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Cystic Echinococcosis in Children: Addressing Research Needs, Filling Knowledge Gaps

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ABSTRACT

Cystic Echinococcosis (CE) is a common neglected disease in many communities around the world, causing substantial costs on the endemic communities. CE has been considered a disease of adulthood, mostly affecting age groups within 20-59 years. However, CE can be seen in early life even in patients younger than 5 years. While the disease is frequently reported from children in the endemic areas across the globe, children CE is even more neglected and under-represented in the literature. Here we present an overview on this topic, summarizing main features of pediatric CE, current findings, existing knowledge and information gaps and research needs on this issue.

In adults the lungs are involved in less than 30% of CE cases, however in children, pulmonary hydatid disease has been reported to be up to 67%. Different patterns of hydatid cyst and multiple organ involvement have been frequently observed in children, probably due to the immature filtering mechanisms of the liver and lungs during infancy and childhood and the role of intestinal lymphatic channels in dissemination of the parasite. It is believed that children immune system is less responsive to hydatid cysts, therefore serological assays of CE in children are likely to result in more false negative outcomes. As the proportion of internal organs occupied by the cyst is much greater in children than the adult patients, CE in children is more likely to be symptomatic than adults.

Another peculiar aspect of pediatric CE is that the disease has been more frequently observed in boys than girls. According to the data recently published by the European Register of Cystic Echinococcosis the contribution of male patients is more than the females in children and adolescents. While males constitute 65% of the CE patients in 0-9 years age group, the proportion decreased to 50% and 45% in 30-39 and 70-79 years age groups, respectively.

Considerable gaps of knowledge exist in pediatric echinococcosis and further investigations are required on this topic. Major information gaps in children CE include the lack of age-specific data, natural history, detailed clinical picture, clinical trials of non-surgical approaches, genotype data, specific guidelines for diagnosis and treatment and WHO ultrasound classification.

Keywords: Pediatric hydatid disease, Children hydatid cyst, Adolescents, Knowledge gaps

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INTRODUCTION

Cystic Echinococcosis (CE) is a common zoonotic infection in many communities around the world. CE is caused by larval stages of different genotypes within *Echinococcus granulosus* sensu lato. Adult worms of E. granulosus develop in dogs and other carnivores as the definitive hosts excreting eggs in feces to infect sheep and other herbivores as the intermediate hosts. Humans are accidentally infected by food and water contaminated with the parasite eggs. Basically, the parasites reach the liver and lungs through the small intestine and portal veins (1).

The disease is distributed worldwide extending from South America to North Africa, Mediterranean basin, the Middle East, Central Asia and Western China. CE imposes substantial animal and human costs, estimated at 0.01-0.04% of the gross domestic products in different endemic countries (2,3). According to WHO, it is estimated that one million people around the world are suffering from CE. Patients undergoing treatment will have a lower quality of life, with an estimated annual burden of 871000 disability-adjusted life-years with an approximate cost of US$ 3 billion associated with CE including monetary burden for treating patients and livestock-related losses.

Surgery and chemotherapy are the main modalities of CE treatment. However, 6.5% of patients exhibits a relapse of disease after surgery, and 2.2% post-operative death (4,5). Several retrospective studies have been conducted on the recurrence of CE. Findings of recent studies demonstrated the relapse rates of CE ranges from 0-22%. Current evidence indicates that CE recurrence is rather a technical/clinical issue and is not linked to epidemiological variables. A number of factors including incomplete peri-cystectomy, previous complications of the cyst, inadequate treatment, minute spillage of the cyst, a diameter greater than 7 cm, and extrahepatic location are the most important determinants of CE recurrence. CE surgery is not only complicated and should be performed in centers familiar with hepato-thoracic surgery, but also the management of patients with recurrent disease is difficult (6,7).

Cystic echinococcosis in children

CE has been considered a disease of adulthood, mostly affecting age groups within 20-59 years (4). However, CE can be seen in early life even in patients younger than 5 years. The disease is frequently reported from children in the endemic areas around the globe. Nevertheless with the recent influx of immigrants from the Middle East and North Africa to the Europe, CE is being frequently diagnosed in children originating from endemic areas (8,9). Therefore even in European pediatric centers, CE should be suspected in the children with space-occupying lesions in thoracoabdominal cavity.

