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Cystic Echinococcosis: A Review Article

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Abstract

Hydatid cystic or cystic echinococcosis disease remains a major challenge due to its medical and veterinary importance and its widespread spread all over the world as well as the economic losses caused by this disease, whether for humans or farm animals. *Echinococcus granulosus* is the causative agent for this disease, targeting the liver and lungs primarily and in varying proportions of the rest of the body. This disease is characterized by the non-appearance of pathological symptoms for long periods as its appearance depends on the size, number and site of the cysts formed and the type of organ infected and surgery is still the most effective solution for the disposal of hydatid cysts. Dogs and the rest of Canidae family represent the final host of the parasite causing the disease while herbivorous animals are the median host of the parasite, but the human is an occasional host who becomes infected as a result of accidental ingestion of eggs and therefore does not donate to the perpetuation of the parasite's life cycle. The current article discusses cystic echinococcosis disease in several aspects, including the historical background of the disease, the scientific classification of the causative parasite, the life cycle and the stages of the parasite and the structure of each stage of its development and the symptoms caused by the infection of this disease and the treatment used and methods of diagnosis as well as methods of prevention and control of the disease in addition to some studies conducted on this disease.

***Keywords*:** Cystic echinococcosis, *E. granulosus*, Life cycle, Liver, Lung.

1. Introduction

Cystic echinococcosis is one of the most important parasitic diseases common to humans and animals due to their wide geographical distribution and their effect on human health, sometimes causing disease or death, as well as economic losses resulting from sheep and livestock infections (Eckert and Deplazes, 2004). The tapeworm (*Echinococcus granulosus*) is the cause of this disease, leading to the formation of metacestode larval stages in the median host, including humans, called hydatid cysts (Zhang *et al*., 2003), which is a cyst filled with liquid, unilocular, which grows in the host's tissue. Dogs and the rest of Canidae family are the final host of the parasite, who is responsible for transporting the infectious stages which represented by eggs into the external environment (McManus *et al*., 2003).

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2. Historical Information

Cystic echinococcosis is a common parasitic disease amongst humans and animals (Dvorak *et al*., 2008), which man has suffered from ancient times to the present day, as the disease was first mentioned in the Bible, Talmud and resembles a water-filled bladder observed in the livers of sheep and cattle that were scattered in religious ritual ceremonies. Hippocrates was the first to describe it like a water-filled bladder as soon as he noticed it in the liver of one of the dead also noted when its eruption in the abdomen led to the death of the patient, reinforced by Galen and Aretaeus, as referred to by Al-Razi in his book Al-Hawi (Cox, 2002).

Fransisco Redi in 1684 they explain that hydatid cysts were the animal origin, while the adult worms were designated in the small intestinal of dogs by Hartmann in 1695, and Jone Hunter in year 1773 revealed the cysts as sphere-shaped containing a cavity filled with white liquid and a satisfactory nature or causing disease (Thompson, 2001) and Pallas in year 1776 compared between the hydatid cysts that found in mice and those in humans (Cox, 2002). in 1782 Goeze revealed the scolices in the cysts which appear like a small granules and renowned the resemblance them with the front end of the tapeworm, so he proposed that the tapeworm was the pathogen (Bouree, 2001; Cook, 2001), while Batsch called the adult worms *Hydatigena granulose* when he designated it in the small intestines of dogs in 1786, , and in 1808 Rudolphi classified the parasite as *Echinococcus* genus, whereas Von Siebold revealed in 1853 the presence of mature worms in the small intestines of dogs after three weeks they were experimentally fed on hydatid cysts taken as of livestock, thus demonstrating the association between the mature worm and the larvae form. In 1855, Haubner designated in the pigs which infected experimentally with the eggs of *E. granulosus* the development of cysts. Naunyn In 1863 noticeable through experimentally the attendance of mature worms in the dogs feeding them substances of cysts taken from human infected with disease, so demonstrating the association between animal hydatid cysts and human. In 1860, Leuckart complete to whole the cycle of life of *Echinococcus* genus and mentioned their characteristics, as well as the difference between unilocular hydatid cysts resulting from *E. granulosus* parasite and *multilocular* hydatid cysts (Bouree, 2001 Craig and Larrien, 2007; Thompson, 2001).

3. Classification of Parasite

(Gatti *et al*., 2007; Harder and Mehlhorn, 2008).

