Hepatic Hydatidosis Management

Abstract:
Hydatid cyst disease is a tapeworm infection caused by the larvae of echinococcus granulosus, spread through contaminated water and food with. Hepatic hydatid cysts have different clinical manifestations.The investigations include X-rays, ultrasonography, computerized tomography, magnetic resonance and ERCP used to detect deep lesions in all the organs and extent and status of avascular fluid-filled cysts. Antibody test is done to confirm x-ray findings. Medical treatment is influenced by the drug Albendazole.Albendazole chemotherapy proved to be a major therapy preferred in the medical care of cystic echinococcosis. Radical hepatic hydatid cysts surgery refers to peri-cystectomy and Conservative surgery consists of removal of the cystic contents and sterilization of the cavity as well as resection of the part of cyst. Laparoscopic surgery offers the advantages of a short hospital stay, less wound infection incidence rate, and minimal post operative pain. Percutaneous aspiration injection re-aspiration is suitable in patients who are not fit for surgery or are not ready for the surgery and have multiple cysts in the liver. The conclusion of this review article is compared to open surgery for hepatic hydatid cysts, we have shown that laparoscopic surgery can be performed safely even with multiple cysts, large cysts and bile duct cysts.

Keywords: Albendazole **,**hepatic, hydatid cyst disease, pericystectomy, PAIR , liver resection, scolicidal agents.

Introduction:

Hydatid disease is a tapeworm disease caused by the larvae of Echinococcus granulosus, which is life threatening. The incidence of the disease is closely related to certain geographic regions of the world. Hepatic hydatid cysts have different clinical manifestations and many people are infected with cystic hydatid disease (1).

Hydatidosis is very rare in European countries outside the endemic area of the Mediterranean (2). Echinococcus granulosus exists almost everywhere in the world and is most common in countries where sheep and cattle are raised. (<1 case / 1 million) in the United States. No sexual orientation. In 50% -70% of echinococcosis cases, the liver is affected.

E. granulosus is a hermaphroditic flatworm.There are three stages of development. The cyst usually consists of three parts: pericyst , which is formed by the host's inflammatory tissue, the external capsule and the internal capsule, which produce brood capsules with scolices . (3)

Figure:1 Collection of surgery clinic “Colentina” hospital

In some cases hydatid cysts are asymptomatic and are diagnosed when they become symptomatic. The cysts gradually grows (1-2cm/year) and unless the brain is affected, it is rarely diagnosed during childhood or adolescence. The incubation period is months to years and even decades.

Investigations for diagnostic purpose are plain x-ray abdomen, chest showing Calcification, ultrasonography ,computerised tomography , magnetic resonance imaging, Casoni test, endoscopic retrograde cholangiography , liver function test ,routine hematological test showing elevated total leucocyte count and eosinophilia.

Medical treatment consists of Albendazole or Praziquantel. The management of hydatid cysts of the liver usually involves surgery as the main component of treatment. The surgical approach aims to drain the contents inside the cyst as well as the germ layer surrounding the cyst while taking extreme precautions to prevent the contents of the cyst from spilling out (4).

Main aims of hydatid surgery are 1) complete removal of infectious components of the cyst. 2) avoid the spillage of the contents of the cyst during the surgery. 3) residual compartment treatment. 4) minimize operational risk.

Diagnosis and Management:

Investigations:

The existence of cysts in a patient with a history of contact to sheep and dogs in E. granulosus-endemic areas raises the possibility of cystic echinococcosis. Hydatid cysts, on the other hand, must be distinguished from benign cysts, abscesses, cysts caused by pituitary TB, and benign or malignant tumours. The existence of cysts in a patient with a history of contact to sheep and dogs in E. granulosus-endemic areas raises the possibility of cystic echinococcosis. Hydatid cysts, on the other hand, must be distinguished from benign cysts, abscesses, cysts caused by pituitary TB, and benign or malignant tumours.

Confirmation of the non-invasive diagnosis can also be done with the use of a combination of immunologic diagnostic techniques and radiographic imaging. X-rays can detect hepatic hydatid cysts .

Magnetic resonance imaging, computed tomography, and ultrasound are useful for detecting deep lesions in all organs, as well as determining the extent and status of avascular fluid-filled cysts.

Fig 2. Chest x-ray of a 6-year old girl showing hydatid cyst in the left lung in an endemic areas.(4)

Due to its availability and use in detecting the number of cysts, their location, size, and viability, abdominal ultrasound is the most commonly utilised imaging diagnostic tool for echinococcosis.

