Poverty-associated emerging infection of Cystic Echinococcosis in population of Northern Pakistan: A hospital based study

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Abstract. Cystic Echinococcosis (CE) is one of the most important zoonotic parasitic diseases in human, livestock, and wildlife globally. The prevalence of CE depends upon human behavioral risk factors, the diversity and ecology of animal host interactions and the genetic diversity within Echinococcus species which differ in their zoonotic potential and pathogenicity. It is a neglected, economic and socio-cultural problem in Pakistan. The available data about the incidence of CE is very limited and no extensive study has been reported in Pakistan. The current study was aimed to analyze the hospital reported cases of CE and the associated risk factors related to the incidence of CE. The hospital-based data of CE for the time period of January 2012-December 2017 was collected from Islamabad, Rawalpindi and Peshawar. The data covered demographic characteristics including age, gender, and cyst localization of infected individuals and socioeconomic determinants. The data was analyzed based upon different risk factors along with the different socioeconomic parameters that has an important impact on the distribution of disease. A total of 228 cases were presented in the selected hospitals of different cities during the study period. Out of total 228 patients, 59.21% were males and 40.78% were females (P<0.001). Most infections have been recorded in young adults (>20-30) showing 22.8% of total infected individuals followed by children (0-10) showing 10.5% (n=24), respectively (P<0.001). Liver was the most vulnerable organ (58.77%, n=134) followed by lungs (14.47%, n=33) (P<0.001). The infection was higher among rural communities (84.2%) than urban (12.8%) (P<0.001). Socioeconomic and demographic factors had an important impact on the intensity of disease (P<0.001). The occurrence of cases in children and young adults was an important finding as it indicated an active transmission of the parasite in Pakistan along with the poverty index. Emergence of echinococcosis in Pakistan showed that emerging health issues in Pakistan could bring the disease to limelight for future research. This finding, together with the fact that 1 hospital reported 214 cases over 6 years
underlines the need for a program for prevention/control of this disease in Pakistan. The timely measure needs to be taken to hamper the disease development and establishment. In order to control the disease, complete surveillance should be done which in turn weighs down the disease progress.

INTRODUCTION

Echinococcosis is considered as the neglected tropical zoonotic disease. The cestodes of *Echinococcus* in adult and larval stages are the causative agents of the disease. Members of *E. granulosus* species complex include *E. granulosus* sensu stricto, *E. felidis*, *E. equinus*, *E. ortleppi* and *E. canadensis* (Nakao *et al.*, 2007; Hüttner *et al.*, 2008). *E. equinus* and *E. felidis* have not been shown to have zoonotic potential. All remaining members of *E. granulosus* are reported as causative agents of human Cystic Echinococcosis (CE) and hydatidosis in livestock animals (Romig *et al.*, 2015).

During the life cycle of *E. granulosus*, dogs serve as definitive hosts while ungulates (e.g. sheep) are intermediate hosts. Infection occurs through the ingestion of the tapeworm eggs that develop into fluid-filled larvae primarily in the liver and lungs of livestock animals and humans. Although infection can occur in any organ of the intermediate host, liver and lungs are most commonly affected. The parasite completes its life cycle among two hosts which are of medical and public health importance. Humans are an accidental host for the disease and the parasite enters human after the ingestion of parasitic eggs or via direct interaction with definitive hosts (McManus *et al.*, 2003). The hatching of ingested eggs occurs in small intestine of humans and larvae can move to any organ of the body. After the larval development, cysts are formed and can lead to symptomatic and asymptomatic conditions (Eckert *et al.*, 2004).