There are four species of the genus of the taxonomically valid (Dubinsky *et al*., 1998; Thompson, 2008., Lymbery, 2017) these types as follow: -

- *E. granulosus* (Batsch, 1786)
- *E. multilocularis* (Leuckert, 1863)
- *E. oligarthrus* (Diesing, 1863)
- *E. vogeli* (Rausch & Berustein, 1972) The classification site of the parasite can be as follows:

“Phylum: Platyhelminthes

Class: Cestoda

Subclass: Eucestoda

Order: Cyclophyllidea

Family: Taeniidae

Genus: *Echinococcus*

Species: *Echinococcus granulosus"*

E. granulosus has genotype which differ in their Host species, Geographic area, and pathogenicity, identified by using mRNA sequences (Table 1), (Fig.1) (Deplazes ,2010)

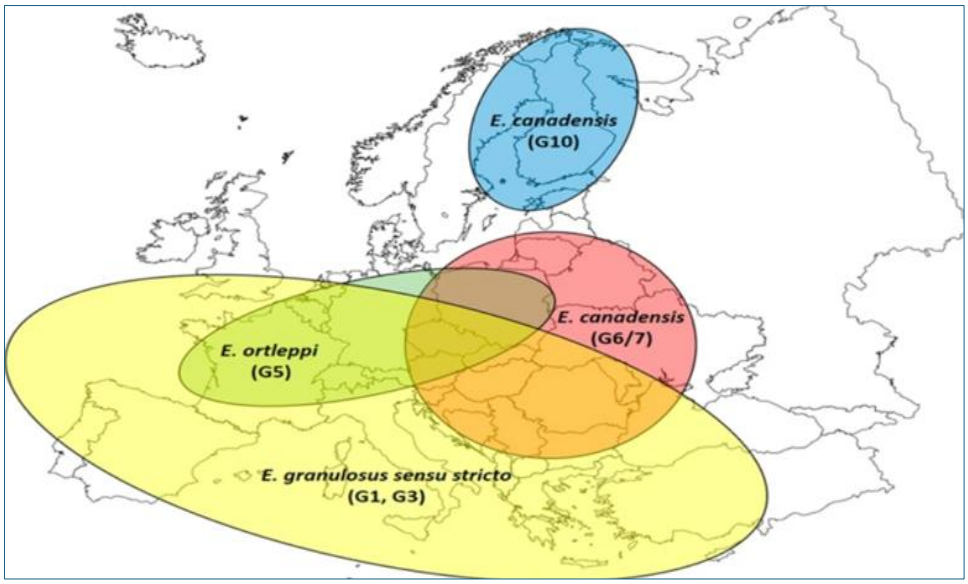
The new classification was *Echinococcosis granulosus*

Echinococcosis granulosus sensu stricto= G1-G3

Echinococcosis equinus =G4

Echinococcosis ortleppi = G5

Echinococcosis canadensis= G6-G10 (Vuitton *et al*., 2020; Umhang *et al*., 2020; Laurimäe *et al*; 2018)



(Fig. 1): geographic distribution of *E. granulosus* genotype (Casulli et al., 2022)

Genotype	classification	Common name	Principal hosts	Notes	Reference
G1	*E. granulosus sensu stricto*	Sheep strain	Sheep, goats, cattle, humans	Major cause of human cystic echinococcosis worldwide	Romig et al., 2015

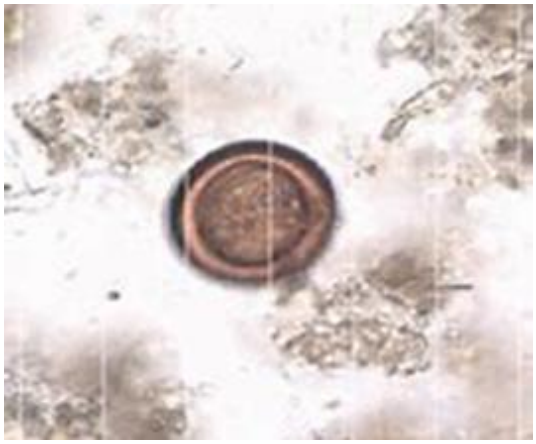
G2	*E. granulosus sensu stricto*	Tasmanian sheep strain	Sheep, goats	Restricted distribution, closely related to G1	Alvarez Rojas et al., 2014
G3	*E. granulosus sensu stricto*	Buffalo strain	Buffalo, cattle, humans	Found in Asia and Middle East	Nakao et al., 2013
G4	*E. equinus*	Horse strain	Horses (not infective to humans)	Distinct host specificity	Ito et al.,2017
G5	*E. ortleppi*	Cattle strain	Cattle, dogs, rarely humans	Zoonotic but rare	Romig et al., 2015
G6	*E. canadensis*	Camel strain	Camels, goats, dogs, humans	Important in Middle East, Africa	Nakao et al., 2013
G7	*E. canadensis*	Pig strain	Pigs, dogs, humans	Reported in Europe, Latin America	Alvarez Rojas et al., 2014
G8	*E. canadensis*	Cervid strain	Moose, elk, deer, dogs	Found in North America, Northern Europe	Nakao et al., 2013
G9	*E. canadensis*	(Pig strain, variant)	Pigs, humans (rare)	Molecularly close to G7	Ito et al.,2017
G10	*E. canadensis*	Cervid strain	Reindeer, elk, dogs	Found in northern latitudes	Romig et al., 2015

All species are dissimilar in adult and larval stage (McManus, 2001; Thompson and Schantz, 2006), also causes different forms of cysts in the accidental and median host (Pawlowski et al., 2001; Morar and Felman, 2003).

