical procedures exhibit a lower relapse rate but the intraoperative risk as well as the postoperative complications are significantly greater.

Laparoscopic surgical management of LHC¹⁶ is gradually gaining ground nowadays. Various techniques like Total Pericystectomy, Puncture and aspiration of contents followed by Marsupialisation, Unroofing and Drainage, Unroofing and Omentoplasty and Omentoplasty using helical fasteners have been described. A major difficulty faced in Laparoscopic management of LHC is the difficulty in evacuating the contents of the cyst, the Daughter Cysts with the laminated membrane¹⁷.

(5) Adjunctive Treatment :

There are evidences which showed that adjunctive measures play a useful role in the management. They are-

a) Prevention of secondary CE and relapses by Albendazole starting 4 days before surgery and continuing up to at least 1 month after surgery, but efficacy is doubtful.

b) Surgical field protection with pads soaked with scolicidal agents.

c) Prevention of Cholangitis – After surgery a search for cystobiliary fistula¹⁸ is mandatory; if such a Phenomenon occurs, injection of scolicidal solution into the cyst cavity is contraindicated.

d) Cysts are always to be removed completely to avoid residual cavities. This prevents secondary infection or biliary fistulas and consequently achieves faster healing.

(6) Image Oriented Stage Specific Treatment Approach

WHO classification	Suggested modality of treatment
CE1	Albendazole alone if cyst <5cm, PAIR + Albendazole if >5cm
CE2	(Surgery + Albendazole) or (Non-PAIR PT + Albendazole)
CE3a	Albendazole alone if cyst <5cm: PAIR + Albendazole if >5cm
CE3b	(Surgery + Albendazole) or (Non-PAIR PT + Albendazole)
CE4 & CE5	Watch & wait

Complications :

Complications include –

(1) Related to parasite –

- Recurrence
- Infection
- Metastasis

(2) Related to medical treatment –

- Hepatotoxicity
- Anaemia & Thrombocytopenia
- Teratogenicity

(3) Related to PAIR intervention

- Spillage and seeding
- Haemorrhage
- Infection
- Mechanical damage to other tissue
- Anaphylactic shock
- Cystobiliary Fistula

(4) Related to scolicidal agents

- Chemical sclerosing cholangitis, especially if formalin is used.
- Hypertatremia, if hypertonic saline is used.
- Acidosis if cetrimide is used.

Prognosis :

In Cystic Echinococcosis, with good surgical evacuation of the cyst without spillage (which occurs in 2 to 25% of the cases) the prognosis is usually good. Operative mortality varies from 0.5% to 4% of the cases. The prognosis is guarded in case of alveolar echinococcosis, with cure being possible only with early diagnosis and complete surgical excision.

Prevention and Control of Hydatid Disease :

CE is a disease that may be easily prevented, with improved public awareness, improved slaughterhouse hygiene and periodic deworming of dogs with Praziquantel; These will ultimately impede disease transmission causing significant reduction in disease burden. A newer modality of prevention in the form of vaccinating sheep with an E. granulosus recombinant antigen (EG95) is nowadays being encouraged with good result.

Conclusion :

Human Hydatid Disease is a globally prevalent, slow growing disease having two phases- an evolving phase, wherein the cyst grows; and an involution phase, wherein the parasite dies, leaving a calcified cyst. Though treatment modalities are many, starting from medical treatment, PAIR and surgical treatment, complication often develop which may be sometimes life threatening. Now the focus is on preventive strategies which are to be adopted more and more to eliminate Cystic echinococcosis in humans in the near future.

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(Continued from page 78)

platelets in patients with active COVID-19 has revealed upregulation of many genes responsible for aggregation. Upstream regulators like JAK3 and Rho family GTPases were also activated in these platelets³.

Compared to the other systemic manifestations of COVID, cardiovascular complications have received much less attention. A Cochrane review of cardiovascular effects of COVID revealed that the Weighted Mean Incidence (WMI) of AMI in hospitalized COVID patients was 1.7%⁴. In our cases, the diagnosis of AMI was established with the help of ECG, cardiac biomarkers and Echocardiography. Isolated elevation of cardiac biomarkers like Troponin T is found in a large number of COVID patients⁴. But in isolation, that does is not sufficient to diagnose AMI as such elevations can be transiently seen in hypoxia induced cardiac damage too. Thus, if the suspicion of AMI in a covid patient is high, a battery of tests should be advised instead of a single one like Troponin T. Both of our COVID-19 patients with AMI had fatal outcome.

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