

Chronic Diseases Journal Chronic



DOI: 10.22122/cdj.v12i3.744

Published by Vesnu Publications

Unusual presentation of hydatid disease with recurrence over five vears in central India

Pravinkumar Ghongade¹, Bharat Patil², Vitaladeuni B. Shivkumar³, Nitin M. Gangane⁴

- 1 All India Institute of Medical Sciences, Nagpur, India
- 2 MGIMS Sevagram, Maharashtra, India
- 3 Department of Pathology, MGIMS Sevagram, Maharashtra, India
- 4 Department of Psychiatry, Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha, India

Abstract

Original Article

BACKGROUND: Human hydatid disease (HD) is a chronic parasitic infection caused by Echinococcus species. Classic human hydatid cystic disease is a neglected zoonotic disease caused by the larva of cestode Echinococcus granulosus, leading to serious life-threatening complications. This study examines the range of presentations, mainly uncommon sites and changes in hematological parameters in recurrence and before and after surgery.

METHODS: Amongst a total of 109 cases of HD, 25 unusual sites of HD were retrospectively studied in central India tertiary care rural hospitals from January 2016 to December 2020. Demographic details, clinical details, treatment reports, hematological reports, histopathology reports, and ultrasonography (USG)/computed tomography (CT)/magnetic resonance imaging (MRI) reports were also retrieved.

RESULTS: Histologically, scolices were found in 40.36% of the cases. Preoperative mean platelet volume (MPV) and platelet count (PLT) were significantly higher and lower, respectively, compared to the postoperative period. The recurrence rate of HD after surgery was 3.6%, while in the case of unusual presentation, recurrence was noted as 8%. All 4 cases of recurrence showed increased PLT (P < 0.0001).

CONCLUSION: Findings of the study highlight essential features of HD, which help early clinical suspicion, prompt diagnosis, and management to reduce morbidity and mortality related to HD. A possibility of HD should be considered in the differential diagnosis of cystic swellings present anywhere in the body, especially at rare and unusual sites. Platelet parameters and eosinophil count could be utilized for early suspicion and ruling out the possibility of recurrence of HD.

KEYWORDS: Hydatid Cyst; Echinococcus; Recurrence

Date of submission: 15 June 2023, Date of acceptance: 28 July 2023

Citation: Ghongade P, Patil B, Shivkumar VB, Gangane NM. Unusual presentation of hydatid disease with recurrence over five years in central India. Chron Dis J 2024; 12(3): 147-54.

Introduction

Human hydatid disease (HD) is a chronic parasitic infection caused by Echinococcus species, granulosus complex, multilocularis, or E. vogeli, more commonly found in sheep-rearing areas like Europe,

Corresponding Author:

Vitaladeuni B. Shivkumar; Department of Pathology, MGIMS Sevagram, Maharashtra, India Email: shivkumar@mgims.ac.in

Africa, South and Central America, and Asia.^{1,2} HD is becoming an endemic disease with emerging incidences in India.1,3,4 However, Tamil Nadu, Andhra Pradesh, and Jammu and Kashmir have a high prevalence in India, with 4-16 per 100000.5 The increased incidence may be due to favorable climatic conditions in India, such as a warm and humid climate, the availability of large numbers of intermediate hosts who rely on

grazing activities, a lack of awareness, and a lack of cooperation between veterinary and medical sciences.