Echinococcosis is endemic in Asia (Ito *et al.*, 2017). The annual incidence of CE can range from less than 1 to 200 per 100,000 inhabitants in various endemic areas (Pawlowski *et al.*, 2001). In China and Central Asia, more than 20 million people are at risk (Craig *et al.*, 2007). Mortality rate (about 2-4%) from CE is low but it may increase considerably if medical treatment and care is inadequate (Pawlowski *et al.*, 2001). Low annual incidence rate of alveolar echinococcosis (AE) is generally reported in most of the endemic areas (0.03-1.2 per 100,000 inhabitants) but in untreated or inadequately treated patients mortality is more than 90% within 10/15 years of diagnosis (Pawlowski *et al.*, 2007; Craig *et al.*, 2007; Ammann *et al.*, 2004).

The disease is initially diagnosed through ultrasonography and then referred for pathological and serological examination. Diagnosis and classification of CE was made using portable ultrasound according to the criteria proposed by World Health Organization Informal Working Group on Echinococcosis for CE (Pawlowski *et al.*, 2001). On the basis of conformational features of cysts, CE lesions (primarily in the liver) were differentiated into 6 types including CL, CE1, CE2, CE3, CE4, and CE5. In general, the CL type refers to a cystic lesion without clear rim indicating the parasite is at an early stage of development if the cyst is of a parasitic origin, while the presence of CE1 or CE2 is suggestive of active stages of the disease, while CE3 suggests the parasite is at a transitional stage, and CE4 or CE5 implies an involution, necrotic or inactive parasite (Pawlowski *et al.*, 2001).

Ultrasound is the gold-standard screening test, whilst computed tomography has a role in emergency presentations and screening for multi-organ involvement. Magnetic resonance imaging is the preferred second-line imaging and demonstrates biliary involvement in a better way. Medical therapy or PAIR (percutaneous aspiration, irrigation with scolicide and re-aspiration) may be appropriate in selected cases; however, surgery remains the definitive treatment for active, large (>5cm), symptomatic or complicated cysts. A variety of surgical techniques have been described, including conservative, radical and minimally invasive
procedures. There is currently no consensus approach; surgical modality should be tailored to patient factors, relevant anatomy, local facilities and surgeons’ expertise (Keong et al., 2017).

Surgery procedures are followed for the removal of cysts. Histopathological examination identifies morphological, microscopic and macroscopic characteristics of cysts along with formation of protoscoleces. The treatment of CE can be carried out through surgical procedures and chemotherapy. The treatment efficacy depends upon various disease characteristics such as cyst size, viability, rupturing of the cyst and many more. Chemotherapy is mostly done with benzimidazoles, albendazole, mebendazole and praziquantel (Nakao et al., 2001). Praziquantel (PZQ) was proposed to be used alongside with benzimidazoles in CE-patients. PZQ exhibited a high efficacy against protoscoleces and metacestodes in animal experiments (Urrea-Paris et al., 1999, 2001).

Only 13 cases have been reported from 1980-2015 based on published data from different areas of Pakistan (Ahmed et al., 2001). So the disease is neglected and published reports are limited from all over the country. To the best of our knowledge, there is no comprehensive study regarding the epidemiological and molecular genotyping of human CE in Pakistan. There is urgent need of a comprehensive survey to determine the incidence rate of CE. Therefore, current study aimed to analyze the incidence of CE in Pakistan. Histopathological reports of hydatid cysts from different hospitals were collected which depicted the emerging trend of disease in Pakistan.

MATERIAL AND METHODS

Study area
The included study sites have diverse environmental conditions and different population size. According to recent census of Pakistan, the population of Islamabad is 2,006,572 with 991,747 in rural area located at 33.43°N 73.04°E in latitude and longitude coordinates. The population of Rawalpindi is 10,007,821 with 6,004,157 in a rural area at 33.6°N 73.05°E. The population of Peshawar is 4269,079 with 2,299,037 in a rural area at 34°012N 71°352E (GOP, 2017-18). Main hospitals in the area were selected for collecting reported cyst data.

