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RESEARCH ARTICLE

SCREENING STUDY OF THE RELATIONSHIP BETWEEN TOXOPLASMOSIS AND ABORTION IN HAIL REGION, SAUDI ARABIA.

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Abstract

Background: Toxoplasmosis is one of the most common parasitic infections with variable prevalence in different countries caused by *Toxoplasma gondii*. The importance of toxoplasma mainly due to the risk of disease transmission during pregnancy and suggested its role in abortion. Chronic toxoplasmosis causes repeated abortion especially at first trimester.

Objective: This study aims to determine the proportion of women with Toxoplasmosis who experienced recurrent abortion among 2 years 1432 and 1433 and the relationship between the incidence of Toxoplasmosis and recurrent abortion in Hail with the effect of treatment.

Subjects and method: Data was collected from Maternity and Children's Hospital in Hail as a representative case in Hail, Saudi Arabia about women who had suffered from recurrent abortion (3 or more) among 2 years 1432 and 1433 and the seroprevalence of *Toxoplasma gondii* antibodies in pregnant women.

Results: indicate that the percentage of abortion due to toxoplasmosis in relation to total abortion due to different causes among 2 years (1432 & 1433) was found to be 2.85%. High percentage was found at first trimester (62.1%) followed by second trimester (31%) and then third trimester (6.9%). There is no significant difference between percentages either in year 1432 or 1433. High percentage of abortion due to *Toxoplasma gondii* was found in participant women with age of 25-45 years old.

Conclusion: We can conclude that it is of great importance to avoid raw or undercooked meat, preventing close contact with cats and early treatment from toxoplasmosis.

Introduction:-

Toxoplasmosis is a parasitic infection caused by *Toxoplasma gondii* (*T. gondii*) with variable prevalence in different countries. Some studies have suggested its role in abortion (Ebadi et al., 2011). There are three main routes of

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toxoplasma transmission through ingestion of raw or undercooked meats, exposure to oocyst-infected cat feces, and vertical transmission. (Elmore et al., 2010).

Detection of IgM antibody in a woman who had abortion indicates the possible role of *T. gondii* in abortion phenomenon in Ahfaz, Southwest of Iran 2015 (Saki et al., 2015). The seroprevalence of *T. gondii* antibodies in pregnant women varies from the 6.1 to 75.2 % based on the geographical region (Elsheikha, 2008). This prevalence is 7.6% in India, 15-41% in Africa, 21% in Pakistan and Bangladesh, 31% in Ireland, 33% in Caribbean, 55% in France and 46% in other European countries (Remington et al., 2006). Other authors found that (53.14%) of women with recurrent abortion and (69.35%) of women with neonatal deaths tested positive IgM antibody against Toxoplasma. Although spontaneous abortion due to congenital toxoplasmosis is well known, it is yet controversial that to what extent toxoplasmosis can cause habitual abortion (Ebadi et al., 2011). Also Toxoplasma antibodies detected by positive serological tests tend to be higher with increased age and parity it seems that they have no role in habitual abortion, the study conducted between January 2000 and May 2001 at King Hussein Medical Center (Qublan et al., 2002). Toxoplasmosis can be involved in etiology of abortion and stillbirth (Ghasemi et al., 2016). The results indicate that the Type II T. gondii is associated with ovine abortion (Chessa et al., 2014). Other study indicates that chronic toxoplasmosis, most probably is significant cause of repeated abortion, also found that toxoplasmosis has a significant relation to abortion at first trimester (Sahwi et al., 1995). Also a higher percentage of antitoxoplasma IgG antibodies positivity in women with repeated abortion than the control group (Ebadi et al., 2011). Other study presents evidence of Toxoplasma infection in Quasseem, Saudi Arabia and directs the attention that toxoplasmosis is an important cause of repeated abortion there (El-Sebai, 1991). There is a relatively high seroprevalence of acute Toxoplasma infection in pregnant women, with the potential for transmission of the parasite to the fetuses (Al-Mohammad et al., 2010). Other study mentioned that one of every three pregnant women in Aydin was at risk of toxoplasmosis at the first trimester of their pregnancy (Ertug et al., 2005). Another study found that the seroprevalence increased significantly with age and was higher in the lower socioeconomic strata (Rossa et al., 2008).

Mwambe, et al. (2013) found that *in Mwanza, Tanzania* about 30.9% were sero-positive for T. gondii-specific antibodies. Infection was higher in urban than those from rural communities (41.5% versus 22.0%). Also, employed women were more likely to get infection than peasants (40.0% versus 25.9%). The risk of infection was increased by 7% yearly also with increased woman's age.

