

Clinical, Radio-Ultrasonographic and Serological Features of Hydatid and Simple Cysts in Human

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Abstract

Introuduction: Hydatid cyst is remain a health problem of significant concern worldwide. Cystic echinococcosis (CE) is considered to be highly endemic in some countries.

Methods: In this study serological, radiographic and clinical features of simple and hydatid cyst were studied. For this purpose, 114 patients (57 male, 57 femle) whom had clinical or/and radio, ultrasonographic signs for hydatid and simple cysts, were referred to cystic infection in Azadi Teaching Hospital in Kirkuk province, Iraq. The serum samples were examined serologically by ELISA.

Results: Depending on the results of clinical or/and ultrasonographic, a rate of 15.8 % were infected with CE and a rate of 84.2 % were have simple cysts (SC). While the results of serological examination by ELISA revealed 14.1% for CE and 85.9% for SC. The most age group which was significantly infected by CE in males was 56-64 year with a rate of 40 %, and the most age group which was significantly infected in females was 65-73 year with rate of 100 %.

The CE was significantly more frequent in the liver of infected patients in both males and females, with rates of 71.4, 100 % for each gender respectively. The size of most of hydatid cysts were larger than 9 centimeter. People in rural area were most infected than in urban area.

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The frequency of CE were significantly highest among housewife females (43.8 %), and unemployed men (31.3 %).

Conclusion: CE can be diagnosed and differentiated from SC serologically, even when the cysts are very small and at beginning stage. The radio-ultrasonographic is good in cysts diagnosing but cannot differentiate between types of small sized one.

Key words: Clinical, Serological features, Hydatid cysts, Simple cysts, Human, Kirkuk, Iraq.

المظاهر السريرية و الاشعاعية والمصلية للأكياس المائية و البسيطة في الانسان

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الخلاصة

المقدمة: داء الاكياس المائية لايزال يشكل مشكلة صحية ذو اهمية معنوية عالميا، ويكون منتشر بدرجة كبيرة في بعض المناطق والدول.

طريقة العمل: في هذه الدراسة المظاهر السريرية المصلية و الصور الصوتية و الاشعاعية للاكياس المائية و البسيطة تم دراستها، لهذا الغرض تم اختيار مئة واربعة عشر مريض (57 انثى و 57 ذكر) ممن كان لهم نتائج الموجات فوق الصوتية و الاشعاعية و الاعراض السريرية يدل على اصابتهم بالاكياس البسيطة او المائية. فحص مصول المرضى مناعيا بطريقة الاليزا.

النتائج: اعتمادا على الاعراض السريرية و النتائج الاشعاعية و الموجات فوق الصوتية، 18 مريض كان موجبا للاكياس المائية و بنسبة 15,8% و 96 عينة كان للاكياس البسيطة بنسبة 84,2% ولكن نتائج الدراسة المصلية لم يختلف معنويا و اظهر 16 (14,1%) عينة للاكياس المائية و 98 (85,9%) عينة للاكياس البسيطة. المرحلة العمرية الاكثر اصابة معنويا في الذكور كان 64-56 سنة بنسبة 40% بينما المرحلة العمرية الاكثر اصابة في الاناث كانت 65-73 سنة بنسبة 100%. الاكياس المائية ظهر يتردد اكثر في اكياد المخمجين و بنسبة 71,4% ، 100% لكل من الذكور و الاناث على التوالي. احجام نسبة عالية من الاكياس المائية كانت اكثر من 9سم. و نسبة الاكياس المائية كانت اعلى معنويا في المناطق الريفية عنه في الحضرية، ظهر الطفيلي بنسبة اكبر في ربات البيوت و الذكور غير الموظفين و بنسبة 43,8 ، 31,3% لكل فئة على التوالي.

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الاستنتاج: الاكياس المائية يمكن تشخيصها وتمييزها مصليا عن الاكياس البسيطة، حتى وان كانت صغيرة الحجم و في المراحل الاولى من التكوين، الطرق الاشعاعية والموجات فوق الصوتية هي طرق فعالة جدا في الكشف عن الاكياس ولكن لا يميز بين المائية والبسيطة منها.
الكلمات المفتاحية: المظاهر السريرية و المصلية، الاكياس المائية، الاكياس البسيطة، الانسان، كركوك، العراق.