Data collection
The collected data was retrospective, from selected hospitals of three different cities, Islamabad, Rawalpindi and Peshawar. Islamabad, the capital of Pakistan located on Pothohar Plateau is inhabited by people from different areas of the country. Rawalpindi and Islamabad are considered as twin cities with no distinct boundary. Pakistan Institute of Medical Sciences, Islamabad (PIMS) and Armed Forces Institute of Pathology, Rawalpindi (AFIP) are the tertiary referral hospitals of twin cities and institutions for medical research. Peshawar is the capital of Khyber Pakhtunkhwa province, inhabited with local people along with Afghan refugees. Rehman Medical Institute (RMI), Peshawar provides surgical services with standard diagnostic facilities to rare and complex diseases.

Demography and Socioeconomic data
Various factors associated with disease were analyzed as potential risks for the disease prevalence, including living standard, hygienic conditions, association with dogs, slaughterhouses, butcher shops, peoples age, gender, and occupation. Migration of the individuals from rural to urban areas is also considered as one of the factors for disease transmission.

Histopathological Findings
Histopathological details of cysts including cyst size, number, nature, and location were also collected.

Study Duration and Human CE Cases
The current retrospective study analyzes the data from January 2012-December 2017. The data for surgery-confirmed cases of human CE were collected from different hospitals including AFIP, PIMS, RMI and CITI Laboratory.
Ethics Statement
The study was approved by the institutional review board under ERB/18/72. The consent to participate in the study was taken from each patient.

Statistical Analysis
The data were evaluated by SPSS 18.0 programme using of Pearson’s Chi square test.

RESULTS

Disease origin
The infected individuals had different occupational modes, most of them acquired disease through contact with infected animals. The infected individuals were interviewed and it was found that they had a close association with livestock animals/dogs before the onset of disease. The stray dogs were not treated with any anthelmintic drugs in the studied area reflecting a potential risk favoring the active transmission of parasite. In the present study, open slaughtering and stray dogs were common in the diseased area. Most of patients lived in underdeveloped areas with poor living conditions. Most of them had no access to clean water and proper sanitation. Therefore, direct contact and lack of animal healthcare became one of the leading cause of disease.

Socioeconomic status
The source of infection for inhabitants in Pothohar Plateau may mostly be stray dogs and other wildlife that consumed infected livestock organs and dog faeces, hence becoming a major source of infection to human. The poverty trend in Pakistan showed that low income and sub-standard poor living conditions contributed significantly in increasing the disease burden (Table 1).

Migration and Nationality
Migration might be one of the important factors that has a major role in the spread of CE in Pakistan especially from rural to urban areas. In Peshawar, 5 out of 228 patients were Afghan immigrants (2.19%), reflecting the transmission of disease from Afghanistan to Pakistan. The migration of individuals from rural to urban areas is also one of the major factors for disease spread (Table 2).

Case distribution
The present study showed an increasing trend of cases diagnosed as hydatid cysts. Our findings indicated that the most number of reported hydatid cyst cases were in 2016 (n=60 followed by 2014 (n=55), 2013 (n=47), 2015 (n=45), respectively while the least number of cases were in 2017 (n=13) and 2012 (n=8), respectively (Fig. 1). These findings clearly indicated the emergence of CE in Pakistan because in past, only a few

Table 1. Trends in poverty incidence and estimated poverty lines (2015-2016)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Pakistan</td>
<td>23</td>
<td>28(2.4)</td>
<td>30(3.6)</td>
<td>33(3.3)</td>
<td>30(-3.0)</td>
<td>38(4.4)</td>
<td>38(0.0)</td>
</tr>
<tr>
<td>Urban</td>
<td>19</td>
<td>25(3.5)</td>
<td>25(0.0)</td>
<td>30(6.7)</td>
<td>28(-2.2)</td>
<td>34(3.6)</td>
<td>32(1.2)</td>
</tr>
<tr>
<td>Rural</td>
<td>26</td>
<td>30(1.7)</td>
<td>32(3.3)</td>
<td>35(3.1)</td>
<td>31(-5.8)</td>
<td>39(4.3)</td>
<td>41(1.0)</td>
</tr>
</tbody>
</table>