Type CL- unicellular cystic lesion with uniform reflectance is one of the classification systems (but ultrasound did not detect any pathological findings).

Type CE-1 single mass cyst with equal echogenicity and pathological findings including visible signs of cyst wall;
Type CE-2, multifocal, multisensory cyst;
Type CE-3, multi-layer membrane from the cyst wall visible as a floating membrane or "water lily sign";
Type CE-4 heterogeneous hypoechoic degeneration content, no cysts;
Type CE-5 the cyst has a thick, arcuate outer membrane of calcifications, producing a conical shadow.

Table 1:

WHO-IWGE classification of the hydatid cyst

Stage	Echographic aspect according to WHO-IWGE Classification
CL	Anechogenic uniloculated cyst, with no echoes or internal sepsis
CE 1	Anechogenic cyst, with fine echoes inside, representing the hydatic sand - active cyst
CE 2	Cyst with multiple septums at the interior, giving it a multivesicular aspect or "honeycomb" aspect,with a uniloculated primary cyst - active cyst
CE 3	Uniloculated cyst with decolated proligere membrane ("waterlily sign") (CE3a) or daughter vesicles associating hypo/hyperechogene images (CE3b) - cyst in transition phase
CE 4	Cyst with mixed content, hypo/hyperechogenic, without daughter vesicles - "wool clew" aspect-cyst in the degenerative phase
CE 5	Cyst with partial or totally calcified wall - inactive cyst

Antibody test is used to confirm X-ray findings, although some patients with cysticercosis lack immune response.

Liver cysts are susceptible to show immune response as compared to hepatic cysts. In any case, the site, the sensitivity of serological tests is inversely proportional to the extent of arrangement of parasitic antigens in the cyst; For example: healthy, intact cysts may produce very less response, while ruptured or leaking cysts gives a good response.
The indirect coagulation test is sensitive but is replaced by an enzyme immunoassay. Specific confirmation of senitivity is obtained by presenting echinococcal specific antigens by immunoblot tests. <24% patients are detected with Eosinophilia.
In seronegative patients, the most likely diagnosis is confirmed by demonstrating pigments or cyst membranes in the fluid taken from percutaneous aspiration of the cyst. Ultrasonographic guidance on punctures, deworming blankets, and predictive abilities needed to treat an allergic reaction minimizes risk.

At times, pigment preservation can be found in sputum or bronchoalveolar lavage; hooks are easier to identify thanks to acid-fast stains. (4)

Medical treatment:

The use of benzopamidazole (albendazole) and mebendazole are studied:

World Health Organization (WHO) compares two multiple periods in Europe to compare albendazole or mebendazole drugs. All medications have had similar efficiency, but the mebendazole needed greater capacity. In RCT, which was carried out in Franchi et al to compare the effectiveness of albendazole or mebendazole, treatment with albendazole showed better results than mebendazole. (4)

Albendazole Chemotherapy proved to be a major therapy that is preferred in the medical care of Cystic Echinococcosis.

Albendazole with praziquantel treated in combination has a high scolicidal and anti-cyst activity and deformation has increased and may cause treatment or improvement over albendazole alone. (6)

Surgical treatment:

RADICAL VS CONSERVATIVE SURGICAL TREATMENT.

Radical hepatic hydatid surgery refers to pericystectomy, while conservative surgery consists of removal of cystic contents and sterilization of the cavity, as well as resection of part of the cyst. . There are a number of retrospective non-comparative studies which conclude the radical surgery is the safest and widely accepted.

In a study of 240 patients, Aydin et al found that individuals who underwent conservative surgery had considerably higher morbidity and recurrence.

The aggressive surgery and cautious surgery were evaluated in a single randomised research with 34 individuals. The researchers concluded that conservative surgery had a higher probability of early recurrence and intracystic complications ($P = 0.012$) than radical surgery (3).

A policy of radical surgery can be followed as far as possible with acceptable morbidity and near zero mortality. However, radical surgery has been judiciously applied and still has an important role in conservative surgery (2).

LAPAROSCOPIC APPROACH FOR HYDATID DISEASE.

The use of laparoscopy to treat hepatic hydatid cysts was first documented in 1992 (3). 8 series have been published, including 5 or more patients, most of which use laparoscopic cystectomy technique (6)

Describes a special trocar system and operating techniques. A total of 76 patients underwent surgery using this technique.