Hydatid cyst disease affects all age groups⁵ and has a multitude of clinical presentations ranging from asymptomatic conditions to acute life-threatening emergencies. HD can affect all body organs except teeth, hair, and fingernails. granulosus mainly involves the (55%-70%), followed by the lung (18%-35%), the two organs being affected simultaneously in about 5-13 percent of cases. Incidence of unusual sites accounts for 8%-10%. The spleen, kidney, peritoneal cavity, skin, and muscles are affected by HD in about 2% of cases. In contrast, the heart, brain, vertebral column, ovaries, pancreas, gall bladder, thyroid gland, breast, and bone are affected in about 1% of cases.6

Cyst fluid spillage can occur during surgery resulting in anaphylaxis and secondary echinococcosis (2%-25% of cases).⁷ It occurs after the incomplete removal of viable cysts and minute spillage during the original operation.⁸ Malki et al. demonstrated higher recurrences in segments II ± III (10.2%), IV ± I (9.9%), and VII ± VIII (9.6%).⁹

Kucukbayrak et al. recruited 72 patients in their study. They demonstrated no statistical difference in platelet count (PLT) for both periods, including preoperative and postoperative. However, mean platelet volume (MPV) (mean: 8.07 ± 0.83 , 7.78 ± 0.87 , P = 0.002) and platelet mass (median: 2456.75, range: 1013.70-5046.60 vs. median: 2280.80, range: 134.20-4042.60, P = 0.039) were noted as statistically higher in the preoperative period than postoperative period.

Mustafa et al. included 33 patients operated on for hydatid cysts. The authors concluded that the patient's preoperative MPV was significantly higher than postoperative MPV values. Therefore, they claimed that MPV was a valuable follow-up marker after surgery in

patients with hydatid cysts. Platelet distribution width (PDW) was not significantly different for both periods.¹¹

HD is one of the most severe parasite infections, producing significant morbidity and mortality in humans and diagnosing HD is primarily confirmed through pertinent history, serological tests, and imaging techniques. Hydatid cysts in odd places might make diagnosis more difficult. Few studies are available in the literature about recurrence and hematological parameters of HD; these studies are scarce in case of unusual location HD.

This study examines the range of presentations, mainly uncommon sites, and changes in hematological parameters in recurrence and before and after surgery.

Methods

A retrospective study was carried out at a tertiary care rural hospital in central India over five years (2016 to 2020). Over a five-year duration (2016-2020), 37413 patients with histopathology specimens were reported that 109 were diagnosed with hydatid cysts. Of these 109 cases, a total of twenty-five unusual cases with a confirmed diagnosis of hydatid cyst on histopathology who had undergone ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI), complete blood count (CBC), and biochemical parameters before excision of sample for histopathology were included in this study. The demographic details, clinical details, and treatment reports were retrieved from the hospital information system (HIS). The histopathology reports and USG/CT/MRI reports were also retrieved. Patients whose hospital records were not available were excluded from the study.

All the specimens were preserved in 10% formalin and were subsequently subjected to histopathological examination with routine Hematoxylin and Eosin (H&E) stain. Two

investigators examined these stained slides for histopathological findings. Visualization of a lamellated structure of a germinal layer, cyst wall, protoscolices, and scolices on H&E-stained sections is considered diagnostic criterion for HD. The data were sorted out depending upon the anatomical site, age, sex, and size based on imaging analysis purposes. modality for hemoglobin (Hb) consisting of level, hematocrit [packed cell volume (PCV)], red cell distribution width (RDW), total white blood cell (WBC) counts, as well as platelet parameters such as PLT, MPV, and PDW values were analyzed in both follow up following surgery. Both values mean ± standard deviation (SD) were calculated.

Statistical analysis: SPSS software (version 21.0, IBM Corporation, Armonk, NY, USA) was used to code and summarize the data. The difference between pre and postoperative hemogram parameters was assessed using the t-test. P-value < 0.05 was used to determine statistical significance.

Results

During the study period (2016-2020), 109 cases of hydatid cyst disease were recorded. These 25 cases showed unusual presentation. Among them, 17 patients were men, 8 were women, and 13 were farmers or agrarian by occupation. The mean age of presentation was 47.13 ± 14.92 years. A maximum number of hydatid cyst disease cases were noted in the age group of 51-60 years, followed by 41 to 50 and > 60 years.