Therapies are based primarily on spiramycin because of the relative lack of toxicity and high concentration achieved in the placenta (Han et al., 1999). The effect of treatment with spiramycin on 122 women with recurrent abortions and 55 women with neonatal deaths who had tested positive for IgM antibody, 115 (94.26%) in current abortion group and 35(63.64%) in neonatal death group delivered normal babies (Zargar et al., 1999). Another study recommended that spiramycin treatment be started as soon as possible once the diagnosis of maternal Toxoplasma infection during pregnancy is proved or strongly suspected, because a prolonged time interval between onset of infection and start of treatment seems to be associated with the presence of severe fetal lesions at the time of prenatal diagnosis (Hohlfeld et al., 1989). Another study found a weak evidence for an association between early treatment and reduced risk of congenital toxoplasmosis (Leproust et al., 2007). Spiramycin may reduce the risk of materno-fetal transmission by 60%, but is in the present doses without influence on an already infected fetus. Pyrimethamine in combination with sulfonamides eradicates more effectively parasites in the placenta, and also in the fetus (Stray-Pedersen, 1992). The early start of treatment resulted in a significant reduction in the number of severely affected infant (Foulon et al., 1999).

Aim of the study:-

This study aims to determine the proportion of women with Toxoplasmosis who experienced recurrent abortion among 2 years 1432 and 1433. Also to discover whether there is a relationship between the incidence of Toxoplasmosis and recurrent abortion in Hail and the effect of treatment on this proportion.

Subjects and methods:-

Data were collected about women who had suffered from recurrent abortion among 2 years (Muharam 1432 to Dhu Al-hijah 1433) by making a survey of the medical records in Maternity and Children's Hospital. The data collected were related to the woman age, Number of pregnancies, Number of abortions, causes of abortions, exposure to treatment (duration and type).

Data were analyzed by using the SPSS software package (Chicago, IL, USA), and the chi-square test was used to compare proportions of cases in Toxoplasmosis infection. A statistically significant difference was assumed when the $p < 0.05$.

Results:-

Data was collected from Maternity and Children's Hospital in Hail as a representative case in Hail, Saudi Arabia. In table 1, the number of pregnant women among years 1432 and 1433 H was about 15319 women, about 50% in each year. The number of newborns among the same 2 years was 11252. The number of cases admitted to abortion department was 4057, and the number of abortion due to different causes was 1014 (6.62%); 7.28% in 1432 and 5.98% in 1433 in relation to the total number of pregnant women. Percentage of abortion due to toxoplasmosis in relation to total abortion due to different causes among years (1432 & 1433) was found to be 2.85% (2.90% for 1432 and 2.80% for 1433).

Table 2 showed the seropositivity of anti-toxoplasma among 2 years, for IgG (86.2%), IgM (0%) and Mixed IgG & IgM (13.8%). In year 1432, 1433 the percentage of positive IgG (93.8% & 76.9%), IgM (0%) and Mixed IgG & IgM (6.2% & 23.1%) respectively. Women with positive antibodies for toxoplasmosis have abortion at different gestational age among years (1432 & 1433 H). High percentage was found at first trimester (62.1%) followed by second trimester (31%) and then third trimester (6.9%). There is no significant difference between percentages either in year 1432 or 1433 H (Fig 1).

Table 2 showed also the frequency of abortion due to toxoplasmosis among 2 years (1432 & 1433) was found to be 69% for women that have abortion for 1-2 times and 13.8% (3-4 times) and 17.2% (≥5 times). These percentages have some variations among years (1432 & 1433), women with abortion 1-2 times (62.4% & 76.9%) and abortion for 3-4 times (18.8% & 7.7%) and abortion for ≥5 times (18.8% & 15.4%) respectively (Fig 2).
Table 3 showed that the age of participant women varies from < 16 to > 45 years old. High percentage of abortion due to toxoplasma gondi was found in participant women with age of 25 – 45 years old. From age of 25 – 34 years old was found to be (41.4%) and from 35-45 years old was found to be 44.8% among 2 years 1432 & 1433. Low percentage was found in women with age of <16 – 24 years old (14.8%) and zero % in women with age >45 years old (Fig 3). Causes of toxoplasmosis among years 1432 and 1433 H was found to be due to cats (3.5%) and due to other causes (96.5%) like uncooked meat, water and others (table 3). Treatment with spiramycin or pyrimethamine in combination with sulfonamides eradicates more effectively parasites in the placenta, and also in the fetus (data not shown).