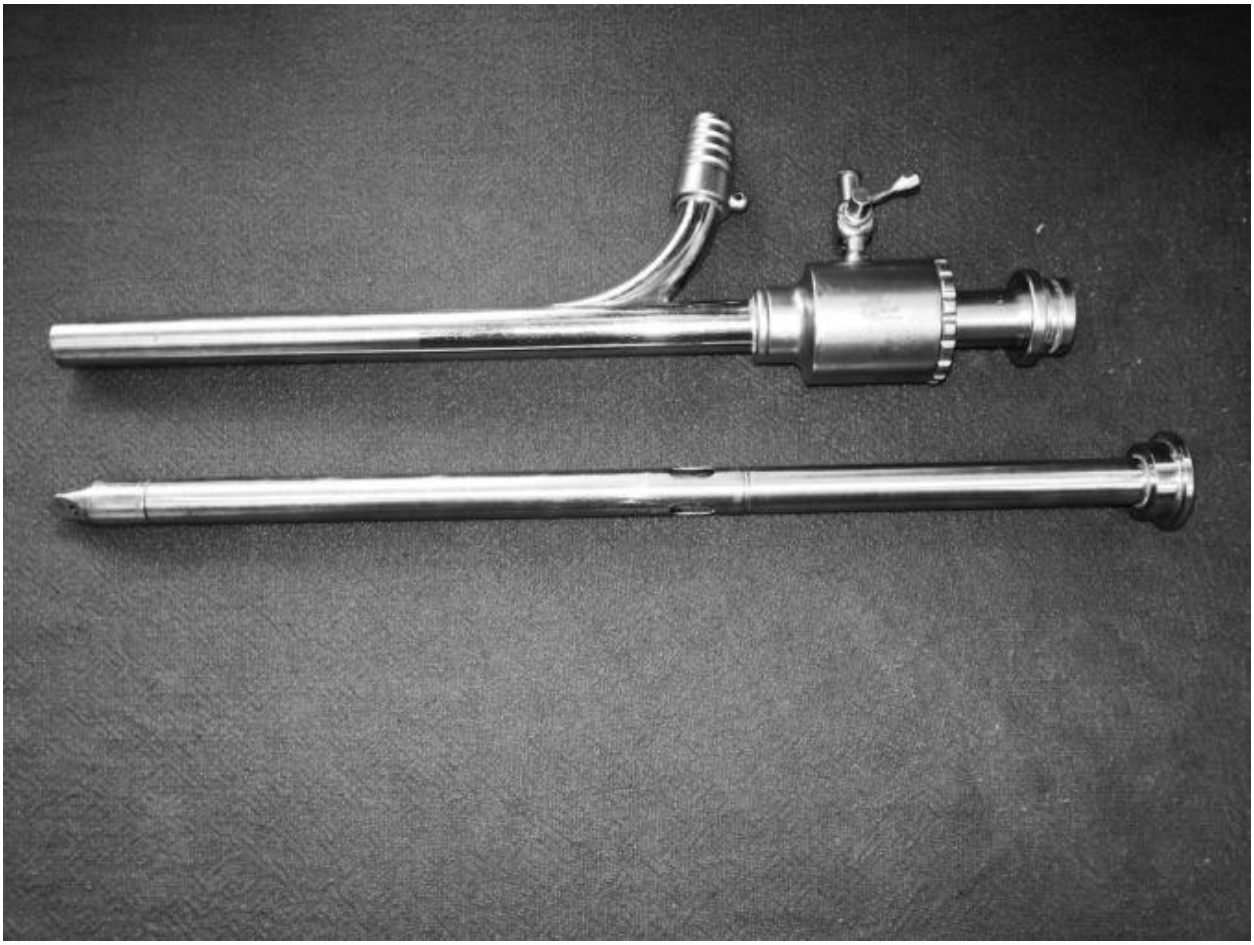

Figure 3: google images.

In 83% of patients, hydatid cysts were eliminated by PHS alone. A left lobectomy was subsequently performed in 13.7% of the patients because the cyst was so large that it occupied almost the whole left liver lobe. The residual cavity is managed by omentoplasty. The mean follow-up time was 5 years, during which there was no recurrence seen. (7)

Compared to open surgery, laparoscopic surgery offers the advantages of a short hospital stay, less wound infection incidence rate, and minimal postoperative pain . The disadvantage is that it is difficult to locate the capsule in certain positions, the risk of overflowing the contents of the capsule increases, and it is difficult to aspirate the capsule.