Localized swelling was a presenting symptom in patients with soft tissue HD. In our study, disorientation was the most common symptom of the brain and vertebral hydatid cyst (Table 1), and HD at the usual location of 79 cases was diagnosed using USG. CT and MRI detected only 5 cases of typical HD. However, 11 unusual cases of recurrent HD were suspected by only USG.

The remaining 13 cases of unusual HD needed CT and MRI for diagnosis. The study noted the size variation of hydatid cysts on imaging modalities. In a maximum number of cases (n = 62), the visualized cyst size was 5-10 cm in diameter. Abdominal USG was done in all patients. On USG, 34.8% of cases showed multiple daughter cysts, calcification in the peripheral wall was seen in 8.3%, while abdominal lymphadenopathy was noted in 3.7%.

Table 1. Presenting complaints of the unusual cases of hydatid cyst disease

Presenting complaints	Number of cases
Pain in the abdomen	6
Abdominal lump	4
Fever	1
Lump and pain in the abdomen	3
Swelling	3
Chest pain	1
Hematuria	1
Breathlessness	1
Breathlessness and pain	
in the abdomen	2
Distension of abdomen	1
Pain in limbs	1
Disoriented state	1

We reported 25 out of 109 hydatid cysts at unusual places, such as five cases involving the spleen, four cases involving muscle, two cases each of bone, retroperitoneal region, and anterior abdominal wall, one from the brain (frontotemporal region), para-vertebral region (T10 to L5), mesentery, anterior mediastinum, and seven instances with kidney hydatid cyst (Tables 2 and 3).

Pre- and postoperative values of Hb, hematocrit (PCV), total leukocyte counts (WBCs), and RDW were not significantly different. PDW did not vary significantly among platelet parameters, but preoperative MPV was significantly higher than postoperative MPV values (P < 0.0001), while the PLT was significantly lower preoperatively (P = 0.035) (Table 4).

Table 2. Location of hydatid cyst with single and multiple organ involvement on imaging modality

Single organ involvement	Number of cases
Liver	52
Lung	10
Multiple organ involvement	
Liver and lung	8
Liver and peritoneum	5
Liver and small bowel	3
Lung and peritoneum	1
Liver, mesenteric,	
peritoneal region	2
Liver, recto-vesicle pouch	1
Liver, peritoneum, right lumbar,	
right iliac fossa, pelvic region	1

In 83 cases, the absolute eosinophil count (AEC) was measured; it was raised in 77 patients before surgery.

Table 3. Unusual location of hydatid cyst with single organ involvement on imaging modality

single organ involvement on imaging modulity			
Location/tissue involvement	Number of cases		
by HD			
Spleen	5		
Kidney	7		
Soft tissue			
A) Back muscle	1		
B) Thigh muscle	2		
C) Inguinal region soft			
tissue	1		
Frontal lobe (brain)	1		
Bone	2		
Retroperitoneal region	2		
Paravertebral region	1		
Anterior abdominal wall	2		
Anterior mediastinum	1		

HD: Hydatid disease

Amongst them, 41 patients had eosinophilia ranging from mild to moderate, and 26 cases had severe eosinophilia. We could follow only 62 cases postoperatively; 49 claims had normal AEC after surgery. We found a total of 4 cases of recurrence of HD after surgery. Amongst them, two cases of recurrence were from liver HD, one from retro peritoneum HD, and one from mesenteric HD. Patients of recurrence from liver HD were presented, one with increased abdominal pain after eight months and the other with chills and rigor that appeared one-and-a-half years later. After six and nine months following surgery, patients with retroperitoneal and mesenteric HD were represented, respectively. In our study, overall recurrence rate of HD after surgery was 3.6%. While in case of unusual presentation, recurrence was noted as 8%. In recurrence of HD, all 4 cases showed eosinophilia of severe degree. 3 cases showed an increase in MPV (P = 0.21), and all 4 cases showed increased PLT (P < 0.0001).

