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Retrospective Evaluation of the Incidence of Cystic Echinococcosis in Humans Between 2012-2023 in Pakistan

Pakistan'da 2012-2023 Yılları Arasında İnsanlarda Kistik Ekinokokkoz Görülme Sıklığının Retrospektif Olarak Değerlendirilmesi

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ABSTRACT

Objective: Present study aimed to determine the demographic, epidemiological and pathological features of human cystic echinococcosis (CE) cases using patients' hospital based clinical history from 2012-2023.
Methods: The current retrospective study was conducted from June-December and aimed to investigate the incidence of human CE in Pakistan. A total of 74 surgically confirmed patients' data was retrieved from the hospital records. All epidemiological, radiological, histopathological and treatment characteristics of the patients were recorded.
Results: The results showed that the highest number of CE cases were recorded in 2019 (15/74, 20.2%), followed by 2018 (11/74, 14.8%). In age categories, the highest frequency of CE cases was recorded in the age group 11-20 (19/74, 25.7%), followed by 31-40 (18/74, 24.3%), 41-50, and 51-60 (9/74, 12.1%), respectively. Gender-wise findings showed that females were more infected (46/74, 62.2%) as compared to males (28/74, 37.83%). Among reported cases, most infected organs were liver (24/74, 32.4%) and the lungs (14/74, 18.9%), followed by the bone, bladder, and abdominal cavity (3/74, 4.1%), kidney, chest (2/74, 2.7%), while and others. Surgery was performed after echinococcal cyst detection by diagnostic imaging methods such as computed tomography, magnetic resonance imaging, or ultrasound. All patients received albendazole anthelminthic medication after their surgical procedures.
Conclusion: The present research reveals that CE is persistently endemic in Pakistan. Lack of knowledge and dedicated work on behalf of public healthcare and veterinarians to control CE pose a challenge in Pakistan. A lot of research and strong management programs are required to combat the disease.
Keywords: Cystic echinococcosis, hydatid cyst, retrospective, surgical, Pakistan

ÖZ

Amaç: Bu çalışma, 2012-2023 yılları arasında hastane kayıtları kullanılarak insan kistik ekinokokkoz (KE) olgularının demografik, epidemiyolojik ve patolojik özelliklerini belirlemeyi amaçlamıştır.
Yöntemler: Bu retrospektif çalışma Haziran-Aralık ayları arasında yürütülmüş olup, Pakistan'da insan KE insidansını araştırmayı hedeflemiştir. Cerrahi olarak doğrulanmış toplam 74 hastaya ait veriler hastane kayıtlarından elde edilmiştir. Tüm epidemiyolojik, radyolojik, histopatolojik ve tedaviye ilişkin özellikler kayıt altına alınmıştır.
Bulgular: Sonuçlara göre en fazla KE olgusu 2019 yılında kaydedilmiştir (15/74, %20,2), bunu 2018 yılı izlemiştir (11/74, %14,8). Yaş gruplarına göre en fazla olgu 11-20 yaş grubunda görülmüş (19/74, %25,7), bunu sırasıyla 31-40 yaş (18/74, %24,3), 41-50 ve 51-60 yaş grupları (her biri 9/74, %12,1) takip etmiştir. Cinsiyete göre değerlendirildiğinde, KE olgularının kadınlarda (46/74,

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%62,2) erkeklere (28/74, %37,83) kıyasla daha yüksek olduğu saptanmıştır. En sık etkilenen organlar karaciğer (24/74, %32,4) ve akciğerler (14/74, %18,9) olmuş, bunu kemik, mesane ve karın boşluğu (3/74, %4,1), böbrek, göğüs (2/74, %2,7), ve diğerleri. takip etmiştir. Ekinokok kistleri, bilgisayarlı tomografi, manyetik rezonans veya ultrason gibi görüntüleme yöntemleri ile tespit edildikten sonra cerrahi müdahale uygulanmıştır. Tüm hastalara cerrahiyi takiben antihelmintik olarak albendazol verilmiştir.