Source: Latest estimates are based on HIES 2015-16. The poverty incidences for other years are taken from Jamal (2013). Consistent methodology and calorie norms are applied for all years. ** In order to ease in interpretation, minimum calorie requirements & converted into per capita term using household demographic data & proportionate minimum requirements. The minimum requirements by age & sex are available in Food Consumption Table for Pakistan (GOP, 2001). Source: Estimated from household level data of HIES, 2015-16.
Table 2. Incidence of human CE and relation with some risk factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Risk Factors</th>
<th>Positive (n)</th>
<th>Positive (%)</th>
<th>Statistical Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Rural</td>
<td>192</td>
<td>84.2</td>
<td>$X^2= 213.47$  $P&lt;0.001$</td>
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<tr>
<td></td>
<td>Urban</td>
<td>36</td>
<td>15.8</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>93</td>
<td>40.8</td>
<td>$X^2=15.47$  $P&lt;0.001$</td>
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<tr>
<td></td>
<td>Male</td>
<td>135</td>
<td>59.2</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0-10</td>
<td>24$^a$</td>
<td>10.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;10-20</td>
<td>6$^c$</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;20-30</td>
<td>52$^a$</td>
<td>22.8</td>
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<td></td>
<td>&gt;30-40</td>
<td>39$^a$</td>
<td>17.1</td>
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</tr>
<tr>
<td></td>
<td>&gt;40-50</td>
<td>48$^a$</td>
<td>21.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;50-60</td>
<td>42$^a$</td>
<td>18.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;60-70</td>
<td>17$^b$</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Punjabi</td>
<td>213</td>
<td>93.4</td>
<td>$X^2=343.89$  $P&lt;0.001$</td>
</tr>
<tr>
<td></td>
<td>Pathan</td>
<td>15</td>
<td>6.6</td>
<td></td>
</tr>
<tr>
<td>Nationality</td>
<td>Pakistani</td>
<td>223</td>
<td>97.8</td>
<td>$X^2=416.87$  $P&lt;0.001$</td>
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<tr>
<td></td>
<td>Afghani</td>
<td>5</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td>Butcher</td>
<td>26$^c$</td>
<td>11.4</td>
<td>$X^2=176.68$  $P&lt;0.001$</td>
</tr>
<tr>
<td></td>
<td>Farmer</td>
<td>50$^b$</td>
<td>21.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>152$^a$</td>
<td>66.6</td>
<td></td>
</tr>
<tr>
<td>Organ Localization</td>
<td>Liver</td>
<td>134$^a$</td>
<td>58.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lung</td>
<td>33$^b$</td>
<td>14.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spleen</td>
<td>11$^c$</td>
<td>4.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Orbit</td>
<td>6$^d$</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatogastric</td>
<td>3$^d$</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Testicular</td>
<td>1$^d$</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pancreas</td>
<td>3$^d$</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ovarian</td>
<td>1$^d$</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Thigh</td>
<td>1$^d$</td>
<td>0.4</td>
<td>$X^2=1324.43$  $P&lt;0.001$</td>
</tr>
<tr>
<td></td>
<td>Renal tissue</td>
<td>2$^d$</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chest wall</td>
<td>1$^d$</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pelvis</td>
<td>3$^d$</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sinus tract</td>
<td>1$^d$</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Retroperitoneal</td>
<td>2$^d$</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peritoneal Cavity</td>
<td>2$^d$</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Uterus</td>
<td>1$^d$</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NOS</td>
<td>23$^b$</td>
<td>10.1</td>
<td></td>
</tr>
</tbody>
</table>

*: a,b,c,d: The difference between the different letters in the same column is statistically significant.

Case reports were available from hospitals. In the present study, majority of cases belonged to AFIP. It might be due to better diagnostic and surgery facilities in the AFIP hospital and secondly the majority of people from Rawalpindi district are concerned with agriculture especially in rural areas with poor hygienic conditions favoring the onset of disease.