Laparoscopic surgery technology has been successfully applied in the management of liver hydatid cysts. Although the use of these procedures is limited to highly endemic areas and units of specific interest, laparoscopic surgery is now a management option for the treatment of hepatic hydatidosis (6).

DRUG TREATMENT WITH SURGERY.

49 patients non-randomized trial was conducted by Akan. Albendazole administered pre-operatively. Albendazole had a significant success rate in treating patients with hydatid cysts.

Albendazole was given one month before surgery and 2 months post surgery to 27 patients. In both the scenarios, the pharmacological treatment was tested for abnormal hepatic enzymes. 22 patients remaining, recurrence was not seen during the average monitoring period (5) of 28 months.

Combination treatment with Albenadazole + surgery is less risky to resort only to surgery.

Percutaneous Aspiration Injection Reaspiration plus Albendazole for hepatic hydatid cysts.

PAIR is suitable for patients who are not fit for surgery and who are not ready for surgery and have many cysts in the liver, spleen,kidneys, and bones. (4)

All patients going for percutaneous drainage were given albendazole orally usually once a day before and post drainage. Perform percutaneous drainage under guidance of ultrasound to closely monitor complications such as allergic reactions, laryngeal edema and bronchospasm.

Procedure usually requires three steps: The puncture and needle aspiration of the cyst, instillation and long-lasting cervical spine solution for about 25-35 minutes, as well as re-aspiration and final flushing of the cyst. Of the 770 patients, 73 (10%) received needle decompression and catheter drainage for type 3 and 4 cysts, and left the catheter in place for 1 to 11 days after drainage. Immediately after aspiration or catheter drainage, perform cytological, histopathological, and parasitological examinations of the cyst fluid or surgical tissue sample to confirm the diagnosis and evaluate the success rate of the drainage. Motility and staining pattern with an optical microscope is observed and neutral red staining is done(to prove active parasites) and methylene blue (to prove inactive organisms) to assess the viability of the protocranial segments. (8)

In the reviewed study, the following stated criteria are used for the success of PAIR treatment

(A) Under ultrasound, the internal cyst is separated from the cyst in the polycystic cyst and the secondary vesicle ruptures. The size of the cyst gradually decreases until it disappears. The size does not increase during the follow-up period. Level of echogenic material, or disappear completely and have an uneven echo pattern (pseudotumor formation);

(B) On CT, the cyst density increases;

(C) In serological and parasitological examinations, the serological titer is Negative with no complication.

The patient was observed for approximately 5 months, during which continuous ultrasound and CT was performed to evaluate the ultrasound mode,the size of the liver cyst cavity which was currently present. ELISA detects serum IgG and/or IgM antibodies. Serological titer >1:150 is considered positive.

Surgical intervention includes : Conservative and Radical methods. Conservative methods include tube drainage, marsupialization , capping (by suture Opposite surfaces are brought closer

together to surgically close the cyst cavity), open top, simple partial cystectomy. Radical surgery includes lobectomy, complete cystectomy, and partial hepatectomy.

Disadvantage of PAIR treatment with the drug albendazole usually are tolerated at a great extent by the patients. Infections are treated with antibacterial treatment; leak during drainage procedure can cause fever, hypotension, and allergic reactions, but can be expected and well treated with paracetamol, epinephrine injection as intravenous fluid or subcutaneoulys is administered .

PAIR may be the best treatment for hepatic hydatid cysts, but there is very less evidences to continue its use as a drug of choice in above procedure for patients with uncomplicated cysts (5).

Scolicidal agents:

Protoscolices are larvae of the parasites that develop into adults in the host's intestine. In surgical treatment of human echinococcosis, the effusion of the protocrops of living organisms is the most commom cause of the recurrence of echinococcosis.

To prevent this problem, a neck killer such as hypertonic salt is used to kill the anterior cervical spine that may spread to the patient's tissues during the operation. However, they may have some unacceptable side effects (9). Numerous related studies were reviewed(10-14).