Sonuç: Bu araştırma, KE'nin Pakistan'da sürekli endemik olduğunu ortaya koymaktadır. Halk sağlığı uzmanları ve veteriner hekimlerin KE'yi kontrol altına alma konusundaki bilgi eksikliği ve yetersiz çalışmaları, ülkede hastalığın kontrolünü zorlaştırmaktadır. Bu hastalıkla mücadele için daha fazla araştırma ve etkili kontrol programlarına ihtiyaç vardır.

Anahtar Kelimeler: Kistik ekinokokkoz, hidatik kist, retrospektif, cerrahi, Pakistan

INTRODUCTION

Cystic echinococcosis (CE) is a global zoonotic disease in humans and livestock caused by *Echinococcus granulosus* tapeworms. Globally, CE has been detected in populations on every continent excluding Antarctica, while alvelolar echinococcosis (AE) is confined to the northern hemisphere (1). An estimated 1.2 million people worldwide are affected by human CE, and 1 to 3 million disability-adjusted life years are lost worldwide, although these numbers are probably underestimated (1-3). *E. granulosus* ranked second among the top 8 food-borne parasites of worldwide public health significance in 2012, according to a joint FAO/World Health Organization (WHO) expert committee (4).

The life cycle of parasites involves two mammalian hosts: A definitive canine host in which parasite adult form develops and an intermediate host (domestic and wild ungulates) harboring the larval stage of parasite (5), while humans are accidental and dead-end host of parasite (6). Humans are infected by accidental ingestion of parasite eggs via contaminated food and water (7,8).

Human echinococcosis is a worldwide common disease (9). Among all the species of *Echinococcus*, two are of public health concern: CE caused by *Echinococcus granulosus* sensu lato and *Echinococcus multilocularis*, the causative agent of alveolar echinococcosis, due to their wide distribution and their medical and economic impact (10). *Echinococcus granulosus* s.l. is a cosmopolitan species, as it is widely distributed (1) causing CE echinococcosis in humans, and has a broad range of intermediate hosts (5).

The primary stages of CE are always asymptomatic until complications occur, which depend on the size of the cyst, numbers, localization, and CE stages. Cyst rupture by chance and subsequently cyst contents spilling could be the outcome of secondary infection (11). Disruption of the cysts can be lethal due to anaphylactic shock. *Echinococcus* can infect any organ, but the most common infected organs are the liver and lungs. Other organs like the spleen, kidney, muscles, and bones are less frequently infected by CE (12).

Numerous imaging techniques such as ultrasound (US), radiography, computed tomography (CT), and magnetic resonance imaging (MRI) as well as laboratory testing techniques like antibody, antigen, and cytokine detection are used for CE diagnosis (13). Early detection of CE is very difficult because of the complicated life cycle of *Echinococcus granulosus* and the fact that the disease develops very slowly after infection (14), but there are several factors on which the detection of CE depends. These factors include cyst size, multiple or single cyst, organ that is infected, cyst localization, integrity of the cyst, and immunity of the infected individual (15). Recently, researchers have introduced various techniques for the detection of *Echinococcus* spp. These molecular techniques include nested polymerase chain reaction (PCR), real-time quantitative PCR, multiplex PCR, and nucleic acid isothermal amplification technology (14).

For treatment of CE, percutaneous therapy, surgery, and anti-infective medication are viable alternatives; however, they are image-based, stage-specific methods. In some cases, a wait-and-watch strategy is recommended, based on the cyst's stage (16). In 2003 a standardized ultrasound-based classification for CE was created by WHO Informal Working Group on Echinococcosis, providing visibility of all cyst stages (17). This system further classifies cysts according to clinical groups to aid in treatment options according to stage of disease (e.g., operation, medication, percutaneous, observation) (18). It enables individualized, economical treatment depending on the character of the cyst and the parents features and local conditions. Nevertheless, such a strategy is not used in many endemic countries resulting in non-optimized care and unnecessary health costs (19).

