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Upper Gastrointestinal Cancer In Yemen: A hospital-based study

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Abstract

Background: The incidence of gastroesophageal cancer has shown a rapid change in several areas of the world. **Aim:** to determine the sub site distribution of upper gastrointestinal cancer among patients underwent endoscopic clinic at Al-Thowrah hospital, Sana'a city, Yemen. **Methods:** Descriptive, hospital based study was carry out to study the sub site distribution of upper gastrointestinal cancers in Yemen. 1006 patients referred to Al-Thawra hospital-Sana'a from several public and privet hospitals. All gastric and esophageal cancer patients diagnosed during the period from January 2008 and July 2012 were included in the study. All patients admitted to this study were studied according to clinical protocol consisting of a standard questionnaire, clinical examination and endoscopic findings. The questionnaire was included demographic characteristics and endoscopic findings. The data were analysis using statistical package for social sciences (SPSS, Version 18.0.) descriptive statistics were apply. **Results:** A total of 1006 patients with upper gastrointestinal cancers were identified, 31.2% of the patients were referred from Amran, followed by 26.8% from Sana'a and 25.9% from Saada. 54.7% of the patients' had EC and 43.3% had GC. Adenocarcinoma accounts for 46%. **Conclusion:** There were considerable variations in the sub site of upper gastrointestinal cancers in the Yemen.

Keywords: Cancer, Upper GI cancer, Gastric cancer, esophageal cancer, Yemen.

Introduction

Cancer is and will become an increasingly important factor in the global burden of disease in the decades to come. According to estimates from the International Agency for Research on Cancer (IARC), there were 14.1 million new cancer cases in 2012 worldwide, of which 8 million occurred in economically developing countries, which contain about 82% of the world's population. The corresponding estimates for total cancer deaths in 2012 were 8.2 million (about 22,000 cancer deaths a day)-2.9 million in economically developed countries, and 5.3 million in economically developing countries. The estimated number of new cases each year is expected to rise from 10 million in 2000 to 15 million by 2020¹.

Upper gastrointestinal cancer (UGIC) is a major contributor to mortality and morbidity worldwide. 952 000 new cases of gastric cancer in 2012 (6.8% of the total number of cancer cases), making it the fourth most common malignancy in men and the fifth most common in women worldwide. More than 70% of cases occurred in developing countries, and about half of the global total occurred in East Asia. GC was the third leading cause of cancer death in both sexes worldwide in 2012 (723 000 deaths, 8.8% of the total¹. GC shows regional variations because of differences in dietary patterns, and the prevalence of *Helicobacter pylori* infection². There has been a steady decline in recent years in most developed countries and in countries with high incidence rates

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in Asia³. GC is a multifactorial disease. A positive family history of gastric cancer has been associated with a two to three-fold increased risk of the disease, which suggests a genetic basis⁴. Diet is considered to play an important role in the occurrence of gastric cancer. Salty food and smoked or marinated food deficient in vitamins and antioxidants significantly increases the probability of gastric cancer^{4,6}. Vegetables, especially non-starchy and allium vegetables, fruits and pulses (legumes) decrease the risk of gastric cancer⁵, and green tea also reduces the risk.⁷

In Yemen, the knowledge about the UGIC remains poor, and there is little information available on this issue in the international literature. According to GLOBOCAN 2012, the incidence of gastric cancer in Yemen was 422 new cases per 100 000 (3.7% of the total number of cancer cases), making it the seventh most common malignancy in both sexes. In men, it was the sixth most common malignancy with 279 new cases per 100 000 (5.2% of the total) but in women, it was the 11th most common malignancy with 143 new cases per 100 000 (2.4% of the total)¹.

Aim of the study:

to determine the subsite distribution of upper gastrointestinal cancer in underwent endoscopic clinic at Al-Thowrah hospital, Sana'a city, Yemen.

Subjects and Methods

The study was conducted at Al-Thowrah Modern General Hospital (AMGH), Sana'a city, Yemen, endoscopic clinic. Al-Thowrah hospital is public and it is a referred hospital in Yemen AMGH provides primary, secondary and tertiary health care for the patients. A descriptive, hospital-based study was

conducted to study the subsite distribution of upper gastrointestinal cancers among Yemenis patients. In this study, we investigated 1006 patients underwent upper gastrointestinal endoscopy clinic from a different part of Yemen. All patients admitted to this study were studied according to clinical protocol consisting of a standard questionnaire, clinical examination, and endoscopic findings. The questionnaire was included the following: demographic and behavioral characteristics (age, sex, and provinces) and endoscopic findings. All patients with GC and esophageal cancer (EC) diagnosed during the period from January 2008 and December 2012, were included in the study. An essential inclusion criterion was that the patients were residing there for at least the last 10 years.

Endoscopic and pathologic tests were performed by the specialist team, according to the study protocol performed. Uniform endoscopic, criteria were used to define the tumor sub site. The subsite of esophageal tumors were recorded as upper, middle, or lower based on the endoscopy. If the location of the main tumor bulk was not obvious, the cancer was recorded as "esophageal". Non-cardia gastric cancer was defined as those were the center of the tumor was located over 2 cm distal to the gastro-esophageal junction. The gastro-esophageal junction was defined as the most proximal site of the gastric folds. Non-cardia gastric cancers were further divided into antrum, body, and fundus, according to the location of the main bulk of tumor⁹. If the main bulk was not obvious, the cancer was recorded as "gastric". Adenocarcinomas of the gastro-esophageal junction area were classified according to the WHO/IARC guidelines as a tumor

which crosses the gastro-esophageal junction regardless of the main site of the tumor bulk. Adenocarcinoma of the esophagus was located entirely above the gastro-esophageal junction, and adenocarcinoma of gastric cardia was located below the gastro-esophageal junction and was centered within 2 cm from the junction.

The data were loaded into a personal computer and statistical analysis was conducted using SPSS, Version 18.0. Copyright SPSS Inc., Descriptive statistics (frequencies, percent, and Mean \pm SD) was applied. Differences between variable measurements related to demographic characteristic were analyzed using ANOVA and Chi-square tests. P -Value <0.05 was taken as the level of significant.