4. Parasitic stages

4.1. The parasite's eggs (Fig. 2) are characterized by their ovoid shape, ranging in diameter from “30-40 µm”, and contain a fully grown hexacanth embryo, with a diameter of 25 µm

(Bouree, 2001; Thompson and Mcmanus, 2001).



(Fig. 2): eggs of *E.granulosus* (Rahman, 2015)

4.2. Larval stage (Hydatid Cyst):

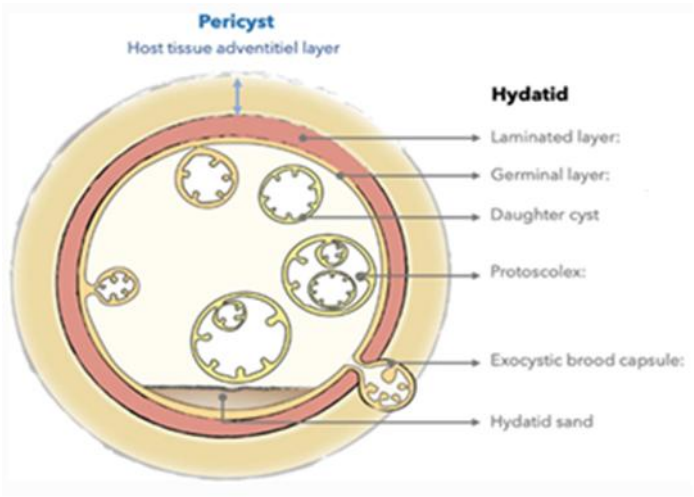
The hydatid cyst (Fig. 3) consists of two layers: an inner layer with a nuclei called germinal layer and is supported from the outside by a non-cellular elastic layer with a contrasting thickness called laminated layer and surrounded from the outside by a fibrous layer produced by host tissues called the adventitious layer (Handa *et al*., 2005; Martinez et al., 2005). The germinal layer represents the living part of the hydatid cyst wall, as it is characterized by its thinness and consists of two areas: the first is called the tegument region and the second area is known as the cells region, which is characterized by containing several types of cells,

(Kang *et al*., 1992). The germinal layer is responsible for the formation of primary scolices and brood capsules (Gutierrez, 2000), which is connected to the germinal layer by a thin stalk and consists within it of the initial scolices if the brood capsules and the primary scolices separate from the germinal layer and they hang inside hydatid fluid to be the so-called hydatid sand (Rumboldt *et al*., 2003). Hydatid cysts are described as fertile or sterile based on the presence or absence of primary hydatid (Kamenetzky *et al*., 2000). Germinal layer also performs numerous roles, controlling the porousness of the hydatid cyst and asexual reproduction, protection and support for the constituents of the cyst and the construction of the hydatid fluid (Galindo *et al*., 2003).

The laminated layer is described by acellular with a rough conformation, elastic and white color that provides support and sustenance for the germinal layer (Flisser, 2003). This layer arises from the germinal layer and has two laminates: the first appears three days after the stability of the embryo and it is in the form of a dense interstitial material consisting of microfibrils, while the second laminate appears within 8-6 days of the appearance of the first laminate and features a material more dense than the first laminate (Holcman and Heath, 1997). This layer consists of a protein complex associated with polysaccharide-protein complex, providing mechanical support and support to the cyst as well as protecting the parasite from direct contact with immune host cells (Irigoin *et al*., 2004). The laminated layer is associated with the germinal layer through micro-finger protrusions extending from the germinal layer towards the laminated layer (Holcman and Heath, 1997). Together, the two layers form the endocyst, which

is derived from the larva itself and surrounded from the outside by the pericyst, which derives from the host's tissues at the site of the hydatid cyst. The pericyst consists of three layers, the outer