Research assessing CE epidemiology in Central Asia confirmed that *E. granulosus* is a public health concern. Pakistan's economy is primarily based on the animal husbandry, and because of poor hygienic conditions, CE continues to be a health concern for humans (20). Even though echinococcosis is endemic in neighboring countries, there is paucity of information regarding the circulating genotypes of *E. granulosus* in Pakistan (21). Keeping facts about CE in mind, the present study was designed to determine the demographic, epidemiological and pathologic features of human CE cases using patients' hospital-based history from 2012-2023.

METHODS

Study Area

The present retrospective study was conducted in Islamabad, Pakistan. The capital city of Pakistan, Islamabad, is located at 33.43°N 73.04°E, near the base of the Margalla Hills and on the northern edge of the Pothohar Plateau. The entire area of Islamabad city is 906.50 km^2, of which 220.15 km^2 are urban and 466.20 km^2 are rural. It is situated in Pakistan's northern area, which has a subtropical humid climate with cold winters, hot summers, and a monsoon season (22).

Study Duration and Sampling Procedure

A total of 74 clinical reports on human CE were collected from the Pakistan Institute of Medical Sciences (PIMS) hospital located in Islamabad from June 2021 to December 2023. The histopathology department of the hospital postoperatively confirmed the patients' clinical data from 2012 to 2023, which was also included in this investigation. Samples were collected from the hospital with the written informed consent of patients and hospital administration for sample characterization.

The epidemiological (age and gender), histopathological (size, cyst location, number of cysts, macroscopic and microscopic) and treatment data of each patient were retrieved from hospital records. According to the medical records, during CT scans and biopsies examination, only infected organs with cysts were removed from the patient body and preserved in block form (formalin-fixed paraffin-embedded tissue) so that they could be studied further.

Statistical Analysis

All collected data were compiled in a Microsoft 365 Excel database to calculate the frequency of human CE cases. Statistical analysis was performed using SPSS (Version 26.0). Chi-square test (X^2) was used to evaluate the association between different groups and variables. The p-value <0.05 was considered statistically significant.

RESULTS

A total of 74 patients with CE were diagnosed and surgically treated in PIMS hospital, Islamabad during 2012-2023 and their age and gender wise distribution is shown (Figure 1). The clinical data of the CE patients provided the framework for the current findings. The findings showed that a highest number of CE patients were reported in the year 2019 (15/74, 20.2%), followed by 2018 (11/74, 14.9%), 2016 (8/74, 10.8%), 2012 and 2022 (7/74, 9.5%), 2013 and 2015 (5/74, 6.8%), 2017 and 2021 (4/74, 5.4%), 2014 and 2020 (4/74, 5.4%), and 2023 2/74 (2.7%). The statistical analysis showed that CE cases were statistically significant across different study years (Table 1). The highest number of positive cases was recorded in the age group 11-20 (19/74, 25.7%), followed by 31-40 (18/74, 24.3%), 41-50 (9/74, 12.1%), 51-60 (9/74, 12.1%), and 21-30 (7/74, 9.5%) (Figure 2).