Results

A total of 1006 patients' aged ranged from 18-96 years with a confirmed diagnosis of gastric and esophageal cancer were identified and the mean age was 63 \pm 12 years. There was no statistical difference with respect to the age of the patients and provinces (ANOVA= 2.7, P = 0.64). Male represented 667 (66.3%) of the total patients while female 339 (33.7%) (Ratio 2:1). There was no statistical differences in the sex between the provinces (χ^2 = 9.16, P =0.10).

Distribution of UGIC by Provinces

As regards, the distribution of upper gastrointestinal cancer among patients by provinces 314(31.2%) of the patients were

referred from Amran, 270 (26.8%) from Sana'a and 261(25.9%) from Saada. More details present in table 1.

Distribution of provinces by site of UGIC

Regarding to the distribution of provinces by sites of upper gastrointestinal cancer among patients, the data showed that there were 203(20.2%) with esophageal and 111 (11.0%) with gastric from Amran, followed by 102 (10.1%) with esophageal and 168 (16.7%) with gastric from Sana'a and 144 (14.3%) with esophageal and 117 (11.6%) with gastric from Saada. More details present in table 2.

Distribution of provinces by type of UGIC

The results of the study regarding the distribution of provinces by type of upper gastrointestinal cancer showed that, 88 (8.7%) with Squamous cell carcinoma, 111(11.0%) with Adenocarcinoma and 115 (11.4%) with A-S (Cardia of the stomach) from Amran followed by 58 (5.8%) with Squamous cell carcinoma, 176 (17.5%) with Adenocarcinoma and 36 (3.6%) with A-S (Cardia of the stomach) from Sana'a, and 47(4.7%) with Squamous cell carcinoma, 117 (11.6%) with Adenocarcinoma and 97 (9.6%) with A-S (Cardia of the stomach) from Saada. More details present in table 3.

Table 1: Distribution of upper gastrointestinal cancer by provinces

Provinces	Upper Gastrointestinal Cancer	
	F	%
Amran	314	31.2
Sana'a	270	26.8
Saada	261	25.9
Hajja	80	7.9
Taiz	35	3.5
Hadramout	3	0.3
Abian	10	0.9
Aden	12	1.2
Al-bida	10	0.9
Mareeb	6	0.6
Al-Guf	5	0.5
Total	1006	100

Table 2: Distribution of provinces by site of upper gastrointestinal cancer

Provinces	Site				Total	
	Esophageal		Gastric			
	F	%	F	%	F	%
Amran	203	20.2	111	11.0	314	31.2
Sana'a	102	10.1	168	16.7	270	26.8
Saada	144	14.3	117	11.6	261	25.9
Hajja	49	4.9	31	3.1	80	8.0
Taiz	22	2.2	13	1.3	35	3.5
Hadramout	2	0.2	1	0.1	3	0.3
Abian	7	0.7	3	0.3	10	1.0
Aden	7	0.7	5	0.5	12	1.2
Al-bida	6	0.6	4	0.4	10	1.0
Mareeb	5	0.5	1	0.1	6	0.6
Al-Guf	3	0.3	2	0.2	5	0.5
Total	550	54.7	456	45.3	1006	100

Table 3: Distribution of provinces by types of upper gastrointestinal cancer

Provinces	type of cancer						Total	
	Squamous cell carcinoma		Adenocarcinoma		A-S (Cardia of the stomach)			
	F	%	F	%	F	%	F	%
Amran	88	8.7	111	11.0	115	11.4	314	31.2
Sana’a	58	5.8	176	17.5	36	3.6	270	26.8
Saada	47	4.7	117	11.6	97	9.6	261	25.9
Hajja	38	3.8	30	3.0	12	1.2	80	8.0
Taiz	16	1.6	13	1.3	6	0.6	35	3.5
Hadramout	2	0.2	1	0.1	0	0.0	3	0.3
Abian	2	.2	3	.03	5	0.5	10	1.0
Aden	4	0.4	5	.5	3	.3	12	1.2
Al-bida	6	0.6	4	0.4	0	0.0	10	1.0
Mareeb	5	0.5	1	0.1	0	0.0	6	0.6
Al-Guf	3	0.3	2	0.2	0	0.0	5	0.5
Total	269	26.7	463	46.0	274	27.2	1006	100

Distribution of sex by site of UGIC

Out of 1006 patient, 523 (52.0%) were male had esophageal cancer and 144 (14.3%) had gastric cancer while 27 (2.7%) were female had esophageal cancer and 312 (31%) had gastric cancer. Table 4.

Distribution of sex by type of UGIC

Out of 1006 patient, 259 (25.7%) were male had squamous cell carcinoma, 329 (32.7%) had adenocarcinoma and 79 (7.9%) had A-S (Cardia of the stomach) while 10 (1.0%) were female had squamous cell carcinoma, 134 (13.3%) had adenocarcinoma and 195 (19.4%) had

A-S (Cardia of the stomach). Table 5.

Distribution of type of UGI C by Site

Out of 1006 patient had upper gastrointestinal cancer, 268 (26.6%) were esophageal cancer and had squamous cell carcinoma, 276 (27.4%) had adenocarcinoma and 6 (0.6%) had A-S (Cardia of the stomach) while 1 (0.1%) were gastric cancer and had squamous cell carcinoma, 187 (18.6%) had adenocarcinoma and 268 (26.6%) had A-S (Cardia of the stomach). Table 5.

Table 4: Distribution of sex by site of upper gastrointestinal cancer

Sex	Site of Upper GI Cancer				Total	
	Esophageal		Gastric			
	F	%	F	%	F	%
Male	523	52.0	144	14.3	667	66.3
Female	27	2.7	312	31.0	339	33.7
Total	550	54.7	456	45.3	1006	100

Table 5: Distribution of sex by type of upper gastrointestinal cancer

Type	Sex				Total	
	Male		Female			
	F	%	F	%	F	%
Squamous cell carcinoma	259	25.7	10	1.0	269	26.7
Adenocarcinoma	329	32.7	134	13.3	463	46.0
A-S (Cardia of the stomach)	79	7.9	195	19.4	274	27.2
Total	667	66.3	339	33.7	1006	100

Table 6: Distribution of type of upper gastrointestinal cancer by site

Type of upper GI cancer	Site of Upper GI Cancer				Total	
	Esophageal		Gastric			
	F	%	F	%	F	%
Squamous cell carcinoma	268	26.6	1	0.1	269	26.7
Adenocarcinoma	276	27.4	187	18.6	463	46.0
A-S (Cardia of the stomach)	6	0.6	268	26.6	274	27.2
Total	550	54.7	456	45.3	1006	100

Discussion

To the best of our knowledge, this was the first study which reported the distribution of UGI cancer among different provinces in Yemen. Mortality rates for gastric and oesophageal cancers have been changing dramatically over recent years. Incidence and mortality rates for GC have been declining for more than half a century. By contrast, EC is becoming more common. Tumours at the junction between the stomach and

the oesophagus are increasing particularly rapidly. All these cancers are more common among men than women⁸.