Discussion:-

The importance of toxoplasma from the perspective of public health is mainly due to the risk of disease transmission during pregnancy (Elsheikha, 2008). Between 350 and 1,000 HIV-infected persons with seropositive for toxoplasmosis and have impact of congenital and AIDS-related symptomatic toxoplasmosis on morbidity and mortality in Kyrgyzstan (Minbaeva et al., 2013).

In this study, the number of abortion due to different causes was 1014 (6.62%), 7.28% in 1432 and 5.98% in 1433 in relation to the total number of pregnant women. Percentage of abortion due to toxoplasmosis in relation to total abortion due to different causes among 2 years (1432 & 1433 H) was found to be 2.85% (2.90% for 1432 and 2.80% for 1433). Elsheikha et al., (2008) said that the seroprevalence of toxoplasma antibodies in pregnant women varies from 6.1% to 75.2% based on the geographical region. In pregnant women worldwide, there are seroprevalences of toxoplasmosis from 7% to 51.3% and in women with abnormal pregnancies and abortions the seroprevalences vary from 17.5% to 52.3% (Galvan-Ramirez, et al., 1995). The prevalence of anti-Toxoplasma antibodies in Japan was 10.3%, and it was significantly higher in women aged above 35 years (Sakikawa et al., 2011), and in pregnant women in Tanzania (Mwambe, et al., 2013). In year 2012, congenital toxoplasmosis was estimated in France at 2.58 per 10,000 live; births and 204 cases of congenital toxoplasmosis were observed (Nogareda et al., 2014).

Our finding reported that, the sero-positivity of anti-toxoplasma among years (1432, 1433), for IgG (86.2%), IgM (0%) and Mixed IgG & IgM (13.8%). Our result was higher than the result of Vado-Solís et al. (2013). They found in Yucatan, Mexico that, 55.2% of the samples were positive to IgG, (3.4%) to IgM, (8.6%) to IgG and IgM. It is also higher than that reported by Ashraf et al. (2010), they found 41.90 % were seropositive for anti T.gondii IgG and 11.88 % for anti T. gondii IgM. It is also higher than that reported by Al-Harthi, et al. (2006) among pregnant

women in Makkah (Saudi Arabia) was (29.4%) for anti-Toxoplasma IgG, (5.6%) for anti-Toxoplasma IgM. Other authors reported that among pregnant women in Hebron district (Palestine) was (27.9%) for anti-IgG and (17.6%) for anti-IgM (Nijem and Al-Amleh, 2009). Other authors reported lower prevalence of Toxoplasma IgG (17.9%) and Toxoplasma IgM (12.8%) in Gaza city (Al-Hindi, 2009).

In Accra, Ghana, Seropositivity was found to be 51.2 % pregnant women for IgG anti-*T.* gondii antibodies, but 0% for mixed IgG and IgM, (Ayi, et al., 2016). The result of Murata et al., (2016) indicate that serum of pregnant women were positive for IgG (50%), and for IgM (91.9%).

This study found that high percentage of abortion was found at first trimester (62.1%) followed by second trimester (31%) and then third trimester (6.9%). This result was in agree with the result of Zargar, et al. (1998) who found that 48% of the abortions had occurred in first trimester followed by 36% and 16% in second and third trimester respectively.

In the current study, the frequency of abortion due to toxoplasmosis among years (1432 & 1433 H) was found to be 69% for women that have abortion for 1-2 times and 13.8% (3-4 times) and 17.2% (≥5 times).

In this study, high percentage of abortion due to toxoplasma gondi was found in participant women with age of 25 – 45 years old. From age of 25 – 34 years old was found to be (41.4%) and from 35-45 years old was found to be 44.8% among 2 years 1432 & 1433. Low percentage was found in women with age of <16 – 24 years old (14.8%) and zero % in women with age >45 years old. Our findings were in agree with the study carried out in Makkah Al-Mukkarmah, the highest IgG and IgM seroprevalence were among participants aged 35 to 43 years (48.8% and 12% respectively) (Al-Harthi, et al., 2006). And also in agree with the study of Ashraf et al. (2010) in Sana'a, Yemen, participants women aged 31-40 years (45.3%), then age group 21-30 years 42.1%. found that toxoplasma antibodies detected by positive serological tests tend to be higher with increased age (Qublan et al., 2002). In Japan, the overall prevalence of anti-Toxoplasma antibodies was significantly higher in women aged above 35 years (Sakikawa et al., 2011).