layer represents the tissue cells in which the hydatid cyst is buried, while the middle layer consists of a severe filter of the host's lymphocytes as well as the formation of the inner layer of the glycogen in the form of a fibrotic capsule (Lewall and Nyak, 1998; Khuroo, 2002). The hydatid liquid found in the central cavity of the cyst consists of a complex combination of parasite-derived components and host-derived serum components (Rigano *et al*., 2001). Hydatid liquid is a colorless or slightly yellowish-slanted smaller liquid, with a qualitative weight of 1.012, which is pH 6.7-7.2 and consists of proteins, enzymes and salts (Muller and Waklelin, 2001). It contains some ions and a number of inorganic elements (Pedrosa *et al*., 2000). The hydatid liquid also contains many antigens, but antigen 5 (5 Antigen) and Antigen B are the most abundant in the hydatid liquid, and the proportions of hydatid cysts components vary reliant on the kind of medium host , tissue present and the parasite strain (Radfar and Iranyar, 2004).



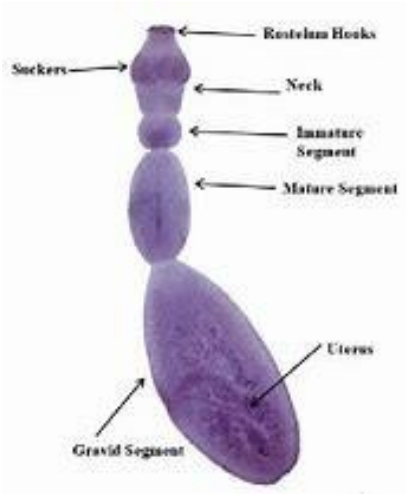
(Fig. 3): Larval stage (Hydatid Cyst) of *E.granulosus* (Calame, 2022).

4. 3. Adult Worm:

The cystic echinococcosis parasite(Fig. 4) belong of Taeniidae, with a stage length of 6-3 mm, “the strobila consists of scolex and a short neck followed by three or four proglotteds body pieces of altered maturity” (Flisser, 2003; Vincent, 2004). The head is characterized by its pyriform shape, carries four suckers cup-like with a muscular composition, and rostellum provided with two rows of hooks of altered measurement and decided mutually (the total of hooks reach to 50-28 hook, with large hook being 40-30 µm long, and small hooks reaching 22-34 µm (Muller and Wakelin, 2001). After the head region there is a small slender area whose main function is to add segments to the body constantly and is called the neck, followed by the neck 3 or 4 pieces, the first segment was immature,

not distinct and has the primordial of the genitals organs which is a group of cells appears as a dark patch. Mature segment, which contains the matured genitalia for female and male, and it

is bigger than the immature segment. The gravid proglottid, which it is characterized by having a greater length and width than the remainder of the segments, and formed almost the hemi length of the body and holding a uterus loaded with hundreds of enriched eggs (800-500). The uterus is distinguished by its elongated sac-like irregular and it is consist of15-12 short side branches (Muller and Wakelin, 2001; Wernery and Kaaden, 2002).



(Fig. 4): Adult worm of *E. granulosus* (Rahman, 2015)

5. Life Cycle:

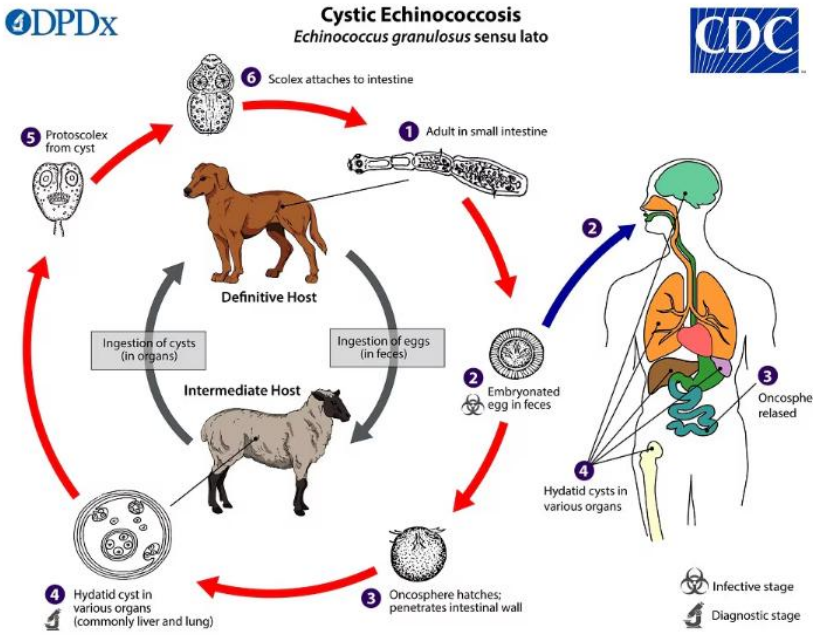
Cystic echinococcosis parasite has complex life cycle (Fig. 5), including a definitive host from carnivore animals which the parasite resides within its small intestine and is in sexual maturity while the other host is the median host, from herbivorous animal where the parasite multiplies within its organs and tissues asexually (Nepalia *et al*., 2006; Filippou *et al*., 2007). Human is an occasional host as it represents the dead end of the parasite's life (Eckert and Deplazes, 2004).