Introduction

Echinococcosis (Hydatid disease) is an infection caused by the larval instar of cestodes tape worms of the genus *Echinococcus*, family *Taeniidae* [1]. Nowadays, four species of *Echinococcus* are known to infect human (*E. granulosus* (dog tapeworm), *E. multilocularis*, *E. oligarthrus* and *E. vogeli*). The parasites are continued their life-cycles in carnivores as final hosts and herbivores as intermediate hosts. The egg-producing adult stage is harbored in the intestine of the definitive host, and the metacestode in intermediate host is develops after oral ingestion of the expelled eggs. Metacestodes may also develop in humans causing various forms of echinococcosis [2]. The cyst is diagnosed radiologically, ultrasound and serologic screening are also methods for detection [3, 4, 5].

Some areas of the world such as Central Europe, the Mediterranean countries, the Middle East, South America, Australia, New Zealand, and South Africa are known to be endemic. It is prevalent sheep-cattle raising regions [6]. Alike with many other parasitic infection, it is tough to summaries data on the occurrence or frequency of CE in humans. In Iraq as in other area the CE is endemic, in Arbil province in northern Iraq, 99 cases were documented between 1990 and 1998 resulting in an yearly average of 12.4 cases and an expected occurrence of 2 cases per 100,000 [7]. In Kirkuk and Tikrit cities, from 2000 to 2003, a 125-hydatid cyst cases were recorded, 82 in Kirkuk and 43 in Tikrit [5]. In Baghdad in 2006, 94 patients were diagnosed for hydatid cyst, 20 of them were urgent [8]. In Hilla also 61 patients were recorded to have CE in 2011-2012 [9]. Of all general surgeries in Saudi Arabia 0.3% of them were accounts CE, the prevalence is estimated to be 1.6-3.6 cases per 100,000 population in Kuwait, *E. granulosus* had apparently low prevalence in Oman animals and humans due to their unusual

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epidemiological conditions [10]. In the entire Iran more than 5,000 patients of CE were treated surgically in a 14-year period (1980-1993) [11]. A 676 CE surgical cases in Jordan have been recorded between 1985 and 1993, and the annual rates in different areas of the country were valued to be 0.5 to 8.2 cases per 100,000 [12]. Recent records accentuate that CE continues to be public health problem in humans in Morocco, Algeria, Tunisia and Libya and seemingly to a smaller degree in Egypt where the yearly frequency of hospital cases is expected to be less than 1 per 100,000 population [13]. Since the increase of emigration and trade, the hydatid cyst can befall also in non-widespread countries [6].

Simple cysts are comparatively more common. The simple cyst histopathologically characterized by wall composed of a thin layer of epithelial cells and having serous fluid on sonography. Hydatid cysts are generally asymptomatic and discovered accidentally on sonography. The appearance of hydatid cysts on sonography is inconstant and hinge on the stage of maturity and the diagnostic accuracy of sonography is required for cysts with a noticeable cyst wall [14]. The hydatid cyst is a fluid-filled cavity, consisting of an outside thick host formed fibrous wall and two inner parasite-derived layers, which is an external laminated and internal germinal layer[2]. The ordinary investigative methodology for cystic echinococcosis comprises imaging techniques, mainly ultrasonography, computed tomography (CT), X-ray examinations, and by detection of specific serum antibodies by immunodiagnostic tests. Enzyme linked immunosorbent assay (ELISA) test using hydatid cyst fluid has a high sensitivity (>95%) [4].

Because there is very little studies on CE in Kirkuk city and the necessity of distinguishing the CE from SC especially at the first steps of formation, the aim of the present study was to detect and differentiate the CE from SC sonographically, radiographically, serologically and by clinical features in patients of Kirkuk province.

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Materials and Methods

1-Population Study:

From January to November of the year 2014, a total 114 patients were eligible for sero-screening for hydatid cyst, according to the examination of the physician, and the clinical signs which referred to cystic infection. Data's including gender, age, location of cyst, size of cyst, type of cyst, residential areas and occupation of all patients were recorded. The patients were referred to Azadi Teaching Hospital in Kirkuk province, Iraq. The ultrasound, x-rays diagnosis of the patients was discussed with the physician.

2-Serum samples collection:

2-3 ml of venous blood was drained cautiously and transferred into disposable plan tube, the specimen was left for (15-30) then centrifuged at 300 rpm for (5min) to isolate clear serum, sera were kept at (-20 °C) till they were assayed by ELISA [4]. (Blood was taken from the patients after they had finished the x-rays or sonography tests).