GC is the third most common malignancy in the world. Defining the exact origin of GC is sometimes difficult especially when the gastro-oesophageal junction is involved. This difficulty often leads to misclassification of cancers, especially those arising from the gastric cardia and the lower esophagus. The incidence of cancer of the gastric cardia and the lower esophagus has shown a rapid change in several areas of the world. This rapid change offers

a unique opportunity to study the etiology of these cancers. Many scientists are working on the epidemiologic characteristics of these changes in order to identify the etiologic factors. Thus, the exact determination of the sub site of origin of cancers and their epidemiology is very important.

In total, 550 cases of esophageal cancer (EC) and 456 cases of GC were referred to the endoscopic clinic at Al-Thowrah hospital, Sana'a City. Assuming that the proportion of UGI cancer cases referred to the endoscopic clinic was independent of tumour site, we can conclude that EC is approximately slightly higher as common as GC in our study. In addition, almost half of the GC cases occurred in the cardia of the stomach. A predominance of EC cases over GC cases and a large number of GC cases originating in the cardia are common findings in populations at high risk for EC, but are unusual findings for other areas of the world. For example in Linxian, China, another area with very high rates of EC, the EC: GC ratio is also greater than one but in most areas of the world, the opposite proportions are found⁹.

Relative to UGI cancer, EC was significantly more common in Amran, Saada and Sana'a provinces than other. Interestingly these areas are those where shamma and water pipe smoking are known to be widely prevalent. While gastric cancer was more in Sana'a, Saada and Amran. No data on substance use habits were available, future research could conduct whether these habits are associated more with UGI cancer. The disparity in the relative frequencies of upper GI cancers in different regions could be explained by variations in the environmental and geographical factors.

There are several reports that dietary, behavioral, life style and environmental factors may play a causative role in high-risk populations^{10,11}.

In our study the majority of the patients had upper GI cancers was male 66.7%. The reasons for such differences are not clear. Environmental or occupational exposures may play a role. For example, men have been historically more likely to smoke tobacco products, although elevated rates in men appear to persist even in countries where men and women have similar smoking patterns¹². Alternatively, sex differences may reflect physiological differences. Estrogens may protect against the development of GC. In women, delayed menopause and increased fertility may lower the risk of GC, whereas anti-estrogen drugs, e.g., tamoxifen may increase the rates of GC^{13,14}. These hormones may provide protection against GC during the fertile years of women but their effect is diminished after menopause, such that females develop GC in a manner similar to males, albeit with a 10 to 15 year lag after their male counterparts^{15,16}.

In our study EC was significantly more common in male 52% than female 2.7% while GC was significantly more common in female 31% than male 14.3%. However, the male preponderance seen in our result is not consistent with the fact that GC is more common in males as reported repeatedly in the literatures^{17,18,19}. In the neighboring gulf countries, the incidence of gastric cancer in males was approximately twice that of females. In Oman in 2006, GC was the most common cancer in men and the fourth most common cancer in women²¹, and the incidence has shown no apparent decline over the last decade. With improved longevity in Oman [20], the absolute burden of GC may become even greater in the future. GC is the fourth most common cancer worldwide²². Its poor prognosis makes it the second most frequent cause of cancer deaths. Incidence data show wide variation between nations²³. High incidence rates are recorded in Eastern Asia, Eastern Europe and South America. Conversely, Australia, North America, Western Europe and the Arab world have lower incidence rates. Oman, in contrast to the neighbouring Gulf Cooperation Council (GCC) countries, is estimated to have higher incidence rates. In Oman, stomach cancer is the most frequent neoplasm among males²¹. This problem, although known about, has not been explored.

A study done in Hadramout, Yemen, in 2006, showed that gastric cancer was the second most common type of gastrointestinal cancer after colorectal cancer. It was the sixth most common type of all cancers among men and the ninth among women⁸. In Yemeni society, the habit of chewing khat (*Catha edulis*) is highly prevalent among adults of both sexes and most of them start chewing in childhood²⁴.

Several studies reported that GC incidence rates vary wildly between men and women and across different countries. Rates are 2- to 3-folds higher in men than women²⁵. Comparing nations, the highest incidence rates are observed in East Asia, East Europe, and South America, while the lowest rates are observed in North America and most parts of Africa²⁶. Ecological and nutritional studies conducted by IARC and IPHR to establish the epidemiologic features and to investigate the aetiology of EC throughout the Caspian Littoral including Golestan Province²⁷ found geographical associations of incidence with a number of variables.

A subsequent case-control study investigated these associations further and established some risk factors, especially poverty and a restricted diet very low in fresh fruit and vegetables²⁸, factors that have since been shown to be associated with an elevated risk for oesophageal cancer in almost all countries where diet has been studied²⁹, but it found no clear evidence for other potential risk factors such as hot tea or nass consumption. However, the studies in Iran were discontinued due to the sociopolitical changes there in 1979, before the complete patterns of incidence and the full complement of risk factor results could be established.

Adenocarcinoma accounts (32.7%) for the highest number of GC with male preponderance. The large majority approximately (90%) of gastric cancers are adenocarcinomas, which arise from the glands of the most superficial layer, or the mucosa, of the stomach. Therefore, if not specified otherwise, our discussion of gastric cancer (GC) mainly pertains to adenocarcinomas. There are, however, other types of cancer arising from the stomach, including mucosa-associated lymphoid tissue (MALT) lymphomas, which

originate from the lymphoid tissue of the stomach, and leiomyosarcomas, which arise from the muscles surrounding the mucosa³⁰. Similar results was reported by Al-Samawi & Allawi³¹. Adenocarcinoma accounts, for the highest number of GC with male preponderance. This study is however, useful in highlighting the distribution of the histological types of GC in Yemen. The cause of the high incidence of GC and EC in our country is unknown. We strongly feel that supported research is needed as well as further environmental and immunohistochemical studies to find out the influence of genetic predisposition and local risk factors especially insecticides used in Khat agriculture.