Caroline Paquet, RM et al. (2013) stated that, spiramycin should be offered for fetal prophylaxis if pregnant women were infected but the infection not reached the fetus. Combined therapy of pyrimethamine, sulfadiazine, and folinic acid should be started with toxopasmosis infected women and fetus. Repeat testing should be performed within 2 to 3 weeks, if acute infection is suspected starting therapy with spiramycin immediately without waiting for the repeat test results. Moreover, treatment of pregnant women can modify the results of serological tests (Rodrigues, et al., 2014; Pomares and Montoya , 2016).

In this study, causes of toxoplasmosis among 2 years 1432 and 1433 was found to be due to cats (3.5%) and due to other causes (96.5%) like uncooked meat, water and others. On the other hand, Al-Hindi (2009) said that animal breading was reported for 33.3% of the aborted women. A history of raw meat intake, exposure to oocyst-infected cat feces, and vertical transmission was identified to be a risk factor related to toxoplasmosis (Skariah et al., 2010; Elmore et al., 2010; Sakikawa et al., 2011).

Recommendations:-

Our study showed a moderate seroprevalence of T. gondii antibodies among pregnant women in Hail, KSA. Hence we recommend the implementation of health extension program among pregnant women in order to prevent primary infection during pregnancy. Screening of women for Toxoplasma antibodies before and during pregnancy and periodic surveillance of the disease among population all over the country is also recommended. It is of great importance to avoid raw or undercooked meat, handling raw meat safely and preventing close contact with cats. Also, the early start of treatment with spiramycin or pyrimethamine in combination with sulfonamides resulted in a significant reduction in the number of severely affected infant.

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Table 1:- Correlation between the total numbers of pregnant women, number of abortion due to several causes, number of cases admitted to abortion department and the number of abortion due to Toxoplasma gondi in Maternity and Children's Hospital in Hail, Saudi Arabia.

Year of Investigation		Number of pregnant women	Number of newborns	Number of cases admitted to Abortion Department	Number of Abortion due to different causes	Number of Abortion due to Toxoplasma gondi.
1432 H	First 6 months	3734	2704	1030	266 [7.12%]	11 (4.14%)
	Last 6 months	3823	2726	1097	284 [7.43%]	5 (1.76%)
	Total	7557	5430	2127	550 [7.28%]	16 (2.90%)
1433 H	First 6 months	4012	3020	982	268 [6.68%]	5 (1.87%)
	Last 6 months	3750	2802	948	196 [5.23%]	8 (4.08%)
	Total	7762	5822	1930	464 [5.98%]	13 (2.80%)
Total 1432 & 1433		15319	11252	4057	1014 [6.62%]	29 (2.85%)

[ ] Percentage change from number of pregnant women.

( ) Percentage change from number of Abortion due to different causes.

Table 2:- Seropositivity of Anti- Toxoplasma IgG and IgM in relation to the gestational age of abortive women due to Toxoplasmosis infection and frequency of abortion among 2 years (1432 & 1433 H) in Maternity and Children's Hospital in Hail, Saudi Arabia.

Year of Investigation		Gestational age			Antibodies For Toxoplasmosis			Frequency of Abortion			Total
		1st Trimester	2nd Trimester	3rd Trimester	+ ve IgG only	+ ve IgM only	+ ve IgG + ve IgM	1 -2	3- 4	≥ 5	
1432 H	First 6 months	7 (63.6%)	4 (36.4%)	0 (0%)	10 (90.9%)	0 (0%)	1 (9.1%)	8 (72.7%)	1 (9.1%)	2 (18.2%)	11
	Last 6 months	3 (60%)	1 (20%)	1 (20%)	5 (100%)	0 (0%)	0 (0%)	2 (40%)	2 (40%)	1 (20%)	5
	Total	10 (62.5%)	5 (31.3%)	1 (6.2%)	15 (93.8%)	0 (0%)	1 (6.2%)	10 (62.4%)	3 (18.8%)	3 (18.8%)	16
1433 H	First 6 months	5 (100%)	0 (0%)	0 (0%)	4 (80%)	0 (0%)	1 (20%)	3 (60%)	1 (20%)	1 (20%)	5
	Last 6 months	3 (37.5%)	4 (50%)	1 (12.5%)	6 (75%)	0 (0%)	2 (25%)	7 (87.5%)	0 (0%)	1 (12.5%)	8
	Total	8 (61.5%)	4 (30.8%)	1 (7.7%)	10 (76.9%)	0 (0%)	3 (23.1%)	10 (76.9%)	1 (7.7%)	2 (15.4%)	13
Total 1432 & 1433		18 (62.1%)	9 (31.0%)	2 (6.9%)	25 (86.2%)	0 (0%)	4 (13.8%)	20 (69%)	4 (13.8%)	5 (17.2%)	29

( ) Percentage of cases from the total number of women with abortion due to *Toxoplasma gondi* infection.

