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BRUCELLA INFECTIONS IN PATIENTS HOSPITALIZED FOR FEVER: A SEROLOGICAL STUDY AT AL DELENGAT FEVER HOSPITAL, DAMANHUR, EGYPT

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ABSTRACT

Background

Human brucellosis is either an acute febrile disease or apersistent disease with a wide variety of symptoms. Brucellosis, one of the world's major zoonosis, is endemic in many parts of Egypt. It is an occupational hazard for veterinary employees, butchers, dairy personnel, and laboratory workers. It is a true zoonosis in that virtually all human infections are acquired from animals. There is no information available on human brucellosis from Al Delengat Fever Hospital, Damanhur, Egypt. Three species (Br. melitensis, Br. abortus, Br. suis), are important human pathogens; Br. Canis, is of lesser importance portals of entry are the mouth, conjunctivae, respiratory tract and abraded skin (***Centers for Disease Control and Prevention 2000***).

Aim of This Study: To study sero epidemiology of all cases diagnosed as brucellosis admitted to Al Delengat Fever Hospital during period between 2011to 2012.

Methods and Materials

The total number of cases admitted in Al Delengat Fever Hospital were enrolled in this study during period between 2011 to 2012 was 8896 cases. From this number there were 243(2.7%), brucella cases of both sexes (138 males(56.8%) and 105 females (43.2%) with ages ranging between 12 years to 70 years. According to this study patients were found to have brucellosis on the basis of slide agglutination method. All brucella positive patients were admitted in the hospital and subjected to detailed medical history, clinical examination, abdominal U/S, chest X- RAY and laboratory investigations (urine analysis, CBC, ESR, liver function testes, kidney function testes, fasting and postprandial blood glucose and serological studies: Malta test (slide agglutination test) and Widal test Results ; The number of brucella cases admitted in Al Delengat Fever Hospital during the mentioned period is 243 cases 2.7% from the total number (8896), (138 males & 105 females) with average number of 20 cases monthly. The peakincidence of brucella cases increase during summer months. The predominant type of brucella species is **M** type in districts area. The incidence of brucella cases increases among males patients than females especially in rural area.

Conclusion

Brucellosis is a febrile illness transmitted to man fromanimal reservoirs, the peak incidence of brucella cases increase during summer months and increase among males than females especially in rural area. Such individuals may need treatment and follow-up.

KEYWORDS: Brucellaigg ELISA, Brucella Igm ELISA, Brucella Serology, Fever

INTRODUCTION

One of the most difficult problems in clinical medicine is fever of unknown origin (***Sivakumar et al., 2006***). Is one of the world's major zoonosis of public health importance and economic concern. It is caused by bacteria belonging to the genus brucella which are facultative intracellular, gram-negative cocco-bacilli. ***Franco MP, et al; 2007.*** Most patients with prolonged fever do not have rare disease but usually suffer from common disorders that are difficult to diagnose because they present atypically ***(Roth J., 2006).*** Fever of unknown origin (FUO) mean fever of more than two weeks duration, during which time, physical examination, chest X-ray films, blood tests and urine culture do not reveal the cause of fever (***Knockaert et al., 2003***). Bacteria of the genus brucella cause a disease primarily in domestic feral and some wild animal and most are also pathogenic for humans. In animals, brucellae typically affect the reproductive organs and abortion is often the onlysign of disorder ***(Asanda and Agbede 2001***).

Most of the human infections are caused by Br. melitensis and Br. Abortus, but Br. canis is of lesser importance**,** ***Franco MP, et al; 2007.*** The animal reservoirs of these organisms transmit infection to man when he consumes raw milk or eats insufficiently cooked meat. Portals of entry are the mouth, conjunctivae, respiratory tract and abraded skin (***Centers for Disease Control and Prevention 2000A***). Brucella also poses an occupational hazard for veterinary employees, butchers, dairy personnel, and laboratory workers who are often exposed to the infected animals or their tissues, (***Mantur BG. Et al; 2006, &Kumar P. et al; 1997).*** Human brucellosis is either an acute febrile disease or a persistent diseasewith a wide variety of symptoms.

The aim of this Work is to study sero epidemiology of brucellosis in all cases diagnosed as brucellosis admitted to Al Delengat fever hospital during the period between 2011 – 2012.

PATIENTS AND METHODS

The total number of cases admitted in Al Delengat Fever Hospital during the period between 2011 – 2012was 8896 cases. From this number there were 243 (2.7%), brucella cases of both sexes (138 males (56.8%) and 105 females (43.2%) with ages ranging between 12 years to 70 years. According to this study patients were found to have brucellosis on the basis of slide agglutination method. All brucella positive patients were admitted in the hospital and subjected to detailed medical history, clinical examination, abdominal U\S, chest X- RAY and laboratory investigations(urine analysis, CBC, ESR, liver function testes, renal function testes, fasting and post prandialblood glucose and serological studies: Malta test (slide agglutination test). Informed consent was obtained from all patient sprior to participation in this study. The Institutional Review Board (IRB) of the Al Azhar University approved this study. The study was conducted according to the principles of the 1974DeclarationofHelsinki.