3-ELISA (Enzyme Linked Immunosorbent Assay) kit:

For determining the presences of specific human *E. granulosus* IgE (allergenic protein). ELISA kit was used instructed procedure of the BIO RAD (Bio-Rad Laboratories.3Brd R. France).

Principle of the assay: The qualitative immunoenzymatic determination of IgG class antibody against *Echinococcus* is based on the ELISA technique. Micro titer strip wells are pre coated with *Echinococcus* antigen to bind corresponding antibodies of the specimen. After washing the well to remove all unbound sample material horseradish peroxidase (HRP) labeled anti-human IgG conjugate is added. Then this conjugate binds to the capture *Echinococcus*-specific antibodies. The immune complex formed by the bound conjugate is visualized by adding Tetramethylbenzidine-(TMB) substrate which gives a blue reaction product. The intensity of this product is proportional to the amount of *Echinococcus*-specific IgG antibodies in the specimen. Sulphuric acid is added to stop the reaction. This produces a yellow end point color. Absorbance at 450 nm is read using an ELISA microwell plate reader.

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4-Statistical Analysis:

χ^2 (chi-square) test in style of independent and in style of homogeneous were used manually. The significant level used was $P < 0.05$.

Results

This study had included the prevalence of hydatid and simple cyst population of Kirkuk city which was detected by sonography, radiography and serologically. The result (Table1) showed no significant differences ($p < 0.05$) between sono-radiography and serology methods in CE diagnosing. The frequency rate of CE was 14.1, 15.8 % for each of serology and sono-radiography methods respectively .

Table 1. Prevalence of hydatid and simple cysts

Gender	Patient No.	Serology (ELISA)				Sono-radiography			
		Simple cyst		Hydatid Cyst		Simple cyst		Hydatid Cyst	
			%		%		%		%
Male	57	50	87.7	7	12.3	50	87.7	7	12.3
Female	57	48	84.2	9	15.8	46	80.7	11	19.3
Total	114	98	85.9	16	14.1	96	84.2	18	15.8
χ^2 value	Evaluated χ^2 value = 0.28, χ^2 value of $P < 0.05 = 3.84$ (none significant)								

The result in table 2 indicated that there were no significant differences in CE infection between male and female ($P > 0.05$), but significant difference were appeared between age groups in both males and females. The most age group which were infected with the CE in male was 56-64 year with rate of 40%, followed by 20-28 with rate 18.2%, no positive sample were detected in each of 11-19, 47-55, 65-73 age group. In female the highest rate (100%) of infection was in

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65-73 year, followed 29-37 year with rate of 16.7% , the lowest rate (0%) was in 20-28 years old.

Table 2. Seroprevalence of hydatid cyst according to age and sex

Sex	Male					Female					
	Age group in years	Examined numbers	+ve	%	-ve	%	Examined numbers	+ve	%	-ve	%
	2-10	6	1	16.7	5	83.3	4	1	25	3	75
	11-19	9	0	0	9	100	7	1	14.3	6	85.7
	20-28	11	2	18.2	9	81.8	12	0	0	12	100
	29-37	10	1	10	9	90	12	2	16.7	10	83.3
	38-46	6	1	16.7	5	83.3	9	1	11.1	8	88.9
	47-55	7	0	0	7	100	7	1	14.3	6	85.7
	56-64	5	2	40	3	60	4	1	25	3	75
	65-73	3	0	0	3	100	2	2	100	0	0
	Total	57	7	12.3	50	87.7	57	9	15.8	48	84.2
χ^2 value	Evaluated χ^2 value = 16.4, χ^2 value of P < 0.05 = 14.1 (significant)					Evaluated χ^2 value = 14.4, χ^2 value of P < 0.05 = 14.1 (significant)					

The occurrence of hydatid cysts in various sites of the patients organs confirmed by ELISA are illustrate in table 3, 4. The result was significant for both male and female. The most organ which was infected with hydatid cyst in male was the liver with the maximum infection rate of 71.4%. The second highest rate of infection was in the lung with rate of 100% followed by back with a rate of 14.3%. The maximum infection number was 5 with rate of 100% for liver in female, and the lung, brain, kidney, gallbladder all was with the same infection rate (Table 4).

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Table 3. Distribution of simple and hydatid cyst among different organs in males.