The incubation period is believed to be at least one year to more than 5 to 15 years (4,5). Therefore, it has been assumed that many people get infected with E. granulosus eggs early in the childhood and the infection usually remains asymptomatic for a long period of time depending on the cyst size and location and may be accidentally diagnosed during routine clinical / paraclinical workups (10).

Specific features of CE in Children

Liver and lungs are the most common organs affected by the parasite, but it should be noted that hydatid cysts can be located in virtually every organ of the body. In adults 60-70% of the cysts are hepatic, and the lungs are involved in less than 30% of CE cases, however in children, pulmonary hydatid disease has been reported to be up to 67% (5,11). In addition many unusual or atypical presentations of CE in children have been published in the literature (12).

Different patterns of hydatid cyst and multiple organ involvement have been frequently observed in children, probably due to the immature filtering mechanisms of the liver and lungs during infancy and childhood, the role of intestinal lymphatic channels in dissemination of the parasite and different epidemiological features of childhood echinococcosis in various endemic countries (12,13). CE growth is believed to be faster in younger individuals, i.e., children and adolescents, and slower in the elderly (5,14). The growth rate of lung CE has been estimated to be at least five-fold higher than liver CE. It is worth noting that, negative pressure, compressible nature and vascularization are reasons for faster growth of the cyst in children lungs (15-18).

It is believed that children immune system is less responsive to hydatid cysts and antibody production is assumed to be lower in children than adults (4). Therefore serological assays of CE in children are likely to result in more false negative outcomes. Although several sero-epidemiological studies have been performed for diagnosis of CE, most serological methods are unreliable due to poor sensitivity and specificity (19). Furthermore, observations indicate that serology demonstrates less sensitivity in pulmonary CE than in liver CE (20).

CE in children is more likely to be symptomatic than adults as the proportion of internal organs occupied by the cyst is much greater in children than the adult patients. This is especially true for pulmonary hydatid cysts in which children present more severe manifestations and higher risk of cyst rupture (11). Therefore in the pediatric age group, low resistance of the lungs to hydatid cysts may result in the expansion and subsequent tension pneumothorax following rapid growth of the cyst. In such cases, to avoid

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further complications early surgical removal of the cyst is advocated (11). Nevertheless, randomized controlled trials are required on different treatment modalities of CE in children as very few studies are available on the surgical and chemotherapeutic management of CE in pediatric settings (21).

Allergic manifestations and anaphylactic reactions are usually observed in the ruptured hydatid cysts. More than 30% of patients with pulmonary CE present with ruptured cysts (11,22,23). Several factors can lead to the rupture by destroying the cyst membranes, e.g., age, anthelmintic treatment, chemical reactions, cyst size, and host immune system (17). The bronchopleural fistula, pneumothorax, pleural thickening, lung collapse, large residual cavity, and empyema are among the complications of pulmonary hydatid cysts ruptured into the pleural or pericardial cavity (24). Running hydatid fluid and cyst membranes into the bronchial tree, can cause suffocation and anaphylactic shock following cyst rupture. Age has been considered as a risk factor for anaphylactic shock in CE, however this warrants further investigations (25).

Another peculiar aspect of pediatric CE is that the disease has been more frequently observed in boys than girls. This is in contrast to the findings of several studies in adult population indicating a slight gender difference towards females (5,26). According to the data recently published by the European Register of Cystic Echinococcosis the contribution of male patients is more than females in children and adolescents and it is gradually declined towards adulthood and elderly (27). While 65% of the patients in 0-9 years age group were boys, the rate decreased to 50% and 45% in 30-39 and 70-79 years age groups, respectively. This is partly because of the fact that in CE endemic countries boys spend more time in outdoor environments and have more chance of contact with dogs and soil, while adult females are more at risk of infection due to the daily activities of food and vegetable preparation and handling livestock. However our knowledge on the nature of echinococcosis in children and adolescents is poor.