Scolicidal agent	Concentration	Time	Results
ABZ or ABZ-SO	50, 10, 1, and 0.1 μg/mL	-	Combined compounds had better protoscolicidal activity
PZ, ABZ	Low PZ + ABZ concentrations	Within 15 days	PZ and ABZ displayed better protoscolicidal activity when applied in combination
Monensin	10 μm	36 h	All protoscoleces were dead
AmB	AmB (20 mg/mL)	60 min	82.3%
AgNPs	AgNPs (0.5-4 mg/mL)	60 min	71.6%
Foeniculum vulgare	1 mg/mL	5 min	100%
Hypertonic saline	20%	10 min	100%
Fungal chitosan isolated from *Penicillium waksmanii* and *Penicillium citrinum*	50, 100, 200, 400 μg/mL	10, 30, 60 and 180 min	Showed strong scolicidal activity
Chitosan from *Penicillium viridicatum*, *Penicillium aurantiogriseum* and commercial chitosan	50, 100, 200, 400 μg/mL	10, 30, 60, and 180 min, respectively	Commercial chitosan showed highest degree scolicidal activity
Endophytic *pestalotiopsis* spp. from neem plant	-	Within 30 min	Up to 97% scolicidal activity
Se NPs	Concentrations 500 and 250 μg/mL	10 and 20 min of application, respectively	Had potent scolicidal effects
Extract of endophytic fungi *Eupenicillium* and *Chaetomium* spp.	-	6 h	Had significant anti-cestodal activity
CsA	100 μg/mL and 50 or 20 μg/mL	For 3 days and 5 days, respectively	CsA is an effective scolicidal agent *in vitro*
AgNPs derived from the aqueous aerial extract of *Penicillium aculeatum*	0.1 and 0.15 mg/mL	120 min	Showed 83% and 90% scolicidal activity, respectively
Methanolic extract of *Sambucus* (S.) ebulus fruit	1, 10, 50, and 100 mg/mL	5, 10, 30, and 60 min	Showed a high scolicidal activity *in vitro*
Warm water	50°C, 55°C, and 60°C	1, 2, 5 min	100% scolicidal activity
a) Aqueous extracts of *Olea europaea* leaves b) Hydroalcoholic extracts of Satureja khuzestanica leaves	a) 0.1% b) 0.1% and 0.01%	a) 30, 60, and 120 min b) 120 min	Strong
Methanolic extract of *Allium sativum*	50 mg/mL	10 min	100% scolicidal activity
a) Acidic solutions and b) alkaline solutions	a) With pH 1, 2, 3, and 4 b) With pH, 13, and 14	a) 5 and 10, min b) 5 and 15 min	100%
Nigella sativa (*Ranunculaceae*) essential oil	Various concentrations of the essential oil (1 mg/ml)	10 min	Had potent scolicidal activities
Ajowan (*Trachyspermum ammi*) the	5 mg/mL	60 min	100% scolicidal activity

Table 2: Effect of different scolicidal agents on protoscolices of *Echinococcus granulosus* hydatid cyst *in vitro*.(9)

Prevention:

Avoid multilocular E. coli from wild animal hosts is impractical. So, in infected areas avoid contact with dogs and foxes. Preventing human infections depends on awareness to improve

personal hygiene and environmental sanitation. Monthly praziquantel treatment can be used to prevent infections in dogs that are likely to eating infected rodents.

DISCUSSION:

Mebendazole was the drug of choice to treat echinococcosis. afterwards, due to its great absorption properties, albendazole was introduced (5).

In an Randomized controlled trial by GilGrande et al., All patients underwent for the surgery: 17 patients did not get albendazole drug treatment, 20 patients were given Albendazole for 1 month, and 20 patients were given the same for about 3 months. 8 cysts (50 percent) in the control, 12 (71 percent) in the Albendazole for one month group, and 15 (93 percent) in the ALB for three months group were not alive (P = 0.018).

A research by Keshmiri et al. found similar findings in 28 individuals with 241 cysts who were randomly randomised to receive ALB (3 months) or placebo. When ALB is combined with surgery, the best results are attained (5).

Several studies comparing aggressive surgery and conservative surgery have been published. Despite the limited sample size, Yüksel. observed that cautious surgery was associated with considerably higher recurrence and morbidity rates in their single randomised trial (5).

Almost all types of liver hydatid cysts can be treated safely and effectively with laparoscopic surgery. Large-scale prospective and randomised trials have failed to prove its superiority. (Open laparoscopy).

Percutaneous drainage combined with albendazole is more successful than monotherapy in treating liver hydatid cysts and is both safe and efficacious. Complications, on the other hand, are conceivable. Khuroo and his colleagues (5).