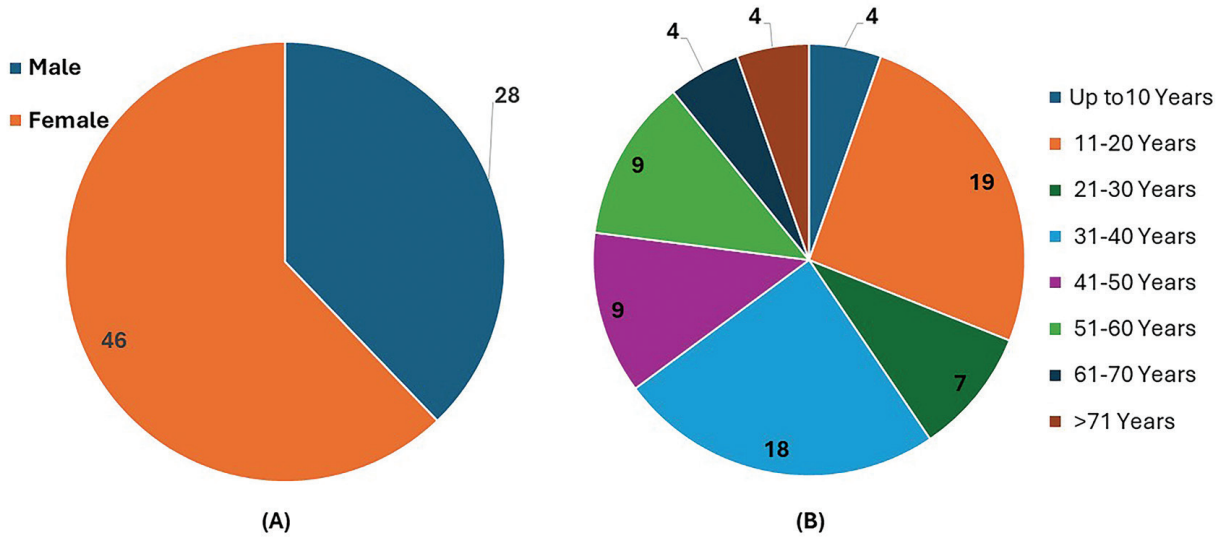

Figure 1 (A, B). Gender and age wise distribution of CE patients
CE: Cystic echinococcosis

Table 1. Year-wise frequency and chi-square analysis of human CE cases in PIMS Hospital, Islamabad, Pakistan

S. no	Year	Total	Frequency (%)	Statistical analysis (X^2)
1	2012	7	9.5	X^2=25.24 df=11 p<0.008
2	2013	5	6.8	
3	2014	3	4.0	
4	2015	5	6.8	
5	2016	8	10.8	
6	2017	4	5.4	
7	2018	11	14.9	
8	2019	15	20.2	
9	2020	3	4.0	
10	2021	4	5.4	
11	2022	7	9.5	
12	2023	2	2.7	

CE: Cystic echinococcosis

The frequency of human hydatid cyst disease was 37.8% in males and 62.2% in females, respectively. The results showed that more CE cases were observed in females (46/74, 62.2%) compared to males (28/74, 37.83%) (Figure 3). Statistical analysis showed there is a significant association between the frequencies of both the genders (Table 2).

In the present study, hydatid cyst disease was observed in different organs. The study showed that in most CE patients, the liver was the most infected organ (24/74, 32.4%), followed by the lungs (14/74, 18.9%), bone, bladder, and abdominal cavity (3/74, 4.1%), kidney, chest (2/74, 2.7%), while others (Table 3, Figure 4). Statistical analysis ($p<0.000$) showed that there is a significant association across different organs (Table 3). With respect to organ involvement, multiple organ involvement was less (19/74, 25.6%), as compared to single organ involvement (55/74, 74.3%). Table 4 shows that most cysts (9/74, 11.0%) had a diameter of less than 4 cm, followed by 7-8 cm (8/74, 11.0%).

Surgery was performed after echinococcal cyst detection by diagnostic imaging methods such as CT, MRI, or US. All patients received albendazole anthelminthic medication after their surgery. Albendazole is usually recommended for CE patients who underwent surgery in Pakistan.