Cyst location	Total cyst No.	Simple cyst	%	Hydatid cyst	%
Face	7	7	100	0	0
Head	10	10	100	0	0
Hand	13	13	100	0	0
Foot	4	4	100	0	0
Back	7	6	85.7	1	14.3
Neck	7	7	100	0	0
Liver	7	2	28.6	5	71.4
Gallbladder	1	1	100	0	0
Lung	1	0	0	1	100
Total	57	50	87.7	7	12.3
χ^2 value	Evaluated χ^2 value = 36.09, χ^2 value of P < 0.05 = 26.3 (significant)				

Table 4. Distribution of simple and hydatid cyst among different organs in females.

Cyst location	Total cyst No.	Simple cyst	%	Hydatid cyst	%
Face	6	6	100	0	0
Head	7	7	100	0	0
Hand	12	12	100	0	0
Foot	2	2	100	0	0
Back	3	3	100	0	0
Ovary	12	12	100	0	0
Neck	6	6	100	0	0
Liver	5	0	0	5	100
Brain	1	0	0	1	100
Lung	1	0	0	1	100
Kidney	1	0	0	1	100
Gallbladder	1	0	0	1	100
Total	57	48	84.2	9	15.8
χ^2 value	Evaluated χ^2 value = 58.44, χ^2 value of P < 0.05 = 36.4 (significant)				

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The relationship of CE with the residential area is illustrated in table 5. The result showed that the most significant residential area which was infected by hydatid cyst was in Chamchamal, Hawija, Tuz with rates of 66.7, 42.9, 50% respectively for each area. Krfri, Failak, Daquq had same rate (33.3%) of infection. While in the city center the infection with the hydatid cyst in the Wasti, 1 Huzairan, Qadisiyah, Shroiija were with rates of 20, 16.7, 14.3, 13.3% respectively for each area.

Table 5. Distribution of simple and hydatid cysts according to patient's residence

Residential area	Total cyst No.	Simple cyst	%	Hydatid cyst	%
Wasti	10	8	80	2	20
Raheem awa	15	15	100	0	0
1 huzairan	6	5	83.3	1	16.7
Imam qasim	2	2	100	0	0
Panja ali	6	6	100	0	0
Shorijh	15	13	86.7	2	13.3
Al-huria	9	9	100	0	0
Tariq bagdad	6	6	100	0	0
Hai al-askari	12	12	100	0	0
Tuz	4	2	50	2	50
Dbbs	3	3	100	0	0
Kefri	3	2	66.7	1	33.3
Chamchamal	3	1	33.3	2	66.7
Failak	3	2	66.7	1	33.3
Hawija	7	4	57.1	3	42.9
Daquq	3	2	66.7	1	33.3
Qadisiyah	7	6	85.7	1	14.3
Total	114	98	85.9	16	14.1
χ^2 value	Evaluated χ^2 value = 27.96, χ^2 value of P < 0.05 = 26.3 (significant)				

The main presenting symptoms in CE infected individuals (Fig.1) were jaundice with rate of 74 % followed by right upper quarter (RUQ) pain with rate of 62.5%. The less symptoms appeared were hematuria and intracranial pressure having the same rate (6.3%).

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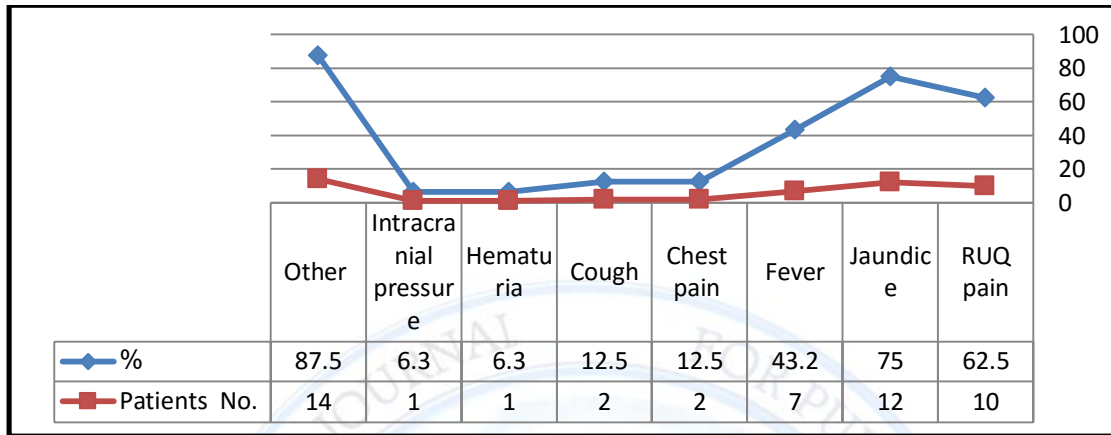


Figure 1. Cystic echinococcosis symptoms

Regarding the occupation of the patients significant difference was appeared between them (table 6). The significantly highest incidence of the disease in females were among housewives with rate of 100% while in men were among unemployed with rate of 100%. The incidence of the hydatid cyst in the students were 18.8 %.