Different organs were reported to be affected by the disease. Of all the cases 58.7% (n=134) cysts were in liver, 14.4% (n=33) in lungs, 4.8% (n=11) in spleen, 2.6% (n=5) in orbit and various other organs as presented in Table 2.

**Socio-demographic aspects**
The study area was comprised of both rural and urban population. According to most recent census, 2017, of Pakistan, 49.42% population of Islamabad, 59.99% of Rawalpindi and 53.85% of Peshawar comes from rural areas. Among the 228 cases, 192 cases were from rural areas with 51.75% males and 32.45% females while 36 cases were from urban areas consisting of 7.45% males and 8.33% females. Within the gender wise distribution, of the 228 patients, 59.2% were males and 40.8% were females. Different age groups showed differential number of cases. It was found that the highest number
of individuals infected with CE were under the age group >20-30 with 22.8%. The young ones are more associated with livestock and dogs and might have more chance to get infected with *E. granulosus*. The age group >10-20 years was least infected with 2.6% of the total patients. Surprisingly, total of 24 cases (10.5%) were children with age 0-10, indicating children were also vulnerable to hydatid cyst infection (Table 2).

**Role of occupation and ethnicity in disease susceptibility**

The echinococcosis cases identified in the present study were from two major ethnicities of Pakistan. Among studied cases, 15 individuals (6.6%) were Pathan and 213 (93.4%) were Punjabi. The infected individuals were associated with different occupations. Out of 228, the first two most vulnerable occupations were farmer (n=50, 21.9%) and butcher (n=26, 11.4%). Other 152 individuals (66.66%) had different professions (Table 2).

**DISCUSSION**

The ubiquitous nature of CE made the disease endemic to certain regions with approximately 270 million people (58% of the total population) at risk of CE in Central Asia including areas of Turkmenistan, Kyrgyzstan, Kazakhstan, Mongolia, Tajikistan, Afghanistan, Uzbekistan, Iran, Pakistan and Western China (Zhang *et al.*, 2015). Lack of data was reported for the epidemiological status and actual prevalence of CE in Pakistan. To the best of our knowledge, from 1980 to 2015, only three reports based on prevalence data and 13 case reports on CE in humans were reported from 1980-2015. Such a lack of research on CE in Pakistan greatly underestimates the real status of this serious NTD in Pakistan (Ahmed *et al.*, 2017).

The current analysis included selected hospitals from three different cities of Islamabad, Rawalpindi, and Peshawar in Pakistan. These three cities have a different range of population and geographical conditions. These cities have a significant population of stray dogs and other wildlife. The slaughterhouses and butcher shops in these areas have frequently reported the presence of stray dogs which act as a major mean of CE transmission. Unhygienic conditions and poor waste management creates environment for the transmission of CE to humans. Dogs are the definitive hosts for *Echinococcus* spp. The dogs are infected when fed with offals of livestock infected with hydatid cysts, usually dumped by butchers around slaughterhouses. The cysts are developed into adult cestode in Figure 1. Year-wise trend of hydatid cyst disease in the study area.
the intestine of dogs and eggs are passed through feces to the environment to infect intermediate hosts such as livestock and humans. The whole life cycle is perfectly completed in the endemic areas which contain evil cycle of dogs and livestock. Humans become vulnerable for infection of cysts due to unhygienic life style, interaction with dogs and other potential risk factors for the spread of disease to humans. Similar observations were reported by Ahmed et al. (2017) and Khan et al. (2018a, 2018b, 2018c).

Risk factors for CE include previous episodes of echinococcosis, occupational and domestic exposure to dogs and travel to or from endemic areas (Keong et al., 2017). The infected individuals belong to different occupations including butchers, farmers, and other professions, most of them acquire disease through contact with *E. granulosus* eggs. The butcher shops having stray dogs may be infected with *E. granulosus* and their feces near vicinity serve as an important risk factor of disease spread. The farmers are also in direct contact with the dog’s feces. Individuals with professions other than farming and meat slaughtering got infection either by eating contaminated vegetables or by interaction with infected dogs.