Conclusion

We conclude that the largest report from Yemen identifying subsite involvement of upper GI cancers. The present analysis contradicts hospital-based study which reported higher relative frequencies of UGI cancer in all regions of Yemen. 31.2% of the patients were referred from Amran, followed by 26.8% from Sana'a and 25.9% from Saada. 54.7% of the patients' had EC and 43.3% had GC. Adenocarcinoma accounts for 46%. We observed different patterns of subsite involvement in different parts of Yemen. This difference could indicate different etiologies.

Recommendations

The importance of health education and increased awareness about risk factors. Further epidemiologic studies aimed at identifying the probable risk factors are required.

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Prevalence and associated factors of intestinal parasitic infection in basic school children in Sana'a Yemen.

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Abstract

Background: Intestinal parasitic infection is the most common endemic infection worldwide and represent major public health problems, mainly in developing countries like Yemen. **Aim:** The study aim is to identify the prevalence and associated factors of intestinal parasitic infection among basic school children in Sana'a city Yemen. **Methods:** A cross-sectional descriptive study involved 500 basic school children was conducted from April to May 2013. 500. Stool specimens were collected from all participants and examined for intestinal parasitic infection using direct microscopy, wet concentration method then sedimentation method. Data entered and analyzed using SPSS software. **Results:** The overall prevalence of intestinal parasite infection among the participants was 31.2% and it was higher in Azal district 35.5%. The predominant parasites was *Giardia Lambela* 48%. The highest prevalence of intestinal parasitic infection 34.4% was among participants from public school and lesser 10.4% among participants from private school. The result was statistically significant ($P < 0.001$). Prevalence of intestinal parasite infection was found among participants for illiterate mothers to be 35.1%, it was high 36% if there is only one bath room in house and the result was statistically significant ($P < 0.001$). Prevalence of intestinal parasite infection 63% was among participants who did not follow hand washing practice after defecation and the result was statistically significant ($P < 0.001$). Most of participants 70.6% don't have water supply during observation. **Conclusions:** Intestinal parasites were prevalent in varying magnitude among the schoolchildren. The prevalence of infections were higher for protozoa compared to helminthes. Measures including education on personal hygiene, environmental sanitation, water supply and treatment should be taken into account to reduce the prevalence of intestinal parasites.

Introduction

Intestinal parasitic infection is the most common endemic infection worldwide and the single worldwide cause of illness¹. Intestinal parasitic infection represents major public health problems, mainly in the tropical and subtropical regions². WHO estimated that 3.5 billion people are affected, and 450 million are ill as a result of these infections, the majority being children³. Intestinal parasitic infections constitute a global health burden causing clinical morbidity in 450 million people⁴. Poor environmental hygiene, poverty, and impoverished health services are closely associated with the high prevalence of intestinal helminthic infestations⁵.

Intestinal parasitic infections are one of the major health problems in several developing countries⁶. In developing countries, intestinal parasitic infections are common, varying from one country to another, depending on the socioeconomic status, degree of personal and community hygiene, sanitation and climatic factors. Intestinal helminthic infestations are most common among school age children, and they tend to occur in high intensity in this age group^{7,8}. Intestinal parasitic infection is relatively frequent among Yemeni people especially school age children⁹. In Yemen, intestinal parasitic infections are common varying from one area to another, depending on the degree of personal,

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community hygiene, sanitation and climatic factors¹⁰.

Several studies and surveys on intestinal parasitic infections in different localities such as Sana'a province and population such as children and restaurant workers had done and have shown a high prevalence rates¹¹⁻²¹. School children in Yemen form about 25% of the total population. In Yemen, there are still some areas, where epidemiological information regarding intestinal parasitic infection is lacking. Therefore, the aim of the study was to identify the prevalence and associated factors of intestinal parasitic infection among basic school children in Sana'a city.

Subjects and Methods

A descriptive, cross-sectional study was carried out among basic school children in Sana'a, the capital city of the Republic of Yemen from first of April to the end of May 2013. Sana'a city is at an altitude of 2,200 m above the sea level. Sana'a has a population of approximately 1,937,500 (2012), making it Yemen's largest city.

The sample size was calculated using Epi Info version 7.2. Based on the following assumptions (Reference population = 250000, expected frequency = 50% based on the average of finding of previous study²², precision 5%, CI 97%) to be 471, 6% of the calculated sample size had been added to overcome the possible dropout , so the actual sample size is 500 pupils. The multistage random sampling method was used to select the sample proportionately from 23 schools (15 public and 8 private schools). Sample was distributed according to the type of school proportionately. Four hundred thirty three school children from public schools and 67 school children from private schools were enrolled. Three classes were randomly selected from each school. Targets school children were selected following methods, 251 boys and 249 girls. Data were collected through pre-tested interviewer-administered structured questionnaire, obs-

ervation of school environment and stool analysis. The children were interviewed in their mother tongue. Selected school children for the study were interviewed to obtain information about demographic characteristics, habits and behavior such as washing hands before eating and after defecation. Observation of the school environments (availability of safe water) was carried out during the field visits to each school. Fecal specimens were collected at home in the morning and transferred to private specialized laboratory within 20 minutes and examined by direct microscopy, wet concentration method then sedimentation method. Data entered and analyzed using SPSS software version 18. Necessary approvals were obtained from general director of Sana'a educational office and directors of involving schools. Participation in the study was voluntary. Written consent from the parent of child was obtained from all participants prior to the study.

Confidentiality of gathered information was assured. Anti-parasitic drugs were provided for infected school children with any intestinal parasitic infection. Leaflets for increasing awareness of school children were distributed during field work in target schools.

Results

A total of 500 fecal samples were collected from participated school children. The response rate was 100%. The overall prevalence of intestinal parasitic infection among the participants was 31.2% (156/500). The prevalence of intestinal parasitic infection in studied directorates was 35.5%, 30.9%, 27.6% and 26% in Azal, AL-Safiah, AL-Tahreer and Old Sana'a directorates respectively. Results as shown in table 1.

Of all intestinal parasitic infections detected among participated school children, the most common parasite was *Giardia Lamblia* 48.1% followed by *Entamoeba histolytica* 46.2%. Details demonstrated in table 2.