Knowledge gaps and research needs

Considerable gaps of knowledge exist in pediatric echinococcosis and further investigations are required on this topic. Figure 1 demonstrated specific features and major research and information gaps regarding CE in children. Unfortunately the literature suffers from shortcomings in reporting CE data in humans. One major defect is the lack of age-specific data on many aspects of human CE. For example in most hospital CE studies, the cyst location has not been specified according to different age groups. Therefore the precise distribution of the organs involved in pediatric CE is not known. Details of the clinical picture of CE in children have not been provided in many studies. Natural history of childhood hydatid cysts is not clear and reporting hydatid cyst stage according to WHO ultrasound classification of cystic echinococcosis in children and adolescents is almost absent in the literature.

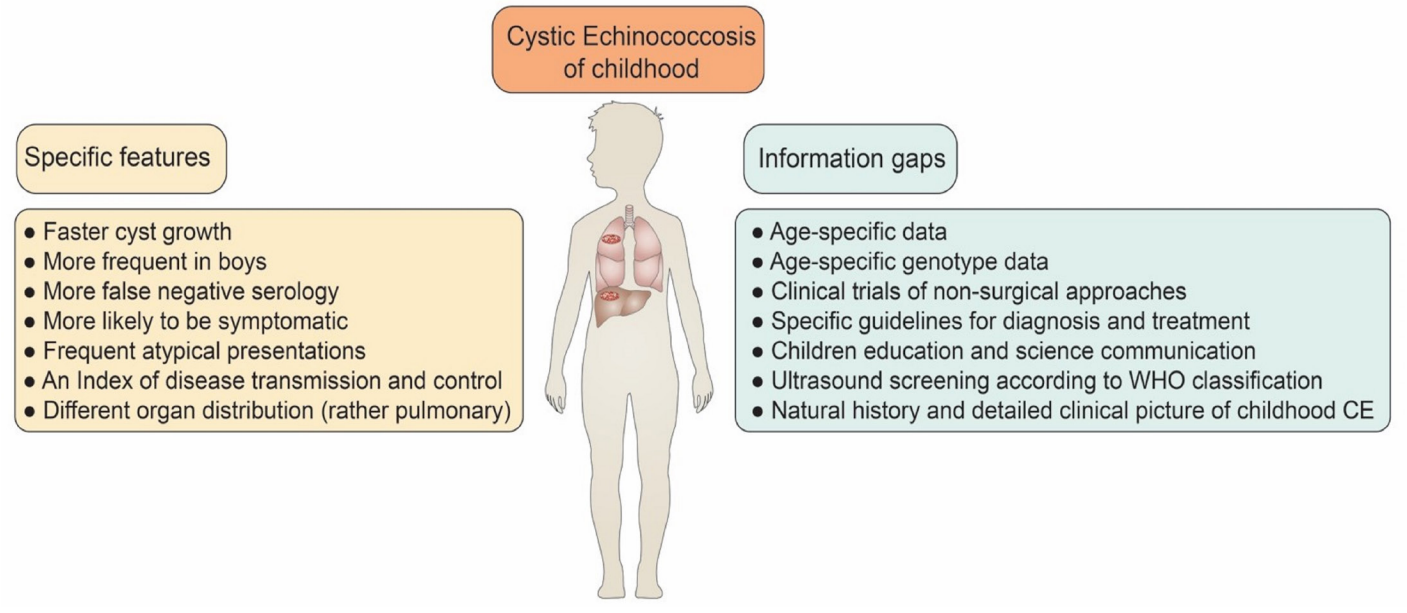

Figure 1. Cystic Echinococcosis of childhood: specific features and major research and information gaps

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Unfortunately dozens of research papers on the molecular epidemiology of CE did not report age-specific genotype data, therefore understanding differential contribution of E. granulosus genotypes in the adults and children CE is not possible. Specific guidelines for the diagnosis and management of CE in children have not been developed, consequently in the absence of relevant clinical trials, the outcomes of particular interventions as well as the pros and cons of various diagnostic and therapeutic approaches have not been clearly demonstrated.