Eggs with the feces from the infected definitive host are infective phase for the middle host. The eggs are able to cause injury when they reach the external environment, and the whole gravid proglottid may be separated and thrown out by recurring contraction movements, therefore spreading eggs extensively in the environment (Dvorak *et al*., 2008). Infection of the median hosts occurs when they swallow fully grown fertilized eggs, which hatch into hexacanth embryos in their small intestine. (Khuroo, 2002). Embryos are activated under the influence of bile salts (Lightowlers *et al*., 2003) after they are released through digestion by trypsin and pancreas (Muller and Wakelin, 2001).

Hexacanth embryos enter to the intestines until to reach to the mucous layer (Sioutis *et al*., 2021), then enter the vascular ducts and pass negatively to reach through three or four hours to the liver (Kuntiz and Kuntiz, 2006), which represent as the first filtrated for embryos, and enormous numbers of them are held as they are filtrated in the liver sinusoids, while the remnant crosses to reach the lungs that represent the another filtrated, where fewer embryos are held. A fewness of embryos continue in the capillary vessels to enter the systemic circulation and then spread to the various other organs (Polat *et al*., 2003 Gurbuz *et al*., 2006). When the embryo settles in the target organ, a series of reorganizations occur within 14-10 days

(Brunetti et al., 2005), consisting of a metacetode with sac-like called hydatid cyst (McManus *et al*., 2003; Morar and Felman, 2003).

When feeding, the final host's infection gets the visceral of median host's infection with the fertile hydatid cyst, and by the digestive enzyme, the primary scolices in the bowels (ileum and jejunum) bulge in reaction to the alteration in pH, exposure to bile salts and increased temperature (Thompson and McManus, 2001), It attaches deeply between the villi within the Crypts of Lieberkuhn by suckers and head hook (Macpherson and Craig, 2001), after which these scolices grown into adult worms within 6-4 weeks (depending on the parasite strain and host sensitivity) (McManus, 2001; Thompson and Gottstein, 2003), and they started releasing eggs or graved segment every 7-10 days (Khuroo, 2002), and adult worms may remain alive in the final host for 5-20 months (Filippou et al., 2007). When accidentally swallowing eggs, a human being is exposed to hydatid cyst, thus being an occasional median host as it represents the dead end of the parasite's life and does not donate to the perpetuation of the life cycle (Eckert and Deplazes, 2004).



(Fig. 5)**:** life cycle of *E. granulosus* (CDC. (2019).

6. Clinical Indications of hydatid diseases:

Cystic hydatid disease in humans is characterized by a different incubation stage from some months to years, and can reach to 20-30 years, particularly once the growth of the cyst is sluggish and in an undetermined place (Craig and Larrien, 2007; Dvorak et al., 2008). Symptoms appear early once the cyst is present in exact and vital places such as the, spinal cord, orbit or brain (Gutierrez, 2000). The early phases of the sickness are characterized by the lack of signs due to the small volume of the cysts (less than 5 cm) and enclosed by a sac from the infected organ, also numerous cysts maybe remain without showing any symptoms for numerous years till they extent a confident size bring about symptoms (McManus et al., 2003). The pathological influence of is shown as a consequence of hydatid cyst pressure and mass

effect upon the injured organ or because of cyst rive and associated problems (Chen et al., 2002). The development of cyst inside the infected tissue reasons an inflammatory response that indications to the creation adventitia capsule's surround the cyst and over time there is obliteration and destruction the tissue and in progressive cases may effect obstruction of the role of the infected organ (Gottstein, 2003). when the cyst rive and release of hydatid fluid, it clues to immune reactions, whether in the form of anaphylactic shock ,urticaria, respiratory symptoms or edema, , which maybe lead to death, in addition to the discharge of primary scolices that develop into secondary cysts in dissimilar parts (Eckert and Deplazes, 2004). Liver is the first organ most likely to be infected with hydatid cyst (75%), followed by second place lungs (20%), and injuries (5%) can appear in other parts for example heart, bones, , kidneys, brain, spleen, and any other part of the body (Paksoy et al., 2005). In theoretical aspect, hydatid cyst can appear in several part of the body except three areas: hair, nails and teeth (Prabhakar et al., 2005; Fortia et al., 2006). when the hydatid cyst growth inside the liver that clues to hepatomegaly liver and formation of palpable mass or without during clinical examination at the upper right quarter, above-stomach pain on the right lateral, nausea, fever, besides some impediments may happen by reason of obstruction or infestation bile canals or hepatic vessels for instance cholangitis, obstructive jaundice, cirrhosis or liver abscesses, and others (Ezer et al., 2006; Schwartz et al., 2008).