Associated factors of intestinal parasitic infection in current study

Regarding the gender, there was no significant difference in prevalence of intestinal parasitic infection between males and females 32.7% and 29.7% respectively. Of the total 500 school children, the highest prevalence of intestinal parasitic infection was found among school children of age group 6-9 years 33.1%. However, this result was not statistically significant. Details are shown in table 3.

We found that the prevalence of intestinal parasitic infection was significantly higher among school children from public school 34.4% compared to children from a private school 10.5%. The result was statistically significant ($P < 0.001$). The vast majority of target school children's parents were educated 89.6% (fathers) and 63% (mothers). Intestinal parasitic infection was found among school children for illiterate parents to be 35.1% and 28.8% (mothers and fathers respectively). There was no significant difference in prevalence of intestinal parasitic infection according to the parents' education level of the school children ($P > 0.05$). For more details present in table 3.

Results showed that intestinal parasitic infections found among participated school children with rented houses 35.2%, while among school children with own houses 27.8%. There was no significant difference in prevalence of intestinal parasitic infection by house possession ($P > 0.07$).

We found that intestinal parasitic infections were 34.3% among school children if the number of rooms in their houses ≤ 3 rooms, while it was 27.3% if the number of rooms in their houses > 3 rooms. There was no significant difference in prevalence of intestinal parasitic infection according to the No. of rooms ($P > 0.09$). The results showed a high prevalence of intestinal parasitic infections 36% if there is only one bathroom in house whereas more than 1 bathroom it was

10.8%. The result was statistically significant ($P < 0.001$). For more details see table 3.

Intestinal parasitic infections were found more common among those school children who used unsafe water for drinking and other purposes 34% in comparison to others 29.5%. There was no significant difference in prevalence of intestinal parasitic infection according to the source of water supply ($P > 0.05$). Results as shown in table 3. The current study found that the number of school children who don't wash their hands before eating was 41 children 8.2% while those who wash their hands before eating were 459 children 91.8%.

The study showing that washing hands before eating is associated with decreased exposure of intestinal parasitic infection. The prevalence of intestinal parasites among school children who wash their hands before eating was 30.3%, while it was 41.5% among those who don't wash their hands before eating. There was no significant difference in prevalence of intestinal parasitic infection according to the washing hands before eating of the school children ($P > 0.05$).

This study found that 94.8% of school children wash fruits and vegetable before eating in comparison to 5.2% of school children who do not wash. Prevalence of intestinal parasitic infection decrease among those who are washing fruits and vegetables before eating 29.9%, in comparison to those who have a habit of eating unwashed fruits and vegetables before eating 53.8%. There was no significant difference in prevalence of intestinal parasitic infection according to the washing fruits and vegetables before eating ($P > 0.05$). Table 3.

Intestinal parasitic infections were found more commonly among those school children who did not follow hand washing practice after defecation 63%, in comparison to others who wash hands after defecation 20.2% and the result was statistically significant ($P < 0.001$). Table 3.

Table 1: Prevalence of intestinal parasitic infection by districts.

Districts	Studied	Infected	%
Azal	180	64	35.6
AL-Safiah	149	46	30.8
AL-Tahreer	94	26	27.7
Old Sanna'a	77	20	25.9
Total	500	156	31.2

Table 2: Prevalence of intestinal parasitic infection by types of parasite.

The parasite	No	%
Ascaris Lumbricoides	2	1.3
EntrobiumVermicularis	1	0.6
Hymenolepis Nana	5	3.2
Taenia species	1	0.6
Entamoeba Histolytica	72	46.2
Giardia Lamblia	75	48.1
Total	156	100

Table 3: Factors associated of intestinal parasitic infection in the current study.

Factors	Studied	Infected	%	P-value
Gender				
• Male	251	82	32.7	0.476
• Female	249	74	29.7	
Age group				
• 6-9	133	44	33.1	= 0.909
• 10-13	298	94	31.5	
• 14-16	69	18	26.1	
Type of school				
• Public	433	149	34.4	< 0.001*
• Private	67	7	10.5	
Mothers' educational level				
• Literate	315	91	28.9	= 0.145
• Illiterate	185	65	35.1	
House possession				
• Own	270	75	27.8	= 0.07
• Rented	230	81	35.2	
No. of rooms				
• ≤ 3 rooms	277	95	34.3	= 0.09
• > 3 rooms	223	61	27.3	
No of bathrooms				
• 1 bathroom	325	117	36	< 0.001
• > 1 bathroom	175	19	10.8	
Source of water supply				
• Pipe	318	94	29.5	= 0.29
• Other (tankering / whvet + pool)	182	62	34.1	
Hand washing practices before meal				
• Yes	459	139	30.3	= 0.138
• No	41	17	41.5	
Washing fruits and vegetables before eating				
• Yes	474	142	29.9	= 0.0104
• No	26	14	53.8	
Washing of hands after defecation				
• Yes	489	99	20.2	< 0.001
• No	11	7	63	

** Statistically significant results*

By observation schools water supply and checking school children for nails cutting during filed work following results were observed: Lack of water supply was found in 69.6% of target basic schools while 30.4% of target basic schools have water

supply.

The prevalence of intestinal parasitic infection was high 40.6% among school children with bad finger nails condition, while it was 14.4% among another group. The result was statistically significant ($P < 0.001$). Results illustrated in table 4.

Table 4: Prevalence of intestinal parasitic infections according to nails condition

Finger nails condition	Studied	Infected	%	P. value
Good	180	26	14.4	< 0.001*
Bad	320	130	40.6	

**Statistically significant results*

Discussion

Intestinal parasitic infections have been recognized as one of the most significant causes of illnesses worldwide. This study attempted to show the prevalence and the associated factors for the prevalence of intestinal parasitic infection among basic school children in Sana'a city.

In the present study, the overall prevalence of intestinal parasitic infection among basic school children was found to be 31.2%. It was different from previous studies conducted in different parts of Yemen. For example in Sana'a studies conducted in 1985 and 2013 showed a high prevalence of intestinal parasitic infection 53%¹¹ and 54.8%¹² than that current study was found and the result was slightly higher than the results reported in 2003 27.5%¹⁶. The present study was in agreement with the study conducted by Alyousfi et al. in 2011 30.9%²¹. Studies conducted in Hadhramout observed that the prevalence of intestinal parasitic infection was 37%¹⁴, 28.7%¹⁸ and 58.7%²⁰.