Regarding the long incubation period and the slow growth of hydatid cysts in human, occurrence of CE in adults can indicate an infection acquired in the distant past, while the incidence of CE in children is indicative of active parasite transmission, and this can be epidemiologically important (28). Therefore the incidence of cystic echinococcosis in children is an important indication of active recent disease transmission in the endemic communities. Frequency of CE in children reflects the recent changes of disease transmission in endemic regions and is an essential indicator for measuring the success of CE control programs. (29).

CE is a neglected tropical disease (NTD) and its control clearly deserves further attention in the endemic regions. Thereby, the need for elaboration of specific strategies and measures for CE control is becoming apparent in endemic regions (30). Dog deworming, livestock vaccination and public/professional education are the main tools of CE control. Children as a target population, play a pivotal role in improving public awareness and hand hygiene of the endemic communities. An effective public education program using mass media communication with available digital / non-digital tools can be achieved via both families and the schools (29).

Lack of detailed epidemiological data on children CE is a pitfall for control programs. To resolve this issue, CE registry systems, reliable national surveillance and community-based ultrasound screening are of paramount importance for providing reliable data regarding children CE (27). A successful control plan needs commitment and coordination of national bodies under a One Health / One Medicine approach.

CONCLUSION

Cystic echinococcosis is a common but neglected disease in pediatric settings in CE endemic countries. The disease is frequently reported from children in the endemic areas around the world. Substantial gaps of knowledge exist in pediatric echinococcosis. Lack of age-specific data, detailed clinical picture of CE in children, lack of age-specific genotype data, unclear natural history of childhood hydatid cysts and under reporting WHO ultrasound classification of cystic echinococcosis in children are among the major information gaps for understanding CE features in children. As CE in children is an important indication of disease transmission dynamics and endemicity in endemic regions, further specific studies on children CE and increased pediatric research activities are required for implementing a successful control program.

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REFERENCES

1. Thompson RCA. Biology and systematics of Echinococcus. Adv Parasitol. 2017;95:65-109.
2. Deplazes P, Rinaldi L, Rojas CAA, et al. Global distribution of alveolar and cystic echinococcosis. Adv Parasitol. 2017;95:315–493.
3. Borhani M, Fathi S, Lahmar S, et al. Cystic echinococcosis in the Eastern Mediterranean region: Neglected and prevailing! PLoS Negl Trop Dis. 2020;14:e0008114.
4. Pawlowski ZS, Eckert J, Vuitton DA, et al. Echinococosis in Humans: clinical aspects, diagnosis, and treatment. In: Eckert J, Gemmell, MA, Meslin FX, Pawlowski ZS. (Eds.), Manual on Echinococcosis in Humans and Animals: A Public Health Problem of Global Concern. World Health Organization for Animal Health and World Health Organization (OIE/WHO), Paris, 2001:20-66.
5. Kern P, Da Silva AM, Akhan O, et al. The echinococcoses: diagnosis, clinical management and burden of disease. Adv Parasitol. 2017;96:259-369.
6. Jaén-torrejimeno I, López-guerra D, Prada-villaverde A, Blanco-fernández G. Pattern of relapse in hepatic hydatidosis : Analysis of 238 cases in a single hospital. J Gastrointest Surg. 2020;24:361–7.
7. Prousalidis J, Kosmidis C, Anthimidis G, et al. Postoperative recurrence of cystic hydatidosis. Can J Surg. 2012;55:15.
8. Vázquez-Pérez Á, Santos-Pérez JL. Cystic echinococcosis in a Moroccan boy: a silent and neglected disease among refugee and migrant children. BMC Glubal Heal. 2022;15:e246399.
9. Richter J, Esmann L, Lindner AK, et al. Cystic echinococcosis in unaccompanied minor refugees from Afghanistan and the Middle East to Germany,

International Journal of Echinococcoses 2022;1(2):49-53
DOI: 10.5455/IJE.2022.02.03

July 2016 through June 2017. Eur J Epidemiol. 2019;34:611–2.