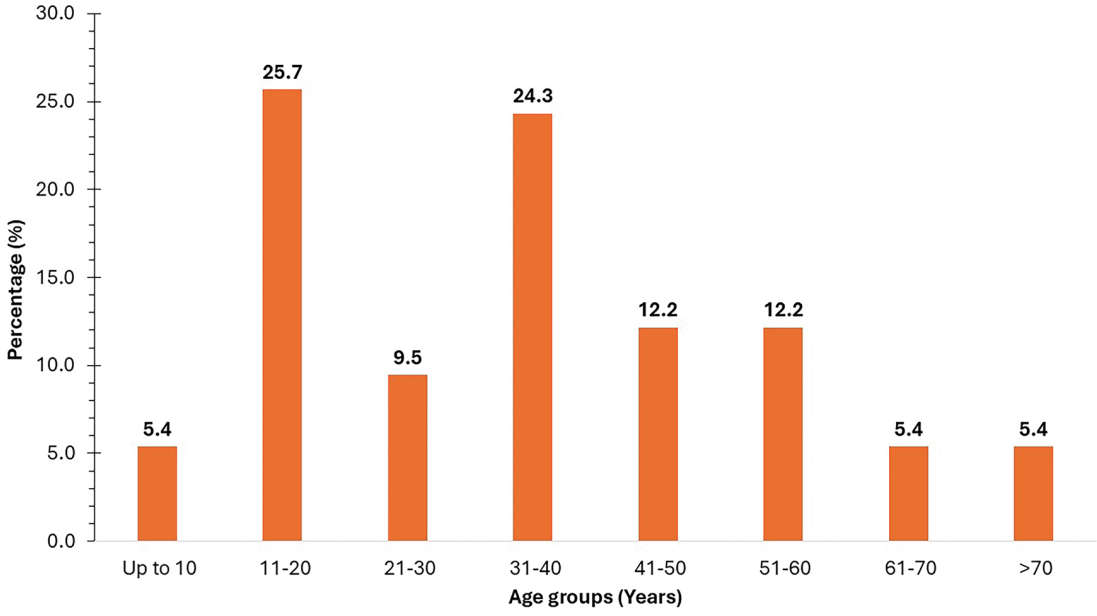

Figure 2. Age wise frequency (%) of human hydatid cyst disease

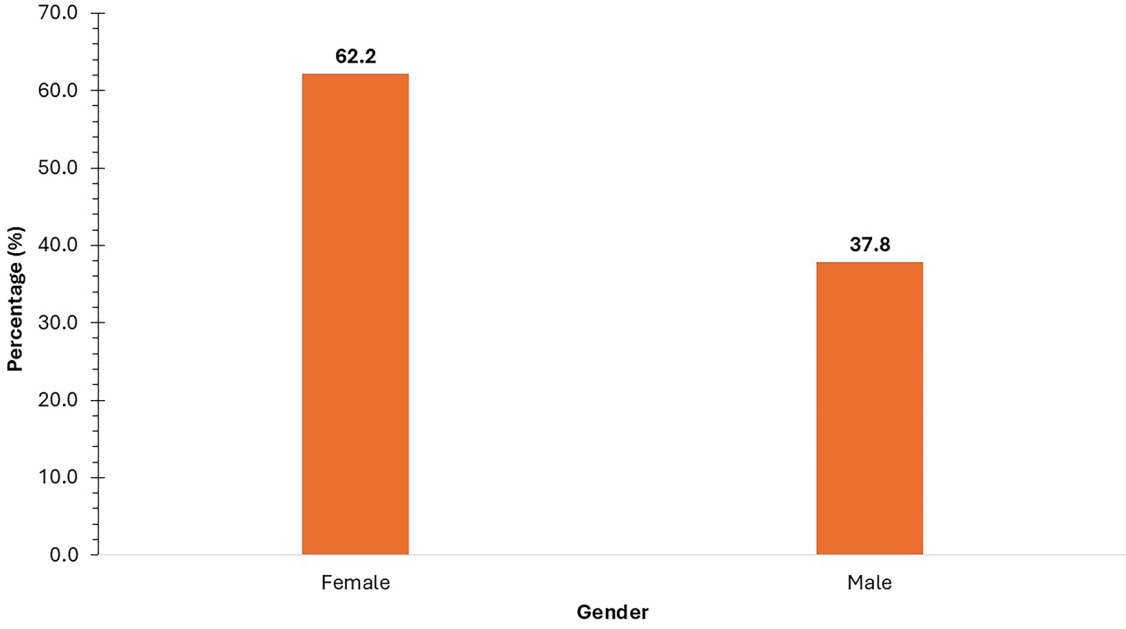

Figure 3. Gender wise frequency (%) of human hydatid cyst disease

Table 2. Gender-wise frequency of human CE cases

S. no	Gender	Total	Frequency (%)	Statistical analysis (x^2)
1	Female	46	62.2	X^2=4.38; df=1; p<0.03
2	Male	28	37.8	

CE: Cystic echinococcosis

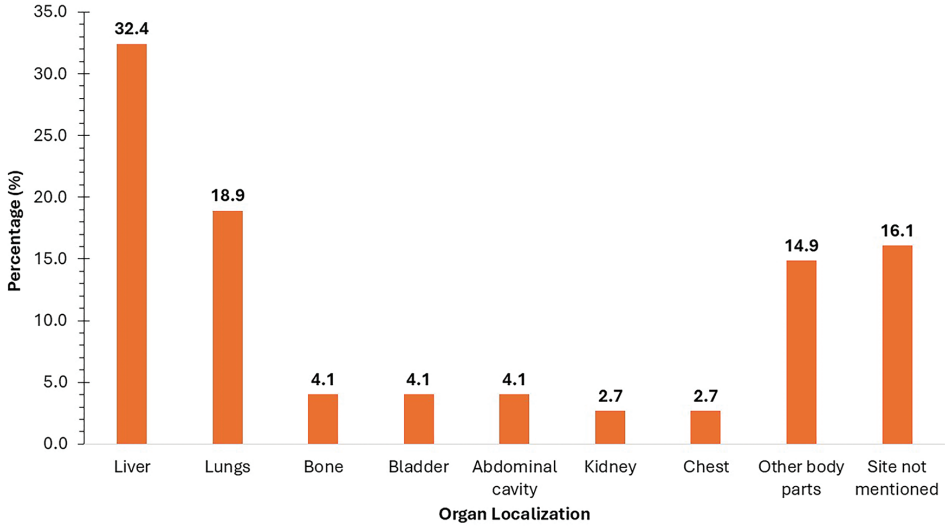

Figure 4. Organ wise localization of human CE cases
CE: Cystic echinococcosis

Table 3. Site of involvement of the cyst

S. no	Organs	Total	Frequency (%)	Statistical analysis (X)
1	Liver	24	32.4	X^2=58.56 df=8 p<0.000