Table 6. Distribution of hydatid cysts in relation to patient's occupation.

Occupation	Total cyst No.	%	Male	%	Female	%
Housewives	7	43.8	0	0	7	100
Unemployed men	5	31.3	5	100	0	0
Student	3	18.8	2	66.7	1	33.3
Child	1	6.3	0	0	1	100
Total	16	100	7	43.7	9	56.3
χ^2 value	Evaluated χ^2 value = 14.72, χ^2 value of P< 0.05 =7.81 (significant)					

The size of the cysts detected were significantly different between the simple and hydatid cyst (table 7). The smaller sizes were for simple cyst and the bigger were for hydatid cyst. Most of

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the hydatid cyst detected were between 9-11cm. and bigger size with rate of 100 %. Low percent of hydatid cyst had small size (3-5cm) with rate of 3.3%.

Table 7. Distribution of simple and hydatid cyst by size.

Size of cyst in cm.	Total cyst No.	Simple cyst	%	Hydatid cyst	%
<3	53	53	100	0	0
3-5	30	29	96.7	1	3.3
6-8	19	16	84.2	3	15.4
9-11	8	0	0	8	100
11>	4	0	0	4	100
Total	114	98	85.9	16	14.1
χ^2 value	Evaluated χ^2 value = 85.2, χ^2 value of P< 0.05 =15.5 (significant)				

Figure 2 shows the type of simple cysts detected. The most high frequency of simple cyst were for sebaceous cysts which represented by 59 cysts with rate of 60.2 %, while the lower frequency were for natal cysts which represented by 5 cysts with rate of 5.1 %.

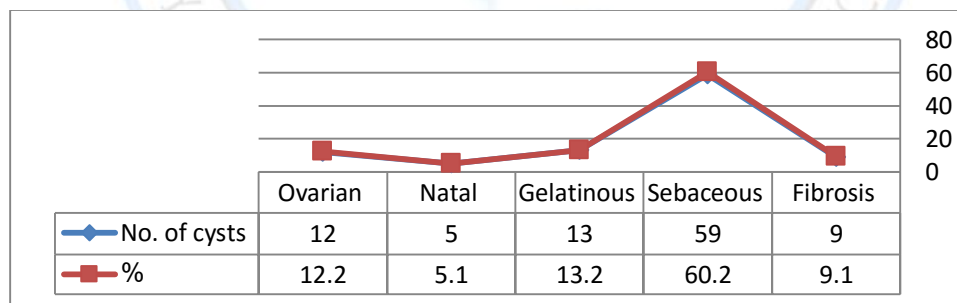


Figure 2. Type of simple cysts.

Comparative diagnosis of hydatid cyst by examination of both ultra sound (US), radiography (RA) and serology by ELISA (Fig.3), revealed 16 positive sample by ELISA while the US-RA were diagnosed 18 sample. Figure (4, 5) shows simple and hydatid cyst diagnosed by US. The

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simple cysts wall is not visible on sonography and its look like ghost (Fig. 4), while the diagnostic accuracy of sonography is high for hydatid cysts with a visible cyst wall (Fig.5).