Discussion

The main objective of the present study was to examine the range of presentations of common and uncommon sites and changes in hematological parameters in recurrence and before and after surgery and to find the recurrence rate in these cases. Histologically, scolices were found in 40.36% of the total cases.

Table 4. Haematological parameters of cases

Parameters	Preoperative values	Postoperative values	P
Hb (g/dl)	11.44 ± 2.04	11.08 ± 1.91	0.1801
RBCs (g/dl)	4.41 ± 0.66	4.44 ± 0.64	0.7337
WBCs (Cells/μl)	8.99 ± 3.32	10.33 ± 4.10	0.0086
Platelet (Platelets per Unit)	282.15 ± 105.50	315.49 ± 126.70	0.0359
MCV (Femtoliters)	79.41 ± 8.37	78.98 ± 8.11	0.7005
RDW (%)	16.26 ± 4.12	16.66 ± 3.72	0.4527
MPV (femtoliters)	9.22 ± 1.26	7.91 ± 1.29	< 0.0001
PDW (%)	14.46 ± 2.46	15.01 ± 3.56	0.1859
PCV (%)	34.94 ± 5.80	33.50 ± 5.69	0.0656
AEC*(Cells/μl)	1765.15 ± 240.27	253.29 ± 202.12	< 0.0001

Hb: Hemoglobin; RBC: Red blood cell; WBC: White blood cell; MCV: Mean corpuscular volume; RDW: Red cell distribution width; MPV: Mean platelet volume; PDW: Platelet distribution width; PCV: Packed cell volume; AEC: Absolute eosinophil count

Due to the hematogenous route or the peritoneal fluid circulation phenomenon, HD can affect any organ in the abdomen. In most diagnosis the early by clinical presentation alone is difficult.12 The clinical presentation of HD depends on the size and site of the lesion with the accessibility of the organ involved for clinical evaluation. In most cases, the initial phase following infection is asymptomatic and may stay for months to years. It may turn symptomatic when the growing cyst exerts pressure on adjacent tissues/organs following rupture of the cyst or if the cyst becomes superinfected. Most cysts become symptomatic when they become larger than 5 cm, but even tiny cysts may produce symptoms in the lung.¹² Due to this, hydatid cyst disease is repeatedly underdiagnosed and detected by chance in evaluation or only when complications occur. Though histopathology is confirmatory and the gold standard for diagnosing HD, imaging modalities, especially together with serology, often specify the diagnosis of hydatid cyst disease.13

Its complications are usually diagnose using USG.¹⁴ However, CT and MRI are the preferred radiological diagnostic modalities for unusual HD. Histopathologically on H&E slides, scolices were noted in 40.36% of the cases. In the rest of the acellular lamellar cyst wall, the germinal membrane and the surrounding host reaction are composed of the foreign body reaction and inflammatory fibrous or granulation tissue (Figure 1a-d). few authors have reported unusual locations like the kidney, spleen, peritoneum, common bile duct, head of the pancreas, and adnexa.15,16

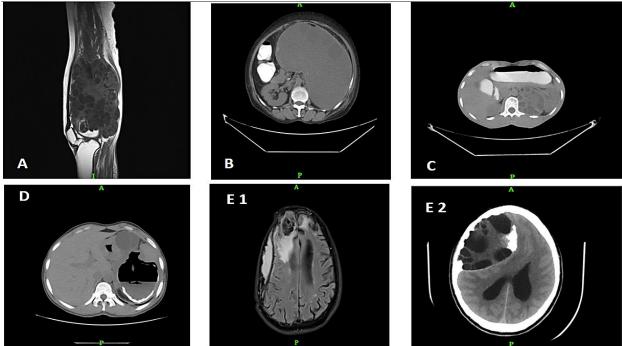


Figure 1. A) Large altered signal intensity lesion involving distal diaphysis, metaphysis of shaft of the femur, semi-membranous, and sartorius muscle [magnetic resonance imaging (MRI)]; B) Large thin-walled peripherally enhancing fluid density lesion with multiple daughter cysts arising from the center pole of the left kidney [computed tomography (CT)]; C) Left paravertebral mass with multiple nonenhancing cysts (CT); D) Enlarged with a well-defined enhancing double-walled exophytic cystic lesion in the middle pole of the spleen (CT); E1 & E2) Well-defined extra-axial minimally peripherally enhancing multi-loculated cystic lesion arising from the inner table of right frontal and temporal bones (CT & MRI)