In Pakistan, the life style in rural areas is a major risk factor for disease transmission. Humans and animals share the same residence boundary which makes the person more susceptible to infection. Home slaughtering in rural areas is also a common practice that usually disposes of the infected body parts of animals to the surroundings thus increasing the chance of infection to the neighboring inhabitants and dogs. Rural area population is in direct contact with dogs which are main hosts for *E. granulosus*. The infected individuals from urban areas are usually from the region surrounded by butcher shops. Improper disposal of animal waste and dogs fed with infected organs at butcher shops increase the chance of infection in humans. Living standards are usually poor in rural areas and near by vicinities of urban areas. In most of the rural areas of Pakistan, wastes are disposed of openly. Even in the urban areas of Pakistan, sanitary conditions are very poor. Besides, knowledge and awareness regarding the disease is insufficient in the population in endemic areas. All these factors attribute to the transmission of CE among the inhabitants in these study areas. These risk factors also include contact with infected animals, association to dogs, unhygienic living conditions, improper sanitary conditions, slaughtering at home, feeding dogs with infected animal organs. Similar observations were reported by Ahmed et al. (2017).

According to Pakistan Economic Survey, poverty estimate for the year 2013-2014 accounted as 29.5% at national level; 18.2% for urban area and 35.6% for rural area with 51% intensity of deprivation. During 2015-2016, 38% population has been declared poor with 41% incidence in rural and 32% urban areas. Educational quality is weighed at 1/24th (4.17%), school going individuals weighted at 16.66% of total population. Only 1/6th of the population receives quality health care facilities. For living conditions, only 4.76% of households had access to clean water, proper sanitation, electricity, and cooking fuel. Livestock keeping is the occupation of major chunk (55.84%) of population (GOP, 2017).

In present retrospective study, increased trend of human CE cases was observed from 2012 to 2017. The increased prevalence of *E. granulosus* infection has been confirmed in livestock (Mustafa et al., 2015; Latif et al., 2010), but the direct link of increase in disease burden in humans is not established yet. There are only three studies from Pakistan, reporting the genotyping of Echinococcus spp. in human and livestock (Khan et al., 2018) reported *E. granulosus* and *E. multilocularis*. Increased infection rate in livestock by *E. granulosus* could be the reason for emergence of human CE. Various environmental factors can also be responsible for disease transmission. The shift between rural and urban area population and migration of population can also contribute to the spread of disease to unaffected areas. Due to excessive traveling, neglected tropical diseases endemic in developing countries are now crossing borders to developed countries. The spread
of diseases from developing to developed countries highlights the seriousness of this public health issue globally. The rural and highly populated areas of urban regions are origin sites of the disease due to the poor hygienic conditions.

In present study, males had increased positive infection rate (59.21%) than females (40.78%). These findings were in concordance to Sharma et al. (2013) where more males were infected (59.37%) than females (40.62%) and in contrast to the Gadahi et al. (2001) with more females (68.18%) getting infected than males (31.81%). Aksu et al. (2013) and Torgerson et al. (2003) also reported more cases of human CE in males than females. The accurate reason for this diverging trend is not clear, possibly because males have more chance of working with sick animals and getting in contact with infected dogs than women during daily routine.

The present results showed age-based distribution of human CE, where the number of reported cases in age group >20-30 years were highest (22.80%) followed by age group >40-50 (21.05%). Similar observations were reported as 50% cases with age group 20-40 years (Gadahi et al., 2001), and in another study, 10 out of 32 cases with cysts were observed for age group >20-30 years (Sharma et al., 2013). Difference in age dependent distribution was observed in different studies because of asymptomatic nature of the disease making diagnosis difficult. Surprisingly, 10.52% of infections were found in children under 10 years old in this study, indicating vulnerability of children to this infection.