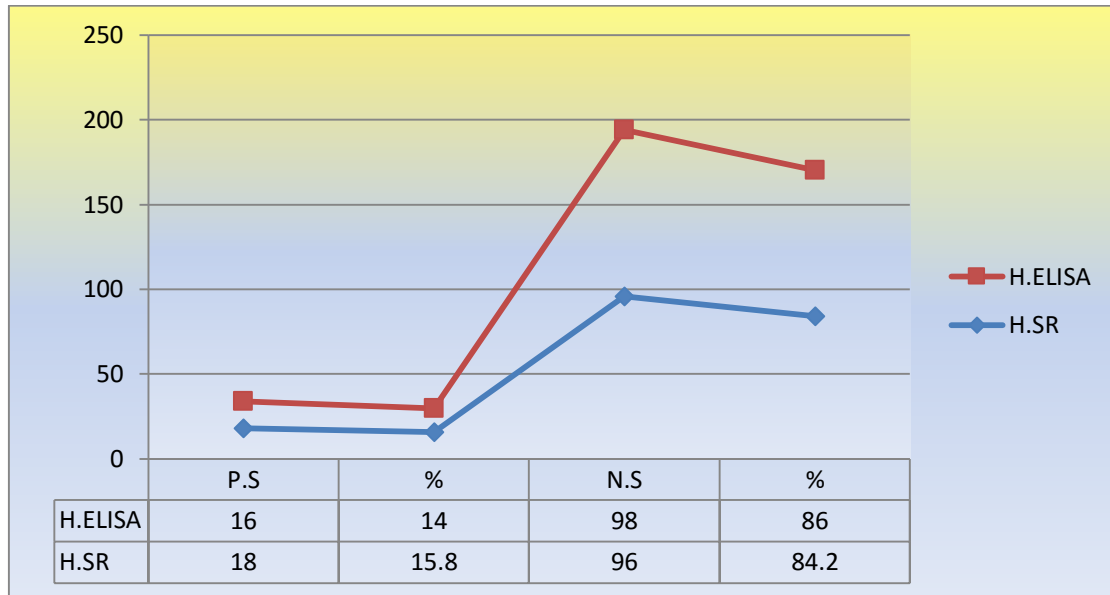


Figure 3. Comparison of ultra sound and ELISA in hydatid cyst detection. (H= hydatid cyst, P=positive, N= negative, S=sample, SR= sono-radiography)

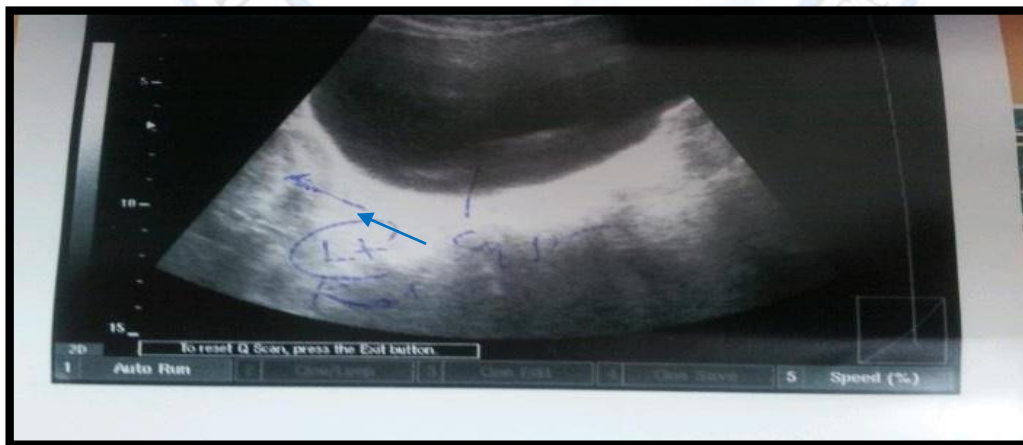


Figure 4. Simple cyst appearance by ultra sound (blue arrow ahead)

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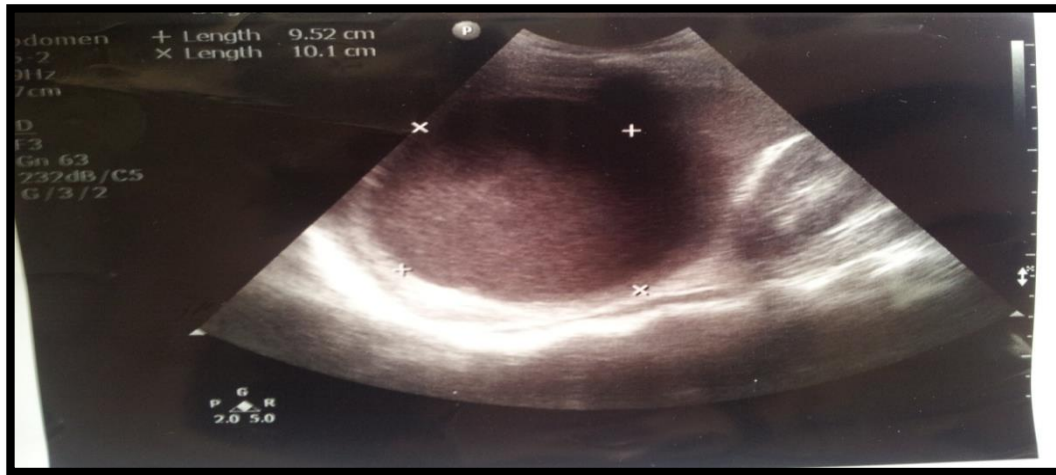


Figure 5. Hydatid cyst appearance by ultra sound (crosses refer to cystic wall layer).