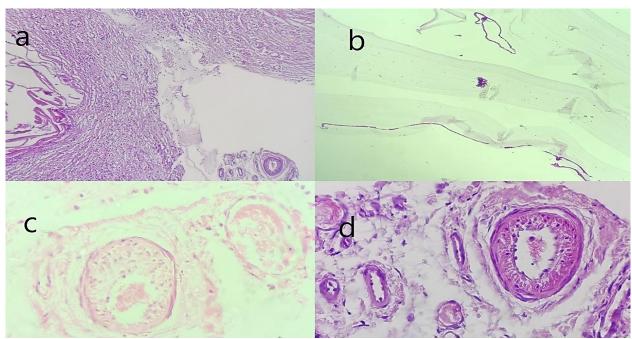


Figure 2. Hydatid cyst in the spleen, the cyst wall is infiltrated by eosinophils, lymphocytes along with proscolex [Hematoxylin and Eosin (H&E), 100X]; Photomicrograph b) Hydatid cyst wall in the kidney with the acellular laminated membrane (H&E) 100X; Photomicrograph c) Protoscolices in the cerebrum (H&E, 400X); Photomicrograph d) Protoscolices with hooklets inside the soft tissue (H&E, 400X)

The spleen is involved in 2%-2.5% of HD cases. It is primarily associated with pulmonary, hepatic, and multi-organ hydatidosis. Renal HD is a rare condition accounting for 1%-3%, and cysts are generally unilateral and in the upper or lower pole. 18% of renal HD can rupture and cause acute colicky pain and hydaturia if they enter the collecting system.¹⁷ We found seven cases of renal HD in our study.

Even in endemic areas, primary soft tissue involvement by hydatid cyst is uncommon, with a 0.5%-4.7% occurrence. In HD, bone involvement occurs in 1%-2.4% of cases. The spine and pelvis are the most frequently affected areas. Approximately, 2%-3% of all cases are found in muscular tissue. Four cases of muscle and soft tissue involvement and two patients with bone involvement were in the present study. The cerebral form has a low incidence of 1%-2%. This localization can be linked to other organ

involvement such as liver or lung or a single brain and spinal column infestation.²⁰ This study noted one case of brain and one case of para-spinal vertebra presentation.

Seventy-seven patients developed eosinophilia, a far more specific sign of parasite infection than the previously considered hepatic syndromes or inflammatory illness. It was also feasible to determine the best treatment based on the imaging (depending on the stage and size of the cysts). Localization is crucial for determining the optimal surgical strategy for minimizing relapse. With difficult-to-access cysts, incomplete endocyst excision is standard, which can be a significant source of recurrence.²¹

Because intra-abdominal adhesions allow for the possibility of leakage or insufficient clearance, recurrent hydatid cysts may experience more challenges during subsequent operations. During the 60.5-month follow-up period, Kapan et al. also found a 4.65% recurrence rate.²² After intra- and extra-hepatic disease treatment, new active cysts develop in recurrent HD; the overall recurrence rate is estimated to be between 2% and 25%.23 Prousalidis et al. reported a recurrence of 8.7%. The two main reasons for recurrence are minute hydatid cyst leakage, ineffective treatment due to missed cysts, and partial pericystectomy.8

In our study, the recurrence rate of HD after surgery was 3.6%, while in the case of unusual presentation, recurrence was noted as 8%. All 4 cases of recurrence showed increased PLT (P < 0.0001). HD location in the liver and the lung was associated with higher recurrence.