The symptoms In the lungs include chest pain, pleuritis, chronic cough, dyspnea ,hemoptysis, as well as allergic responses, and occasionally the release of tiny parts of the hydatid cyst as an consequence of rive of the cyst inside the bronchi (Khuroo, 2002; Marinez et al., 2005). The pathological symptoms resulting from hydatid cysts are diverse and be contingent on a permutation of many factors (Pawlowski et al., 2001; Kern and Pawlowski, 2002):

7. **The type of infectious organ.**

- The location, size, number besides state of the growing cyst inside injured tissue.
- The interaction among growing cysts as well as nearby tissues.
- Complications subsequent as of unexpected bacterial infection, rive, and extent of scolices .
- The incidence of immune responses as a consequence of the liberation of antigenic materials.
- The healthiness condition of the injured.

8. **Diagnosis of Hydatid Cyst Infection**

The diagnosis of the disease in humans depended on numerous steps are (Gonzalez-Sapienza et al., 2000; Filippou, 2007):

i. Epidemiological data is done by confirming the presence of the injury in the particular geographical location.

ii. Clinical features, which are the site, number and size of existing hydatid cyst and associated complications.

iii. Use imaging techniques: The technique is selected dependent on the kind of injured organ as well as the phase of cyst. These techniques include (Khuroo, 2002; Polat et al., 2003):

- Ultra-solography
- Computed Tomography
- Magnetic Resonance Imaging
- X-ray
- Angiography
- Echocardiography
- Cholangiography

iv. Immunological exams: These examinations are utilized to check the attendance of the cyst in suspicious cases in addition to for postoperative assessment as well as curative valuation (McManus et al., 2003). From these examinations as follows:

- Complement Fixation Test (CFT).
- Indirect Haemagglutination Test (IHT).
- Latex Agglutination Test (LAT).
- Fluorescent Antibody Test (FAT).
- Immunoelectrophorsis Test (IET).
- Enzyme linked Immunosorbent (ELISA).

And other tests:

a. Casoni Test

b. Human Basophil Degranulation Test (HBDT)

These tests differ in sensitivity and quality dependent on the nature, pureness as well as quality of the antigen utilized, depending on the sort of immunoglobulin also the sensitivity of this same technique (Zhang et al., 2003a). Diagnostic immune tests of the disease depend on the detection of

the presence of specific antibodies of the parasite in the serum of infected people, so they may give inaccurate results as well as their failure to distinguish the recent infection from the old infection due to the presence of antibodies circulating in the serum even after recovery (Devi and Parija, 2003).

9. Parasites Epidemiology and Geographical Distribution:

Hydatid cystic disease is a widespread global health problem worldwide, as infection can appear in both developing and developed countries, appearing in moderate, as well as tropical and subtropical areas (Gross *et al*., 2012; Siracusano *et al*., 2012). The disease has a global spread and occurs in almost all countries, as the transmission of infection depends on a number of factors: internal factors related to the parasite and host, external climate-related factors affecting both the parasite and the host, as well as socio-environmental factors that affect the parasite's ability to move from hosts animal during the life cycle (Torgerson and Heath, 2003).

The disease is endemic in parts of Asia (central and southern Russia and China), North and East Africa, Central and South America and most regions of Middle East "Iran, Iraq, Kuwait, Saudi Arabia, Turkey, Jordan, and Palestine", and is greatly widespread in portions of "Eurasia, Africa, Australia, South America," nations around Mediterranean Sea (Gross *et al*., 2012), temperate regions and in many Countries of Europe (Mandal and Mandal, 2012).