The studies conducted in other countries of the region reported different results, some of them were in agreement with current study and others were lower or higher than current study, for instance, in Oman 38.7%²³, in Egypt 22.43%²⁴, in Saudi Arabia 33.8 %²⁵, in Iraq 57.9%²⁶, and it extended 70% in Sudan²⁷, 31.8% in

Turkey²⁸, 63.9% in India²⁹, 79.8% in Ethiopia³⁰ and in 84% Colombia³¹.

These variations in prevalence might be due to differences in climatic conditions, geographical factors in the studied areas, poor hygiene, environmental sanitation, socioeconomic and behavioral factors in the residents, educational status of parents and study subjects and previous control efforts. *Giardia lamblia* and *Entameba histolytica* were the first a 48.1% and the second 46.2%, most common protozoa in the present study, both can be transmitted orally through drinking water.

However, the prevalence of *Giardia lamblia* detected in this study was higher than that previous studies in Yemen: it was 10.2%¹¹, 16.1%¹², 20%¹⁴, 17.7%¹⁶, 19.17%²⁰, 16.7%²¹.

The studies conducted in other countries revealed the lower prevalence of *Giardia lamblia* for example: in Oman 10.5%²³, in Egypt 4.46%²⁴, in Saudi Arabia 12.5%²⁵, in Iraq 31%²⁶, in Sudan 12.3%²⁷.

Also, the prevalence of *Entameba histolytica* detected in this study was higher than that previous studies reported for this parasite in Yemen: it was 10.2%¹¹, 21.5%¹², 15.9%¹⁴, & 16.7%¹⁶, 16.83%²⁰, and 17.1%²¹.

The studies conducted in other countries of the region revealed the lower prevalence of *Entameba histolytica* for

example: in Oman 24%²³, in Egypt 23%²⁴, in Saudi Arabia 8.3%²⁵, in Iraq 24.3%²⁶, and in Sudan 0.4%²⁷.

This high prevalence of both protozoa in the current study because all the school children share more or less the same environmental conditions which allowed the transmission and persistence of the parasites. These environmental factors which were observed during this study include lack of water supply in 69.6% of target schools, inadequate sanitation, poor hygiene, improper use of toilets similarity in socio-cultural behavior of the school children. Others intestinal parasites were of low prevalence.

As regard to the gender, the prevalence of intestinal parasitic infection among boys and girls in this study was 32.7% and 29.7% respectively showing that both genders are equally susceptible to infection. The difference was not significant ($P > 0.05$). This result was less than reported in Iraq 59.9% and 56.2%²⁶ and the study conducted in Ethiopia 51.6% and 48.4%³⁰ among boys and girls respectively. This high prevalence associated with males may be due to the fact that they are more often engaged in predisposing activities such as playing in unhygienic playing fields and eating with unwashed hands.

Although the youngest age group (6-9 years) of schoolchildren was more affected 33.1%, the difference between this age group and other age groups (10-13 years) and (14-16 years) was not statistically significant P value = 0.909 and 0.306 respectively. In contrast, another study in Iraq reported that the prevalence was found to be more 71.4%²⁶ in age group (6-11 years). This is maybe because children in these age groups often spend more of their leisure time outdoors, playing and or seeking in garbage dumps. They are also more often in contact with soil and eat indiscriminately with unwashed hands and this could be due to the fact that as the child grows older the exposure to different risk factors for

intestinal parasite infection increases.

Regarding the type of school, the school children in public basic schools were more infected 34.4% than the school children in private basic schools 10.5% with statistically significant difference P -value < 0.001 . This might be because Public basic schools are not providing social services such as water system facilities to the public schools to ensure total eradication of intestinal parasitic diseases. Also, private schools take care of the children more than in public schools.

Current study observed that the prevalence of intestinal parasites was higher among school children of illiterate mothers 35.1% than school children of literate mothers 28.9%. There was no significant difference in prevalence of intestinal parasitic infection according to the mother's education level of the school children ($P > 0.05$). This result is in agreement with a study conducted in Turkey (42.6% and 29.4%)²⁸, it was notably high in a study conducted in Ethiopia (57.8% and 42.2%)²⁹ and in India (68.4% and 41.2%)²⁹. The relation between a child's health and mother's education is well known. Health indicators of children whose mother's education level is lower are always worse.

This study showed a high prevalence of intestinal parasitic infections 36% if there is only one bathroom in house whereas more than 1 bathroom it was 10.8%. The result was statistically significant ($P < 0.001$).

School children who don't practice washing hands before meal more exposed to get intestinal parasites. This study found that the prevalence of intestinal parasites was 41.5% in school children who are not washing hands before eating. This result was in agreement with a study conducted in rural Sana'a rural area by Al-Mekhlafi et al¹² and was in disagreement with the study conducted in Ethiopia 53.6%³⁰.

In this study, the prevalence of intestinal

parasites was high in school children who eat raw fruits and vegetables without washing them 53.8%, while it was 29.9% among another group of school children who wash fruits and vegetables before eating with significant difference ($P=0.0104$). This result was in agreement with a study conducted in rural Sana'a rural area by Al-Mekhlafi et al.¹² and in Ethiopia 77.9%³⁰. This confirms that contaminated hands or foods can play a vital role in transmission wide range of parasites through fecal-oral route. This is probably due to low knowledge of children about the fecal-oral transmission. Washing of hands after defecation was found to be significant risk factor for intestinal parasitic infection ($P<0.001$), the prevalence of intestinal parasites was found more common in those school children who did not follow hand-washing practice after defecation 63%, while it was 20.2% among school children who wash hands after defecation. A similar high result was found in India 74.36%²⁹. Intestinal parasitic infections were found more common among those school children who used unsafe water for drinking and other purposes 34% in comparison to others 29.5%. There was no significant difference in prevalence of intestinal parasitic infection according to the source of water supply ($P>0.05$). This is because Intestinal parasitic infections can be transmitted orally through drinking and use unsafe water.

Prevalence of intestinal parasitic infection was high 40.6% among school children with bad finger nails trims. Similar trend has been reported by Al-Mekhlafi et al.¹² and Shrestha et al. 33.3%³³. The effect of socioeconomic status on risk of intestinal parasitic infections could be attributed to several other factors such as lack of access to safe water, poor hygienic environment, lack of access to education due to financial constraints and overcrowded conditions³⁴.