2	Lung	14	18.9	
3	Kidney	2	2.7	
4	Bone	3	4.1	
5	Chest	2	2.7	
6	Bladder	3	4.1	
7	Abdominal cavity	3	4.1	
8	Not mentioned	12	16.1	
9	Others	11	14.9	

Table 4. Size-wise distribution of single and multiple cysts in human hydatid cyst cases

S. no	Size (cm)	Number of cysts		
		Multiple	Single	Total
1	≤4	3 (16.0%)	6. (11.0%)	9 (12.0%)
2	5-6	0 (0%)	5 (9.0%)	5 (7.0%)
3	7-8	1 (5.0%)	7 (13.0%)	8 (11.0%)
4	9-10	1 (5.0%)	3 (5.0%)	4 (5.0%)
5	11-12	1 (5.0%)	2 (4.0%)	3 (4.0%)
6	13-14	0 (0%)	1 (2.0%)	1 (1.0%)
7	15-16	1 (5.0%)	1 (2.0%)	2 (3.0%)
8	17-18	0 (0%)	0 (0%)	0 (0%)
9	19-20	0 (0%)	0 (0%)	0 (0%)
10	≥21	0 (0%)	1 (2.0%)	1 (1.0%)
11	Not mentioned	12 (63.0%)	29 (52.0%)	41 (55.0%)