10. Todorov T, Boeva V. Echinococcosis in children and adolescents in Bulgaria: a comparative study. Ann Trop Med Parasitol. 2000;94:135–44.
11. Balci AE, Eren N, Eren Ş, Ülkü R. Ruptured hydatid cysts of the lung in children: Clinical review and results of surgery. Ann Thorac Surg. 2002;74:889–92.
12. Gupta R, Sharma SB, Prabhakar G, Mathur P. Hydatid disease in children: our experience. Formos J Surg. 2014;47:211–20.
13. Mohammadi M, Mamishi S, Pourakbari B, et al. Cystic echinococcosis in children: high frequency of multiple organ involvement in North of Iran. Infect Disord Drug Targets. 2020;21:125–9.
14. Romig T, Zeyhle E, Macpherson CNL, et al. Cyst growth and spontaneous cure in hydatid disease. Lancet. 1986;327:861–2.
15. Santivanez S, Garcia HH. Pulmonary cystic echinococcosis. Curr Opin Pulm Med. 2010;16:257–61.
16. Gottstein B. Hydatid lung disease (echinococcosis / hydatidosis). Clin Chest Med. 2002;23:397–408.
17. Goussard P, Eber E, Mfingwana L, et al. Paediatric pulmonary echinococcosis: A neglected disease. Paediatric Respiratory Reviews. 2021; Available from: https://doi.org/10.1016/j.prrv.2021.11.001
18. Durhan G, An A, Ardal S, et al. Radiological manifestations of thoracic hydatid cysts : pulmonary and extrapulmonary findings. Insights Imaging. 2020;11:1–11.
19. Borhani M, Fathi S, Darabi E, et al. Echinococcoses in Iran, Turkey, and Pakistan: Old Diseases in the New Millennium. Clin Microbiol Rev. 2021;34:e00290-20.
20. Herna A, Muro A, Barrera I, Ramos G. Usefulness of four different *echinococcus granulosus* recombinant antigens for serodiagnosis of Unilocular Hydatid Disease (UHD) and Postsurgical Follow-Up of Patients Treated for UHD. Clin Vaccine Immunol. 2008;15:147–53.
21. Rees CA, Hotez PJ, Monuteaux MC, et al. Neglected tropical diseases in children: An assessment of gaps in research prioritization. PLoS Negl Trop Dis. 2019;13:1–14.
22. Hamouri S, Odat H, Syaj S, et al. Rupture of pulmonary hydatid cyst in pediatrics : A cross-sectional study. Ann Med Surg [Internet]. 2021;62(January):31–6. Available from: https://doi.org/10.1016/j.amsu.2021.01.001
23. Aytaç A, Yurdakul Y, Ikizler C, et al. Pulmonary Hydatid Disease: Report of 100 Patients. Ann Thorac Surg. 1977;23:145–51.
24. Haghighi L, Rahimi M, Behniafar H, et al. A Challenging Diagnosis of Two Ruptured and Intact Pulmonary Echinococcal Cysts in a 54-Year-Old Woman: A Case Report. Acta Parasitologica. 2021;66:1605-8.
25. Ye J, Zhang Q, Xuan Y, et al. Factors associated with echinococcosis-induced perioperative anaphylactic shock. Korean J Parasitol. 2016;54:769–75.
26. Şenyüz OF, Celayir AC, Kiliç N, et al. Hydatid disease of the liver in childhood. Pediatr Surg Int. 1999;15:217–20.
27. Rossi P, Tamarozzi F, Galati F, et al. The European Register of Cystic Echinococcosis, ERCE: State-of-the-art five years after its launch. Parasites and Vectors. 2020;13:1–10.
28. Yang YR, Craig PS, Vuitton DA, et al. Children serology of echinococcosis infection as an environmental health indicator to guide preventive activities in Ningxia, PR China. Am Soc Trop Med Hyg. 2007;77:21.
29. Larrieu E, Gavidia CM, Lightowlers MW. Control of cystic echinococcosis: Background and prospects. Zoonoses Public Health. 2019;66:889-99.
30. World Health Organization. Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030. Available from: https://www.who.int/publications/i/item/9789240010352