Development of cyst can take place in any organ of the body. In current analysis, the highest prevalence of cyst was found in liver (58.77%) followed by lungs (14.47%) which is in accordance to many studies (Akcam et al., 2014; Hüttnner et al., 2008; Khazaei et al., 2016; Mousavi et al., 2012; Ernest et al., 2010; Aliabadi et al., 2015). In addition, infection was also found in other body organs including spleen, omentum, breast, testis, pancreas, ovary, thigh, pelvis, and peritoneal cavity as reported earlier (Jamal et al., 1989; Al-Jawabreh et al., 2017). In Pakistan case reports on different infected organs, such as spleen, lungs (Zaidi, 2009), abdomen, ovary (Amin et al., 2009), intra-abdominal (Nadeem et al., 2006), pelvic bone (Khan et al., 2015), cerebral (Khan et al., 2015), cervikal (Sultana et al., 2012), intrarenal (Nadeem et al., 2013), pneumothorax (Fatmi et al., 2010), urin tract (Biyabani et al., 2000), breast (Masroor et al., 2010), mammary and femoral (Shamim et al., 2010), cardiac intraventricular septum (Mustafa et al., 2012), and mitral valve (Khan et al., 2015), have been published. However, rare cases of hydatid cysts of orbit, uterus, chest wall, renal tissue were observed in present study which have not been reported previously in Pakistan.

Previous studies showed different trends of organ infection, age and gender wise distribution of hydatid cysts. Different geographical regions, living standards and various environmental factors could be the reason for the heterogeneous nature of data. Studies on epidemiology and various risk factors contributing to the spread of disease have shown the importance of economic and sociocultural parameters in disease spread globally (Deplazes et al., 2015; Molyneux et al., 2017).

Currently, the incidence of CE has become one of the most emerging and concerning health issues in Pakistan. It is considered as a neglected disease in Pakistan and limited work has been done on the disease. The current report analyzed the data on CE from four different hospitals located in Islamabad, Rawalpindi and Peshawar (2012-2017). The highest number of cases was observed from Rawalpindi (n=216) followed by Peshawar (n=5) and Islamabad city (n=7). Despite of limited area under study, a significant increase in a positive rate of CE was observed which reflected the emerging trend of disease in Pakistan. CE must be brought under consideration for future research keeping in view the lack of research data at molecular and epidemiological level which is necessary for controlling and preventing the disease in Pakistan.
The increasing trend in the burden of disease observed in this study urges the public health authorities to take action on this situation. If left unchecked, the disease can lead to an effective threat to public health. A very confined area of the current study showed a considerable emerging trend of the disease, henceforth, large scale emergence of disease could be expected. This study highlights the need for subsequent investigations across the country to have an exact idea about the disease incidence and burden. The current investigation provides a stronger evidence of an increasing trend of emergence of echinococcosis in Pakistan thus reflecting the importance of the current health issue. The issue needs to be addressed on international forums such as WHO and control/treatment measures should be taken to prevent any economic and health loss.

CONCLUSION

This study showed a picture of geographic distribution and epidemiological situation of echinococcosis cases detected in hospital in three cities in Pakistan. This indicates that the disease is widespread and significant public health problem in the country. The emerging trend of echinococcosis in Pakistan refreeing to an emerging health issue in Pakistan bringing the disease to limelight for future research. The occurrence of cases in children and young adults is an important result as it indicates an active transmission of the parasite in Pakistan. This finding, together with the fact that 1 hospital reported 214 cases over 6 years underlines the need for a program for prevention/control of this disease in Pakistan. Timely measures are needed to be taken to hamper the disease development and establishment. In order to control the disease, complete surveillance should be done which in turn would weigh down the disease progress.

Conflict of Interest

The authors declare that there is no conflict of interest or financial disclosure about this publication.

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