DISCUSSION

Echinococcosis is a global neglected tropical zoonotic disease that affects both human and animals (23). CE is a rapidly growing global health threat, present in many parts of the world, including Pakistan (11). Better human clinical management, CE control programs, by-product management at slaughterhouses especially disposal of contaminated organs may reduce the infection of *Echinococcus* spp. Even though Pakistan's health care system has experienced major changes and advancements recently, there are still many issues, such as inadequate management, a scarcity of trained staff, and a lack of scrutiny of health policy. Main cause of the CE in animals in Pakistan maybe due to socio-cultural practices like home slaughtering, animals' organs feed to the dogs, not deworming of pets and huge number of stray dogs that may support the transmission of the parasite (24). Such ideal conditions increase the probability of contact and may lead to parasitic infection. Humans can become infected with the disease through the accidental ingestion of parasitic eggs excreted by the faeces of definitive hosts such as dogs, foxes, and other canids (15).

The findings of our study revealed variations in the frequency of human hydatid cysts. The highest number of patients were diagnosed in 2019 (20.2%), followed by 2018 (14.8%). The results in accordance with precious published data reports the similar type of observations with higher CE cases in 2019 followed by 2018 (25). The study showed that the most common age group for CE was 11-20 followed by 31-40 and then 41-50 age group. These findings are consistent with past retrospective research that showed increased rates of CE infections in similar age groups (25-28). This study identified a 5.4% infection rate in children under 10 years old. Variations in the distribution of age groups can be due to the asymptomatic nature of the disease, making diagnosis difficult and challenging.

The findings of the current study showed that the incidence of echinococcosis was higher in the females as compared to males, and these results are consistent with study reported in 2022 in the Khyber Pakhtunkhwa region (25). Same results were observed in previous studies (8,26,27) indicating that male were less affected than females. While our findings are contrary with (24), where CE frequency in females were less than males. Gender disparities and social constraints in the country like Pakistan may have influenced the current study's findings towards females.

In the current study, we examined the frequency of human hydatid cyst disease across several organs. The results revealed that the highest frequency rate was observed in the liver followed by the lungs. These results are concord with many previous studies (25,28). Additionally, rare anatomical sites such as kidneys, chest, bones, bladder, abdominal cavity, and ovaries were reported to be infected in the current investigation. This investigation regarding rare infection sites with an extremely low occurrence rate also correlates with published report (29).

CONCLUSION

CE is a zoonotic and neglected tropical disease that has a high prevalence in Pakistan and poses a serious threat to public health. Although there is a paucity of data on the prevalence of CE in Pakistan, the current retrospective research attracts the consideration to CE as a public health concern. Additionally, medical histories remain usually inadequate, as records are unstructured and lack all CE treated cases in the hospitals. Therefore, the current research serves as an initial step in reducing the information gap regarding CE cases in the capital city, Islamabad, Pakistan. Present study will serve as a baseline for evaluating human CE infection and might help in developing preventative strategies in Pakistan.

*Ethics

Ethics Committee Approval: The Departmental Ethics Review Board (ERB) at the COMSATS University Islamabad (CUI), Pakistan has approved the research under no. CUI/Bio/ERB/2021/43.

Informed Consent: Samples were collected from the hospital with the written informed consent of patients and hospital administration for sample characterization.

Footnotes

*Authorship Contributions

Concept: H.S., H.K., H.A., Design: H.S., H.K., H.A., Data Collection or Processing: H.S., N.K., Analysis or Interpretation: A.K., As.K, G-J.Y., R.M.K.S., Literature Search: H.S., H.K., Writing: H.S., H.K., A.K., As.K, G-J.Y., R.M.K.S., N.K., H.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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