In our study, we found more frequent relapses in these groups of patients although differences were not statistically significant. No patient with recurrent Cystic echinococcosis (CE) died as a consequence of recurrent complicated cysts.

We also analyzed the hematological parameters both pre- and postoperatively. Preoperative MPV and PLT were significantly higher and lower, respectively, compared to the postoperative period. Only MPV and PLT differed markedly between pre- and postoperative events. Parameters such as Hb, PCV, RDW, and WBCs were unaffected in both conditions. Platelet parameters like PLT and MPV were significantly altered probably due to changes in shape and pseudopods formation when activated and released inflammatory mediators. Platelets are capable of removing bactericidal compounds and involving and encapsulating microorganisms. They are also effective helminthic infection defenders. Because old platelet shrinks, an increase in the release of new platelet from the bone marrow increases MPV, as seen in conditions involving increased platelet production and destruction. According to Polack et al., platelets have cytotoxic effects on parasites in vivo and in vitro, and these findings suggest that platelets may play a role in infectious diseases.²⁴ Parasitic infections are linked to platelet parameters such as MPV.

Our results were consistent with previous studies. 10,11 We found that preoperative MPV (decreased) and total PLT (increased) of a patient with a hydatid cyst were significantly altered in the postoperative period.

The host's reaction to helminth infection is characterized by eosinophilia. In the presence antibodies or complements, specific eosinophils killed larval stages of parasitic worms in vitro. Eosinophils have long been considered defensive effector cells activated by T helper cells type 2 (Th2).²⁵ In patients with hydatid cysts, we assume that PLT, eosinophil count, and MPV are useful follow-up markers after surgery.

Conclusion

A possibility of HD should be assessed in the differential diagnosis of any cystic lesion present anywhere in the body, especially at unusual and rare sites. We conclude that MPV, PLT, and eosinophil count may be helpful as markers after surgery in patients with hydatid cysts to discover recurrence. Large HD cysts should be carefully monitored for signs of recurrence and regular follow-up, especially in the liver and in unusual locations, is recommended.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

We sincerely appreciate the work of our technical staff members for their tremendous support.

Financials support and sponsorship

This research did not receive any financial support or sponsorship from funding agencies.