About 1 million cases are recorded annually in the world and despite attempts to control the disease (Torgerson and budke, 2003), it represents a health problem in many countries of the world, containing developed countries. 1-8 cases were recorded per 100,000 person tested in Europe and Italy was the leading European country in registering cases of cystic echinococcosis disease in 2005-2003 (Mandal and Mandal, 2012). In endemic regions, human incidence rates for cystic echinococcosis can reach more than 50 per 100 000 person-years, and prevalence levels as high as 5%–10% may occur in parts of Argentina, Peru, East Africa, Central Asia and China(WHO, 2015) .The annual incidence of hydatid cystic disease ranges from 1 to 200 out of 100,000 individual in various sheltered areas (Da Silva, 2010). Iraq is one of the areas where the disease is spreading, particularly in the central and southern regions between the Euphrates and Tigris, where it is inhabited by many farmers and sheep breeders (Al-Muathen and Qasim, 2009). *E. granulosus* species is the only species in Iraq and many researchers have studied the disease in several respects, including the study of Al-Ghariri (2000) on the effect of hydatid cysts on several blood constituents utilizing light and electronic microscopes, as well as Al-Ubaidi (2002) that included cellular and enzyme genetic studies of patients with hydatid cysts. Al-Qadhi study (2005) also showed some immune and chemical aspects in patients with hydatid cysts. The study of Al-Azi (2006) explained some of the immune characteristics of patient with hydatid cysts and the genetic profile of WBC antigens of humans and their title role in the incidence of hydatid cysts, while Al-Fayadh (2010) took a molecular look to describe antigens derived from human hydatid cysts and some median hosts. Taher (2009) studied heamatological, chemical and immunological for patients with hydatid cysts, while the study Saheb *et al,.* (2017) dealt with the spread of the disease in the provinces of the country for the period 2011-2015, with a total infection rate of 476 9 patients with hydatid cysts with 1,451, 1,240, 881, 675,522 patients for 2011, 2012, 2013, 2014, 2015, respectively. Mohammed (2020) study also showed that 90 patients with hydatid cysts were surgically confirmed to five major hospitals in Baghdad from January 2016 to October 2018. Mohamed *et al*., (2021) recorded 64 cases of hydatid cysts in a study conducted in Najaf province in 2018, and in another study conducted in Mosul from 2019-2021, 111 cases were recorded by Omar *et al*. (2021). Studies indicate that there are approximately 1,000 human cases in Iraq recorded

annually in all provinces of the country (Al-Nakeeb, 2004), an increase in recent years (Seda, 2005).

10. Methods of Human Transmission:

The transmission of the parasite to humans is influenced by several factors, including the spread of the parasite in domesticated dogs, human behavior with dogs, the strain of the parasite and human susceptibility to infection (Japhet *et al*., 2006). Hydatid cysts are infected when the parasite's eggs are swallowed by direct contact with infected dogs or feces containing eggs or dealing with soil and plants contaminated with eggs, and the eggs are transmitted directly from hand to mouth (Eckert and Deplazes, 2004). The infection can occur when eating foods and vegetables contaminated with parasitic eggs directly through feces or indirectly through insects such as beetles and flies as well as birds and wind, as water contaminated with parasitic eggs is another source of injury, as well as inhalation of dust containing the parasite's eggs provides an opportunity to acquire hydatid cysts in the lungs (Morar and Feldman, 2003; Kern et al., 2004; Shaikenov *et al*., 2004). Hydatid cystic disease occurs in humans at all ages and in both gender (Campos-Buenc *et al*., 2000; McManus, 2005). However, in some infested areas, the age and gender factor is a serious factor (Eddi *et al*., 2006), where many infections occur in children as a result of toys with dogs, but symptoms of infection do not appear until several years later due to the slow growth of the cysts formed (Boman *et al*., 2006). The incidence in infected areas in females is also higher than that of males, which may be due to the nature of the work done by women, which is more in contact with the final host, which increases the chances of infection (Crompton and Savioli, 2006; Craig and Larrien, 2007).

11. Treatment of Hydatid Cystic Disease:

The nature of the treatment of hydatid cysts in infected people be contingent on the size and site of the cyst in the body and complications resulting from symptoms (Chrieki, 2002) and there are several treatment options (Eckert and Deplazes, 2004) including:

11.1. Surgical Treatment

Surgical intervention continues to be the best way to treat hydatid cystic disease because of the probability of complete elimination of the cyst and the complete reclamation of the patient by up to 90% of the diseases (Pawlowski et al., 2001). Surgery is used in the case of large hydatid cysts, cysts containing daughter cysts, cysts that lie superficially above the organs, cysts hanging from organs, especially in the liver, cysts that are prone to spontaneous explosion or by shocks and infected cysts, as well as cysts that connect to the bile duct or that generate pressure on nearby vital organs. Surgery is not preferred in the case of multiple cysts in one organ or distributed in multiple organs or in the case of cysts in locations where surgery is not easy to perform nor is it used in certain cases such as the patient's age or in case of pregnancy or other severe diseases like heart disease, diabetes and hypertension (Pawlowski et al., 2001; Khuroo, 2002). The seriousness of the surgery lies in the probability of leak of the constituents of the hydatid cyst, which results in the occurrence of anaphylactic reactions, which may be fatal, as well as the spread and growth of primary scolices in different locations of the body and thus the secondary infection of hydatid cyst (McManus *et al*., 2003; Deplozes, 2004). Chemotherapy is recommended to be accompanied by the use of benzimidazole compounds

with surgery and preferably using albendezole (ABZ) four days before surgery and continuing treatment for one month after surgery (Palanivelu, 2005; Filippou et al., 2007). Treatment accompanying surgery helps reduce the internal pressure of the hydatid cyst and thus facilitate surgical treatment with the cyst, and chemotherapy donate to the killing of primary scolices and thus reduces the risk of secondary infection with the hydatid cyst (Pawlowski *et al*., 2001; Eckert and Deplazes, 2004).