Discussion

Hydatidosis is remain a main public health problem in our country as in some other parts of the realm [8]. The adult worm is attached to the small intestinal of animals like dog, fox, wolf, cat and millions eggs are dispersed with each animal defecation [2].

As far as we know the age distribution is apprehensive, the present study appeared the highest surgical prevalence in the 56-64 years in male. Namely, that the maximum age of the incidence was the fifth decade which agreed with [5]. In contrast, apparently conflicted with that recorded by others [15, 5]. High incidence occurred in age between 30-60 years in women [16], was similar to our study result.

In most endemic areas as known, a sizeable amounts of the entire inhabitants at risk are small ages, in contrary the disease mostly affect grown persons at the labor age, high number of hydatid cyst infections are certainly acquired in the period of the childhood but needs several years to patent themselves as harmful lesions .In this study as in usual in hydatid infection, the liver in both sexes was more frequently site involved than in other organs. However, the lung is being the next. These findings are in agreement with results of other studies [5, 16, 17]. In contrast, that some of studies recorded the predominance of the lung hydatid cysts infection

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over the hepatic involvement [18,19]. It is well known that liver is most frequently affected, that is interpreted to the fact that the liver acts as primary filter in the human body. However, conspicuously, the exact mechanism for the hydatid cysts development sites are yet not clear [20]. The main presenting symptoms showed in this study was jaundice, RUQ (right upper quadrant) pain and fever which agreement with other studies [8,9,16].

This study indicated that the rate of hydatid cyst in female is significantly higher than in male, or nearly equal in two sexes, confirming the findings of others [8, 9, 21], perhaps this because the females are more commonly involved in dealing with meat, contaminated food and vegetables, and with animals [9, 22]. In spite of this, investigational studies showed that the males were more prone to contract the disease than the females [23]. In the present study the majority of hydatid cysts cases were among the housewives, this is in agreement with that found by several other studies [5,15,17].

However, high incidence of the disease among housewives may be due to their extreme domesticity in a habitat and handy connotation with infected dogs. Concerning the residence, most of the study cases were from the rural areas (66.7%), This is agreement to other study done in Iraq, in whom they found higher rates (82%, 62.9) in rural areas respectively [9,15]. In this study it was noticed that the majority size of cysts diameters between 9-11 which is agreement with that found by other researchers they recorded high frequency in bigger cyst size (more than 10 cm, mean of 11.4 cm) [8,16]. This is because the symptoms depending on size of cyst and this disease at beginning of infection is asymptomatic until the cyst become large in size then appear of symptoms so then patient feeling there is a problem.

Among simple cysts, sebaceous cyst appeared to be the most common with rate of (51.8%) this in agreement with other studies [24, 25, 26] because they may occur anywhere on the body except in areas where no hair, like hand palms.

The diagnosis of hydatid cyst is usually made by typical sonographic features. The sonography appearance of hydatid cysts is variable and hinge on on the phase of maturity [2]. 25–40% of completely liquid type hydatid cysts appear as well-defined anechoic cysts with no wall structure and thus are sonographically indistinguishable from simple cysts [14] Likewise, on

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MRI the distinguishing morphologic features of cystic echinococcosis types 1, 2, and 3 hydatid cysts are supportive in the differential diagnosis, whereas completely liquid hydatid cysts are indistinguishable from simple cysts [3]. In present study the serologically result had not differed from that of sonography making both of them good tool for diagnosing this is somehow agree with that found by [2] whom revealed sonography to be good tool in CE diagnosing, and with [5] whom revealed serology method (ELISA) to be more sensitive than LATEX in CE diagnosing but The conclusion of our study is that: CE can be diagnosed and differentiated from SC serologically, even when the cysts are very small and at beginning stage. The radio-ultrasonographic is good in cysts diagnosing but cannot differentiate between types of small sized one.

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