References

1. Muni S, Kumari N, Pankaj D, Kumar A, Pintu DK. Hydatid Cyst in Urine: A Case Report. Int J Sci Study. 2017; 5: 257-9.

- 2. Sarkar S, Roy H, Saha P, Sengupta M, Sarder K, Sengupta M. Cystic echinococcosis: A neglected disease at usual and unusual locations. Trop Parasitol. 2017; 7(1): 51–5.
- 3. Kayal A, Hussain A. A Comprehensive Prospective Clinical Study of Hydatid Disease. ISRN Gastroenterol. 2014; 2014: 1–5.
- Rukmangadha N, Chowhan AK, Sreedhar KV, Patnayak R, Phaneendra R, Kumaraswamy MR. Hydatid cyst - different organ involvement: a prospective and retrospective study. Bioscan. 2010; 5: 231-4.
- 5. Dayal R, Rathore SS, Verma D, Parmar S, Yadav RR, Gupta MK. The Study of Hydatid Disease A Retrospective Study of Last 10 Years In Western Rajasthan India. 2016; 15(2): 45–7.
- 6. McManus DP, Zhang W, Li J, Bartley PB. Echinococcosis. Lancet. 2003; 362: 1295–304.
- 7. Karavias DD, Vagianos CE, Bouboulis N, Rathosis S, Androulakis J. "Improved techniques in the surgical treatment of hepatic hydatidosis." Surg Gynecol Obstet. 1992; 174: 176–80.
- 8. Prousalidis J, Kosmidis C, Anthimidis G, Ka-poutzis K, Karamanlis E, Fachantidis E. Post-operative Recurrence of Cystic Hydatidosis. Can J Surg. 2012 February; 55(1): 15-20.
- 9. Malki El HO, Mejdoubi El Y, Souadka A, Zakri B, Mohsine R, Ifrine L, et al. Does primary surgical management of liver hydatid cyst influence recurrence? J Gastrointest Surg. 2010; 14: 1121–7.
- 10. Küçükbayrak A, Oz G, Fındık G, Karaoğlanoğlu N, Kaya S, Taştepe I, Senel E, Küçükbayrak ZS. Evaluation of platelet parameters in patients with pulmonary hydatid cyst. Mediterr J Hematol Infect Dis. 2010 Apr 14;2(1):e2010006.
- 11. Sit M, Aktaş G, Yilmaz EE, Hakyemez IN, Alçelik A, Küçükbayrak A. Platelet parameters in hepatic hydatid cysts. Int J Inflam. 2013;2013:593273.
- 12. Siracusano A, Teggi A, Ortona E. Human cystic echinococcosis: old problems and new perspectives. InterdiscipPerspect Infect Dis. 2009:474368.
- 13. White AC, Weller PF. Cestodes. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Internal Medicine. 17th ed. New York, NY: McGraw Hill Companies;

- 2008. vol 1. p. 1338-40.
- 14. Derbel F, Ben Mabrouk M, Ben Hadj Hamida M, Mazhoud J, Youssef S, Ben Ali A, et al. Hydatid cysts of the liver diagnosis, complications and treatment. Intechopen [Online]. [cited 2012 aug 14]; Available from: URL: https://www.intechopen.com/chapters/38230
- Dagtekin A, Koseogles A, Kara E, Karabag H, Avci E, Tovun F, Bagdatoglu C: Unusual location of hydatid cysts in pediatric patients. Pediatr Neurosurg. 2009, 45: 379-83.
- De U, Basu M: Hydatid cyst of common bile duct mimicking type I cholecochal cyst . J Indian Assoc Pediatr Surg. 2007, 12: 83-4.
- 17. Polat P, Kantarci M, Alper F, Suma S, Koruyucu MB, Okur A. Hydatid disease from head to toe. Radiographics. 2003; 23: 475–94.
- 18. Kizilkaya E, Silit E, Basekim C, Karsli AF. Hepatic, extrahepatic soft tissue and bone involvement inhydatid disease. Turk J Diagn Interv Radiol. 2002; 8: 101–4.
- 19. Kandhrah E, Semercioz A, Metin A, Eroglu M, Uysal B. Non-functioning kidney resulted fromprimary hydatid cyst of the psoas muscle. MMJ. 2006; 19: 145-6.
- Gautam S, Sharma A.Intracranial Hydatid Cyst: A Report of Three Cases in North-West India. J Pediatr Neurosci. 2018: 13: 91–5.
- 21. Haddad MC, Sammak BM, Al-Karawi M. Percutaneous treatmerit of heterogertous predorninantly solid echopattern echinococcal cysts of the liver. Cardiovascular Interventional Radiol. 2000;23(2): 121-5.
- 22. Kapan M, Kapan S, Goksoy E, Perek S, Kol E. Postoperative Recurrence in Hepatic Hydatid Disease. J Gastrointestinal Surg. 2006;10(5):734-9.
- 23. Khuroo MS. Hydatid Disease: Current Status and Recent Advances. Annals of Saudi Medicine. 2002;22(1–2): 56–64.
- 24. Polack, B, Peyron F, and Auriault C. Platelet cytotoxicity against parasites. Nouvelle Revue Française d'Hematologie, 1991;33(4): 317–22.
- 25. Huang L, Appleton JA. Eosinophils in helminth infection: defenders and dupes. Trends Parasitol 2016;32(10): 798–807.