Conclusion

In conclusion, this study indicates that

intestinal parasites are remarkable among school children in Sana'a city especially among public schools, those who do not wash fruits and vegetables before eating, those who do not wash hands after defecation, and those with bad nails condition.

Recommendations

Much work remains to be done to improve the health of the school children. Measures including education on personal hygiene and environmental sanitation, water supply and treatment should be taken into account to reduce the prevalence.

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Impact of duration of Infertility on the Physiological Viability of Sperms Preparing for Intrauterine Insemination among Yemeni Infertile Males

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Abstract

Background: The duration of infertility should be considered as a factor that may affect the outcome of assisted reproductive techniques (ART). **Aim:** The aim of this descriptive study was to examine the outcome of infertility treatment in relation to duration of infertility. **Methods:** Sixty nine couples from Allow in vitro fertilization center (IVF) were involved in this work. Intrauterine insemination (IUI) had been done for all couples using the same ART. **Results:** The mean age of men was 29.37 ± 0.16 years and the duration of infertility was 4.38 ± 0.25 years with range of 1-12 years. Higher pregnancy and life-birth rates were demonstrated in males suffering from infertility for less than 4 years as compared to those who had infertility for more than 10 years ($P < 0.003$, $r = -0.869$). Moreover, abortion rate was higher in men who had infertility for more than 10 years as compared to those who have infertility for less than 4 years ($P < 0.0014$). The linear life-birth rate, in both IVF centers, shows decrease by increase in the duration of infertility. **Conclusion:** The researchers conclude that by increase in the duration of infertility the outcome of assisted reproductive techniques –IUI will be decreased markedly. In addition to the duration of infertility, the present work recommended to consider the different techniques of sperm preparation in relation to the ART outcome.

Key words: Infertility, ART, IUI, Life Birth Rate.

Introduction

Infertility is defined as inability to conceive after 1 year of un-protective intercourse^{1,2}. Pregnancy represents the successful and timely conclusion of series of physiological events: ovulation of a mature oocyte, production of viable sperm, association of oocyte and sperm in the reproductive tract, making of a viable embryo, embryo carriage into the uterine cavity, and embryo implantation within the endometrial cavity. Any disruption in these essential steps will lead to infertility³.

⁴. Secondary infertility is defined as the inability to become pregnant, or to carry a pregnancy to term, following the birth of one or more biological children³. About 30% of the infertile cases are solely attributed to the male partner, 30% to female partner, 25% of cases are caused by a combination of male and female factors and about 15% unexplained infertility^{5, 6}. Most of the infertility treatments are dependent on the underlying cause of infertility⁷. Some infertile couples nevertheless need more complex medical intervention like ARTs which is

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referred to many methods designed to overcome barriers to natural fertilization^[8]. Over all, the estimated number of infertile patients treated by ART is around 20%. The goal is to increase the success rate of ART both in term of achieving pregnancy and in making sure that the pregnancy result in a genetically healthy individual^[9]. The duration of infertility should be considered as a factor that may affect the outcome of ART. It is unclear the effect of duration of infertility on the outcome of infertility treatment especially semen characteristics of infertile males undergoing IUI, and this subject, in general, is not completely understood.

Aim of the study: To examine, retrospectively, the outcome of infertility treatment in relation to duration of infertility in infertile couples from two different centers.

Subjects and Methods

Sixty nine couples from “Allow IVF Center”, Sana’a - Yemen was involved in this study. All couples were evaluated by the infertility consultant and their medical history was recorded. Semen sample was obtained by masturbation with collection of the ejaculate into a clean, dry, sterile and wide mouthed Petri-dish; this was done after 3-5 days of abstinence. The container was labeled with date and time, names of patient and his wife, and their file number. The sample was transported to the laboratory immediately and placed in an incubator at 37°C till complete liquefaction. A drop of 10µL of liquefied and thoroughly mixed semen was taken by Eppendorff automatic pipette, mounted between warm slides and covered with a standard cover slip (22×22) mm. The sample was examined by light microscope under magnification of

40X objectives. The semen was analyzed macroscopically and microscopically using the standardization of World health Organization^[10].

The male factor infertility had been treated by conventional treatment of male infertility and involved in the ART. IUI had been done for all couples involved in the present study using the same ART^[3]. The overall outcome of this treatment had been analyzed in correlation to their duration of infertility.

Analysis were used depending on the nature of the data. In addition to standard statistical methods to determine the mean, standard deviation and standard error of mean (SEM), a typical type of students paired T-test, Chi-square, and Kruskal-Wallis one-way analysis of variance were used for analysis of data. Correlation coefficients were calculated according to Pearson. Data were analyzed using statistical package for the social sciences SPSS 20.5; Inc. Chicago, IL). A power of measurement was considered more than 80% and P-value of less than 0.05 ($P < 0.05$) was as well considered statistically significant.

Protocol of the present study was conducted in compliance with human care standards outcome of Allow IVF center and approval of the Ethical Committee of the Faculty of Medicine and Health Sciences. Informed consent was obtained from each participant in the study, confidentiality of gathered information was granted

Results

The mean age of the recruited 69 infertile couples was 29.37 ± 0.16 years and the mean duration of infertility was 4.38 ± 0.25 years. The semen samples had been obtained from infertile males and seminal fluid analysis (SFA) was done depending on

World Health Organization (WHO) recommended criteria. The percentage of infertile couples with secondary infertility was 76%.

Table (1) showed the parameters of seminal fluid analysis for infertile males classified according to age groups. It was noticed that the highest sperm concentration (million/mL) was within the two age groups (30-39) years (43.29 ± 1.57) and age group (40-49) years (45.11 ± 2.83). Regarding the percentage of sperm motility, best results were obtained within the same two age groups (30-39) years (65 ± 1.37) and (40-49) years (63.69 ± 3.01). A significant difference ($P < 0.05$) was observed in the percentage of progressive sperm motility grade (A), the best results were noticed among age group (40-49) years (10.23 ± 2.13) and the lowest

values were in the age group ≥ 50 years (0.83 ± 0.83). The best results regarding the percentage of progressive sperm motility grade (B) were noticed in the age group (30-39) years (34.94 ± 1.24) and the lowest values were in age group ≥ 50 years (25.83 ± 6.11). The overall percentage of sperm progressive motility (grade A+B) showed a significant difference ($P < 0.01$) with highest percentage in age groups (30-39) years (41.78 ± 1.6), (40-49) years (41.14 ± 3.22) and the lowest value was among age group ≥ 50 years (26.67 ± 6.54). Furthermore there was a significant difference ($P < 0.01$) regarding the percentage of normal sperm morphology. However, the highest results were within age group (30-39) years (52.37 ± 1.5) compared with the lowest results in the age group ≥ 50 years (40 ± 2.58).