The PAIR treatment appears to be the most widely accepted, but it is primarily compared to conservative surgery rather than drastic surgery in the published research. Only 129 patients with liver hydatidosis treated with PAIR drainage (n = 51), radical surgery (n = 62), and conservative surgery (n = 34) patients with cysts were studied by Gupta et al. The PAIR procedure was terminated in 11 patients because to inhalation of bile or cystic debris post initial puncture. Following that, the same patients underwent surgery. PAIR as a regular treatment currently has little or no evidence to support it, and more well-designed research are needed before it can be suggested (5).

This review provides evidences to all the queries related to the management of liver hydatid cysts. The limitations of the review are the different surgical methods stated in the published articles (5)

CONCLUSION:

Hepatic hydatid cysts are usually asymptomatic and are usually diagnosed accidentally. The common symptoms are pain in the upper right abdomen and/or upper abdomen. Surgical methods, including conservative and radical treatment, can affect the outcome of liver hydatid cysts. Compared with open surgery for hepatic hydatid cysts, we have shown that laparoscopic surgery can be performed safely even in large cysts, multiple cysts and bile duct cysts . (10)

References:

1. Regmee S, Maharjan DK, Thapa PB. The Current Protocols in the Management of Hepatic Hydatid Disease. Indian J Surg [Internet]. 2021 Jan 19 [cited 2021 Jul 16]; Available from: https://doi.org/10.1007/s12262-021-02724-2

2. Aeberhard P, Fuhrimann R, Strahm P, Thommen A. Surgical treatment of hydatid disease of the liver: an experience from outside the endemic area. Hepatogastroenterology. 1996 Jun;43(9):627–36.

3. Botezatu C, Mastalier B, Patrascu T. Hepatic hydatid cyst – diagnose and treatment algorithm. J Med Life. 2018;11(3):203–9.

4. Moro P, Schantz PM. Echinococcosis: a review. International Journal of Infectious Diseases. 2009 Mar 1;13(2):125–33.

5. Concepci&oacute, n Gomez i Gavara RL, pez-And&uacute, Jar TBI, Ñez J, Ramia &Aacute M, et al. Review of the treatment of liver hydatid cysts. World Journal of Gastroenterology. 2015 Jan 7;21(1):124–31.

6. Tai Q-W, Tuxun T, Zhang J-H, Zhao J-M, Cao J, Muhetajiang M, et al. The role of laparoscopy in the management of liver hydatid cyst: a single-center experience and world review of the literature. Surg Laparosc Endosc Percutan Tech. 2013 Apr;23(2):171–5.

7. Palanivelu C, Senthilkumar R, Jani K, Rajan PS, Sendhilkumar K, Parthasarthi R, et al. Palanivelu hydatid system for safe and efficacious laparoscopic management of hepatic hydatid disease. Surg Endosc. 2006 Dec 1;20(12):1909–13.

8. Smego RA Jr, Bhatti S, Khaliq AA, Beg MA. Percutaneous Aspiration-Injection-Reaspiration Drainage Plus Albendazole or Mebendazole for Hepatic Cystic Echinococcosis: A Meta-analysis. Clinical Infectious Diseases. 2003 Oct 15;37(8):1073–83.

9. Sharafi SM, Sefiddashti RR, Sanei B, Yousefi M, Darani HY. Scolicidal agents for protoscolices of Echinococcus granulosus hydatid cyst: Review of literature. J Res Med Sci. 2017 Aug 16;22:92.

10. Bayrak M, Altıntas Y. Current approaches in the surgical treatment of liver hydatid disease: single center experience. BMC Surgery. 2019 Jul 17;19(1):95.

11. Manekk RS, Mehta A. Recurrence of Primary Pulmonary Hydatidosis in the Left Lung with No Hepatic Involvement. JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS. 2021 Mar 8;10(10):746–8.
12. Andhale A, Acharya S, Devde K, Shukla S. Disseminated Abdomino-Throracic Hydatidosis Presenting as Mediastinal Syndrome. JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS. 2021 Jun 7;10(23):1807–8.
13. Pratapa, Karthik, Sourya Acharya, Yash Gupte, and Samarth Shukla. "Acute B Virus Hepatitis with Fulminant Hepatic Failure Precipitating Crisis in Sickle Cell Disease." JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS 9, no. 3 (January 20, 2020): 173–75. https://doi.org/10.14260/jemds/2020/40.

14. Raja KK, Acharya S, Inamdar A, Kumar S. Wilsons Disease Presenting as Acute Fulminant Hepatic Failure. JOURNAL OF EVOLUTION OF MEDICAL AND DENTAL SCIENCES-JEMDS. 2021 Apr 19;10(16):1185–6.