11. 2. Treatment by PAIR Method

PAIR is a minimally invasive technique used in the treatment of hydatid cysts in the liver and other abdominal site (WHO 2003a.b). and also is an alternative method to traditional surgical procedures, (Pawlowski et al., 2001). Get best results with PAIR + BMZ are achieved in CE1/CE3a cysts, where it the first-line option treatment (Khuroo *et al*., 1993) PAIR is contraindicated for CE2 ,CE3b, CE4 and CE5, and for lung cysts (Brunetti et al.,2010)

11. 3. Pharmacological Treatment

Chemotherapy is one of the methods used to treat hydatid cysts, as this type of treatment is used in the case of patients who cannot be operated on due to age or pregnancy and patients with many hydatid cysts distributed in more than one organ as well as cysts located in locations where surgery is not possible and in the case of small cysts (Pawlowski *et al.,* 2001). As well as using chemotherapy before and after surgery to reduce the size of the cysts and the risk of a relapse of the disease (Smego *et al*., 2003; Sphicher et al., 2008). Benzaimidazole derivatives are the basis of chemotherapy for hydatid cysts patients, such as Albendazole and mebendazole and others (Reuter et al., 2006). Chemotherapy is affected by several factors, including the patient's age, cysts age, location and appearance features of cysts (Ceballos *et al*., 2008).

Albendazole is currently the drug of choice to treatment CE **(**Franchi et al.,1993), in pre-surgery given Albendazole for 1-4 week in two individual doses, and continue for 1-3 month after dependeding on risk factor(El-On,2003)

The use of Albendazole combined with Praziquantel gives more effective results if each drug is used alone, The combination of Albendazole and Praziquantel in the treatment of cystic hydatid disease is based on both pharmacodynamics synergy and pharmacokinetic enhancement. Albendazole acts by disrupting the parasite's microtubule formation and energy metabolism, leading to death of the larval cysts, while Praziquantel increases the permeability of parasite membranes to calcium ions, causing paralysis and tegmental damage. When used together, these drugs exhibit synergistic effects, resulting in greater protoscolicidal activity and enhanced structural damage to the hydatid cysts compared to monotherapy (Garcia et al., 2011). Additionally, Praziquantel has been shown to increase the bioavailability of albendazole's active metabolite, albendazole sulfoxide, by inhibiting hepatic metabolism and possibly intestinal efflux mechanisms. This interaction leads to higher plasma concentrations and prolonged exposure of albendazole sulfoxide, improving drug penetration into cysts and enhancing treatment efficacy (Lima et al., 2010). Clinical and experimental studies support that this combination yields better cyst degeneration and reduces recurrence rates, making it a valuable therapeutic strategy in cystic hydatid disease (Popova et al.,2023).

Prevention and Control:

Prevention and control of cystic echinococcosis disease use several steps, including:

- Wash your hands with soap and water before eating.
- Wash fresh fruits and vegetables well before eating them.
- Control of stray dog groups.
- Excluding dogs from areas adjacent to massacres, and applying international regulations for dog movement,
- Prevent dogs from feeding on the bodies of infected sheep.
- Treatment of infected dogs.
- Prevent the slaughter of sheep and other livestock in places not intended for slaughter.
- Getting rid of the waste of sacrifices safely.
- Attention to health education for people dealing directly with dogs as well as taking the necessary precautions in laboratories, hospitals and veterinary clinics.

Conclusions

cystic echinococcosis disease are increasing in prevalence in different parts of Iraq and are in remote countries, and may be due to reasons, including environmental conditions, increased livestock breeding, slaughter outside licensed massacres, failure to properly dispose of carcasses, spread of stray dogs and lack of proper control, so it is recommended to develop effective prevention and control several programs, prevent the spread of the disease, increase awareness and educate the community. CE is not only a local or national issue but also a significant global public health challenge, As a neglected zoonotic disease, it requires coordinated efforts at local, national, and international levels to reduce its burden. Strengthening surveillance systems, promoting intersectoral collaboration under the One Health approach, and investing in long-term public health education are critical to controlling CE in global to combat this disease.

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