Mercaptoethanol Brucella Agglutination Test

The 2-mercaptoethanol (2ME) brucella agglutination test is a performed identically to the STA test1. (Standard Tube Agglutination Test) (STA): Agglutination is a clumping result from the cross linking between particles, antigen (agglutinogen) and its specific antibody (agglutinin) in the presence of certain ions (***Kwapinski, 1960***), except for the addition of 2ME to a final concentration of 0.05 ml ineach agglutination tube. The 2 ME disruptsdisulphide bonds making immunoglobulin M antibodies inactive and permitting only brucella agglutination by IgG agglutinating antibodies that are

resistant to 2ME (***Edward et al., 1970***). ***Bucchanan et al. (1974***) observed that the 2ME test is a better indicator for recent infection than the STA test. ***Smits et al., (2003)*** has suggested that apositive 2ME test is evidence of an active infection and the need for antibiotic therapy and Widal test.

RESULTS

Table 1: Symptoms among Patients in the Studied Groups

Items	Total No	%	Male	%	Female	%	Z	P	Sig.
Fever	238	97.94	135	97.82	103	98.095	0.02	>0.05	N.S
Headache	205	84.63	113	81.88	92	87.62	0.48	>0.05	N.S
Bach pain	201	82.7	113	82	88	84	0.16	>0.05	N.S
Sweating	138	56.79	74	53.6	64	60.95	0.75	>0.05	N.S
Abd. pain	102	42	56	40.6	46	43.8	0.38	>0.05	N.S
Vomiting	85	35	47	34	38	36	0.28	>0.05	N.S
Cough	83	34	36	26	47	44.7	2.47	>0.05	N.S

This table shows no significant difference between male and female as regard symptoms

Table 2: Clinical Signs among Patients in the Studied Group

Items	Total No	%	Male	%	Female	A %	Z	P	Sig.
Osteoarthritis	81	33.3	44	32	37	35	0.45	>0.05	N.S
Bronchitis	79	32.5	35	25	44	42	0.24	>0.05	N.S
UTI	77	31.7	35	25.36	42	40	2.01	<0.05	S
HSM	39	16.05	23	16.7	16	15.2	0.28	>0.05	N.S
Ocular pain	33	13.6	21	15.2	12	11.4	0.79	>0.05	N.S
Blurring of vision	29	11.9	13	9.4	16	15.2	1.3	>0.05	N.S
Testicularpain	15	6.17	15	10.87	-	-	-	-	-

HSM =Hepato-splenomegaly, CNS=CentralNervous System, CVS =Cardio-Vascular System.

This table shows no significans between male and female as regard osteoarthritis, bronchitis, HSM, ocular pain, and blurring of vision, but there is significant difference between male and female as regard UTI.

Table 3: Investigations Done to Patients in the Studied Group

Investigation	Sresult	Total		Male		Female	
		NO.	%	NO.	%	NO.	%
AbdominalU\S	**HSM**	139	57	70	50.7	69	65.7
	N	104	43	68	49.3	36	34.3
Brucellatest	**M**	120	49.38	72	52.17	48	45.71
	A	74	30.45	41	29.71	33	31.43
	M&A	49	20.17	25	18.12	24	22.86
Widaltests	**+VE**	138	56.8	67	48.55	71	67.6
	-VE	105	43.2	71	51.45	34	32.4
CRP	**+VE**	202	83.13	115	83.3	87	82.9
	-VE	41	16.87	23	16.7	18	17.1
CBC	**N**	25	10.9	19	13.8	6	5.7
	LL	39	16.5	36	26.1	3	2.9
	LL&An	179	73.6	83	60.1	96	91.4
ESR	**+VE**	243	100	138	100	105	100
	-VE	0	0	0	0	0	0

There is no significance between male and female as regard abdominal ultra sound and brucellatest, but there is significant difference between male and female as regard widal test and CBC.

Table 4: Distribution of Brucella Cases in Relation to Age

Sex Age	Total No	%	Male	E %	Female	E %	Z	P	Sig.
5 -	23	9.46	15	10.87	8	7.62	0.82	>0.05	N.S
15 -	87	35.8	49	35.51	38	36.2	0.09	>0.05	N.S
30 -	102	41.89	57	41.3	45	42.85	0.19	>0.05	N.S
50 +	31	12.76	17	12.32	14	13.33	0.22	>0.05	N.S
Total	**243**	**100**	**138**	**100**	**105**	**100**			

As regard age distribution there is no significant differences between male and female.