Table 3:- Correlation between causes of abortion, women gestational age and participant's age in Maternity and Children's Hospital in Hail, Saudi Arabia among 2 years (1432 & 1433H).

Year of Investigation		Gestational Age			Abortive Women Age				Causes of Abortion		Total
		1st Trimester	3rd Trimester	2nd Trimester	<16 - 24	25 - 34	35- 45	>45	Cats	Others	
1432 H	First 6 months	7 (63.6%)	4 (36.4%)	0 (0%)	2 (18.2%)	4 (36.4%)	5 (45.4%)	0 (0%)	0 (0%)	11 (100%)	11
	Last 6 months	3 (60%)	1 (20%)	1 (20%)	0 (0%)	1 (20%)	4 (80%)	0	1 (20%)	4 (80%)	5
	Total	10 (62.5%)	5 (31.3%)	1 (6.2%)	2 (12.5%)	5 (31.2%)	9 (56.3%)	0	1 (6.2%)	15 (93.8%)	16
1433 H	First 6 months	5 (100%)	0 (0%)	0 (0%)	0 (0%)	3 (60%)	2 (40%)	0 (0%)	0 (0%)	5 (100%)	5
	Last 6 months	3 (37.5%)	4 (50%)	1 (12.5%)	2 (25%)	4 (50%)	2 (25%)	0 (0%)	0 (0%)	8 (100%)	8
	Total	8 (61.5%)	4 (30.8%)	1 (7.7%)	2 (15.4%)	7 (53.8%)	4 (30.8%)	0 (0%)	0 (0%)	13 (100%)	13
Total 1432 & 1433		18 (62.1%)	9 (31.0%)	2 (6.9%)	4 (14.8%)	12 (41.4%)	13 (44.8%)	0 (0%)	1 (3.5%)	28 (96.5%)	29

( ) Percentage of cases from the total number of women with abortion due to Toxoplasma gondi infection.

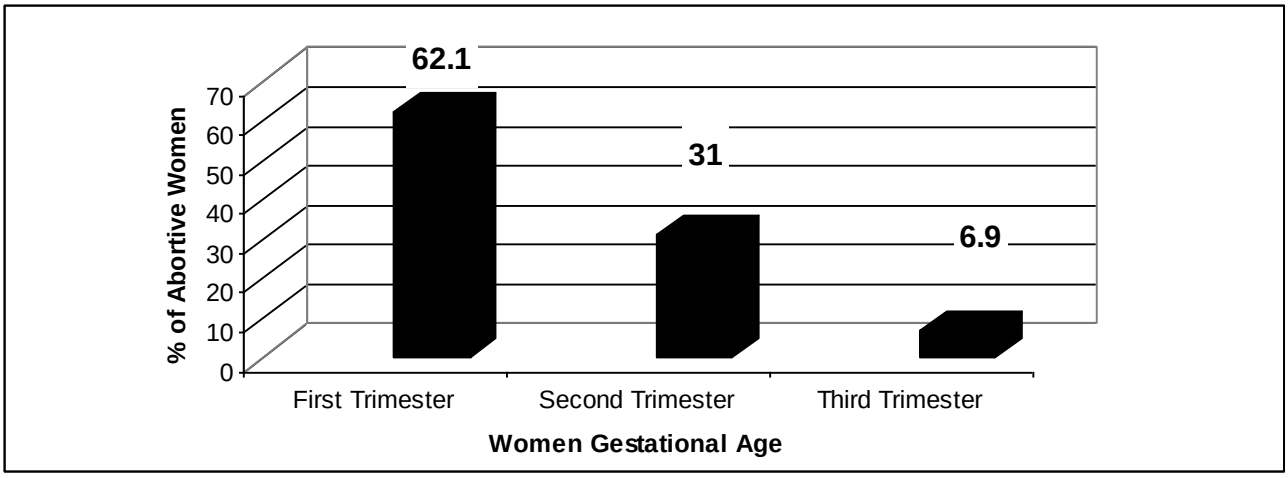

Fig 1:-Women with different gestational age of abortion due to Toxoplasma infection among years (1432 & 1433 H) in Maternity and Children's Hospital in Hail, Saudi Arabia.