Seasonal Variations of Brucella cases in Fever Hospital

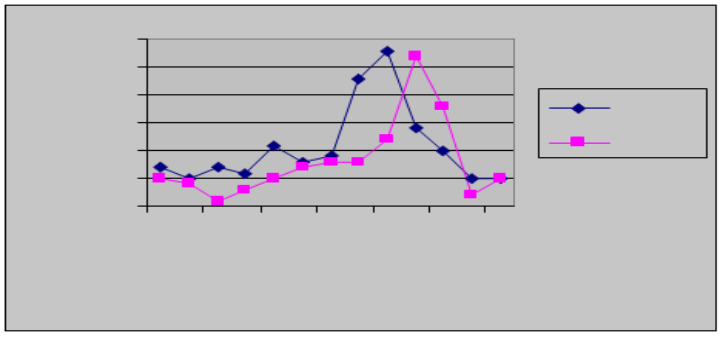

Figure 1

There is marked increase in the incidence of brucella cases in summer months than the other months.

DISCUSSIONS

Human brucellosis is either an acute febrile disease or a persistent disease with a wide variety of symptoms. It is a true zoonosis in that virtually all human infections are acquired from animals. Three species (Br. melitensis, Br. abortus, Br. suis) are important human pathogens; Br. canis is of lesser importance Portals of entry are the mouth, conjunctivae, respiratory tract and abraded skin (***Centers for Disease Control and Prevention 2000A***).The results of this study showed that peak incidence of brucella casesin crease during summer months. The predominant type of brucella species is Mtype in Delengate districts. The incidence of brucella cases increase among males than femalese specially in rural as brucella test was done to all cases subjected to this study. We have 2 main genotypes of brucella species in our area in which this study was done. These types are Brucella Melitensis (M) and Brucella Abortus(A). 120 cases (49.38%) were found to have Bucella Mlitensis (M) of all casessubjected to this study divided into 72 male patients (52.17%) of all male patients included in this study and 48 female patients (45.71%) of all female patients included in this study, and this result is in agreement with ***(Mantur et al., 2006***), 74 patients (30.45%) were found to have Brucella Abortus (A) of allpatients subjected to the brucella test divided into 41 male patients (29.71%) of all male patients included in this study and 33 female patients (31.43%) of all female patients included in this study, and this result is in agreement with (***Marrodan et al., 2001)***. 49 patients (20.17%) were found to have both Bucella Melitensis (M) and Brucella Abortus (A) of all patients

subjected to brucella test divided into 25 male patient (18.12%) of all male patients included in this study and 24 female patients (22.86%) of all female patients included in this study. There is no significant difference between male and female as regard brucella test. This result is in agreement with ***(Orduna et al., 2000***). As regardage distribution in our patients there is no cases under 5 years detected in this period. As regard occupation 83 farmers, 15 abattoir workers 3 veterinarians, 6 herdsmen, no laboratory workers and others 136 in the form of house wives, officers, student. This result is not in agreement with ***Asandaand Agbede (2001)*** which reported that veterinarians, farmers, slaughterhouse workers, meat inspectors, laboratory technicians, and animal handlers are at higher risk of exposure to Brucella organisms. Patients with brucellosis are known to appear normal and complain of many nonspecific symptoms***Wright SG2003.*** We think further studies to confirm the activity of brucellosis in such subjects with serological profile as above are required. Studies with western blotting have shown that active brucella infections are associated with persistence of antibodies to intracellular antigens of brucella (***Goldbaum FA. et al; 1993, & Kwaasi AA. et al; 2005***). Culture studies and detection of brucella deoxyribonucleic acid by ***polymerase chain reaction*** in the sera of subjects presenting with the serological profile of chronic brucellosis may also be useful in establishing the activity of brucellosis. It has been shown that successful therapy of brucellosis results in fall and eventual disappearance of IgG class of antibodies to brucella (***Mantur B. et al. 2010).***

CONCLUSIONS

Brucellosis is a febrile illness transmitted to man from animal reservoirs, and caused by different species of the brucella group of organisms. It is characterized by a series of febrile attacks accompanied by sweating, muscular Pains, arthritis and often an enlarged soft spleen. The peak incidence of brucella cases increase during summer months and increase among males than females especially in rural area. Prevention of brucellosis can be done by avoiding rawdairy food, wear gloves and boots when we deal with sick animals and vaccination of animals. Further studies on isolation and identification of organism from animals and patients would throw more light on the disease.

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CONFLICT OF INTEREST

Specific Authors Contributions

Professor Ibrahim M Abdel Aziz planned and designed the study, conducted patients' recruitment, clinical assessment, follow-up and data collection, data interpretation, sampling size and drafting of the manuscript. Professor Abdel Aziz has approved the final draft submitted.

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LIST OF ABBREVIATIONS

- ELISA: Enzyme ImmunoSorbant Assay. – UTI: Urinary Tract Infections.
- FUO: Fever of unknown origin - ESR: Erythrocyte sedimentation rate
- CBC: complete blood count - C-RP: C. Reactive protein. - Sig: Significant
- N.S: Non-significant. -US: Ultrasound. - STA: Standard Tube Agglutination Test.s
- HSM =Hepato-splenomegaly, - CNS=CentralNervous System, - CVS =Cardio-Vascular System.
- IgG: Immunoglobulin G.