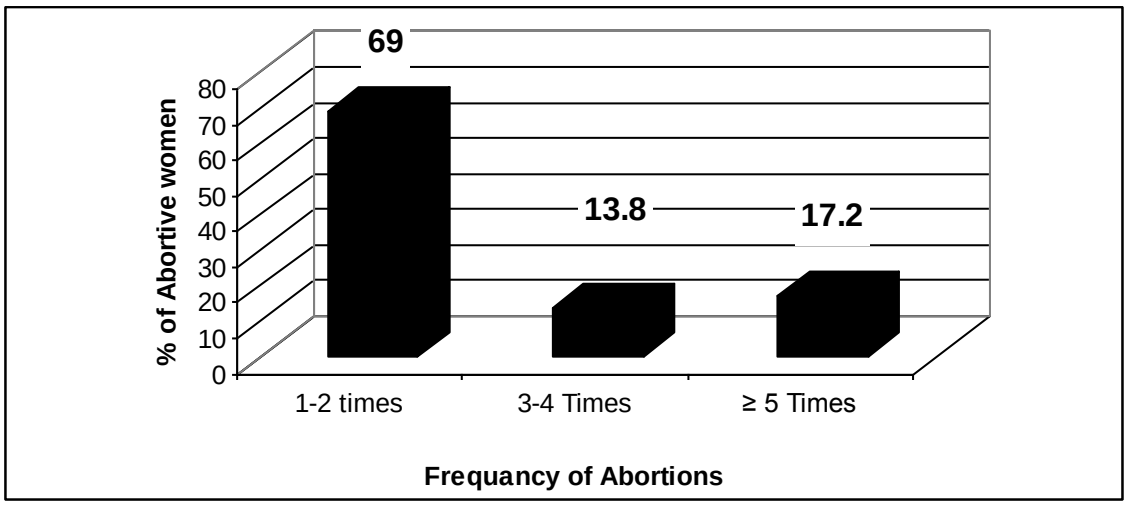

Fig 2:- Frequency of abortion due to Toxoplasma infection among 2 years (1432 & 1433 H) in Maternity and Children's Hospital in Hail, Saudi Arabia.

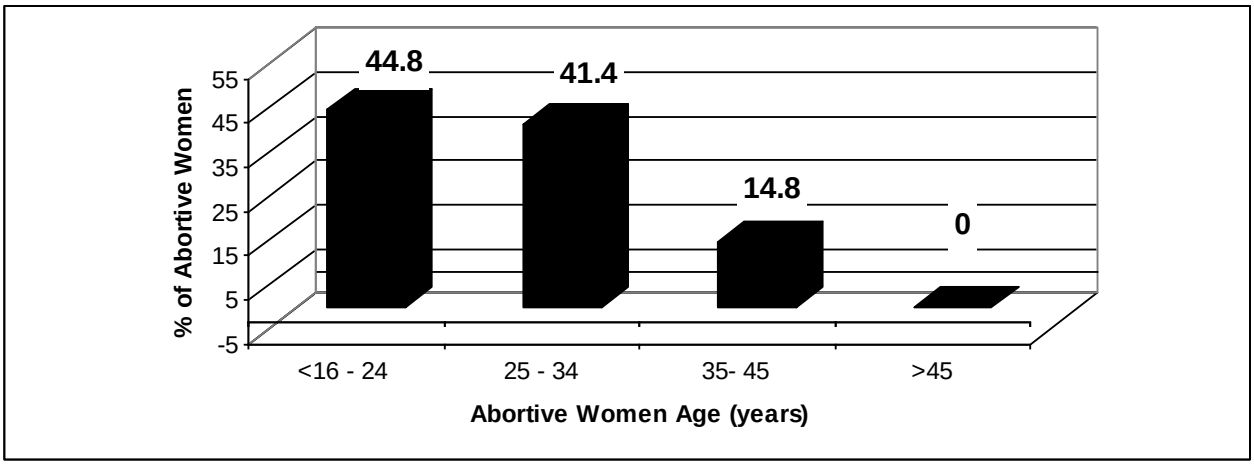

Fig 3:- Abortive Women Age due to Toxoplasma infection among 2 years (1432 & 1433 H) in Maternity and Children's Hospital in Hail, Saudi Arabia.

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