Table 1: The mean of sperms' parameters for infertile males classified according to age group.

Sperm parameters		20-29 years No. 25	30-39 years No. 90	40-49 years No. 35	>50 years No. 6
Sperm concentration (million/mL)		33.88 ± 2.49	43.29 ± 1.57	45.11 ± 2.83	34.17 ± 5.23
Sperm motility (%)		56 ± 2.89	65 ± 1.37	63.69 ± 3.01	57.5 ± 4.43
Sperm grade activity (%)	A	3.4 ± 1.31	6.78 ± 1.06	10.23 ± 2.13	0.83 ± 0.83
	B	29.2 ± 2.91	34.94 ± 1.24	30.91 ± 2.3	25.83 ± 6.11
	C	23.4 ± 1.73	23.5 ± 1.01	22.29 ± 1.61	30.83 ± 3.27
	D	43.6 ± 2.85	34.78 ± 1.31	36 ± 3.02	42.5 ± 4.43
Progressive sperm motility (%)		32.6 ± 2.92	41.78 ± 1.6	41.14 ± 3.22	26.67 ± 6.54
Normal sperm morphology (%)		44.6 ± 2.31	52.37 ± 1.5	46.97 ± 2.45	40 ± 2.58
Sperm agglutination (%)		6.52 ± 1.55	8.22 ± 1.14	12.03 ± 2.33	5 ± 3.42
Round cells count		4.56 ± 1.1	5.46 ± 0.71	7.11 ± 1.36	10.5 ± 4.99

Number of infertile males classified according to duration of infertility is showed in figure 1. It was clear that the largest group of infertile males was with duration of infertility 3-4 years, then the group with duration of infertility 5-6 years. The smallest group 95/69) was observed for infertile

males with duration of infertility ≥ 10 years. Although little variations were assessed for seminal fluid parameters among different groups of infertile males classified according to duration of infertility (Table 2), but it was observed that the percentage of sperm progressive motility grade (A+B)

(32.22±6.62) and percentage of normal sperm morphology (44.78±5.43), were the lowest among the group with duration of infertility >11 years. Moreover, the percentage of sperm The outcome of IUI for infertile males including pregnancy, life birth and abortion rates were demonstrated in the figure 2.

The higher pregnancy and life-birth rates were showed in those males suffering from infertility for duration

agglutination (12.22±4.34) and assessed counts of round cells (6.33±2.58) were with highest results in the group of >11 years duration of infertility.

less than 4 years in compare to those who have duration more than 10 years (P<0.003, r=-0.869). Abortion rate was observed in those men who have duration more than 10 years in compare to those who have duration of infertility less than 4 years (P<0.0014).

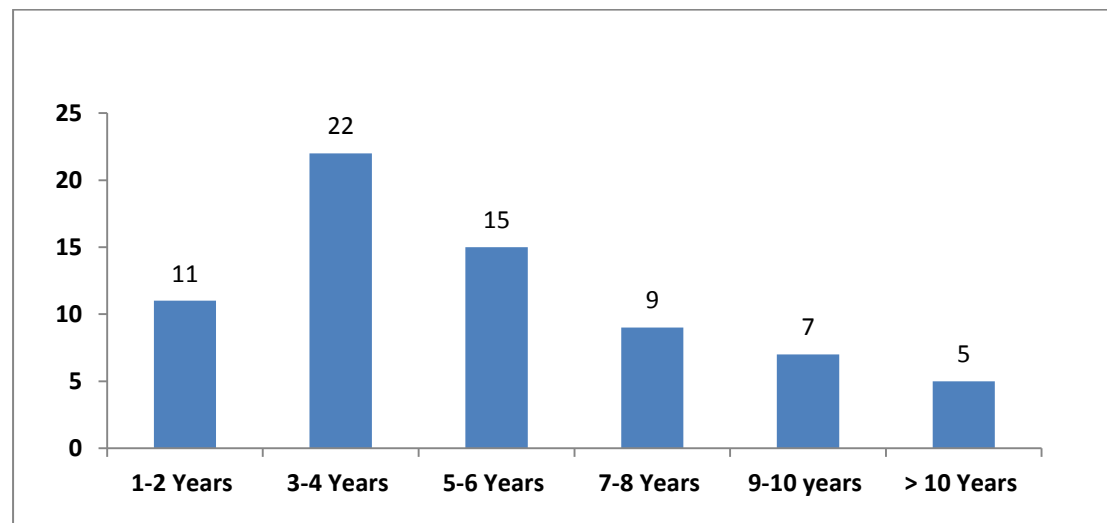


Figure 1: Number of infertile men according to the duration of infertility.

Table 2: The mean of sperm parameters for infertile males classified according to duration of infertility.

Sperm parameters		1-2 years No. 22	3-4 years No. 47	5-6 years No. 32	7-8 years No. 15	9-10 years No. 17	>10 years No. 19
Sperm concentration (million/mL)		42.58±3.77	42±1.86	41.89±2.33	40.22±5.02	42.13±3.19	32.33±4.25
Sperm motility (%)		62.08±2.31	64.31±1.66	63.89±2.3	61.11±4.78	63.44±4.49	45±6.87
Sperm grade activity (%)	A	6.25±1.48	5.67±1.17	7.44±1.8	8.33±3.79	7.5±2.96	4.22±3.45
	B	34.17±2.23	34.71±1.73	32±2.07	30±3.68	32.19±3.32	25±4.93
	C	21.67±1.72	23.94±1.25	24.17±1.68	23.89±2.64	23.75±2.44	22.78±2.9
	D	37.92±2.31	35.48±1.63	35.83±2.3	37.78±4.32	36.56±4.49	45±6.87
Progressive sperm motility (%)		39.58±2.79	40.87±1.92	39.44±2.75	38.33±5.59	39.69±4.29	32.22±6.62
Normal sperm morphology(%)		47.83±2.71	50.12±1.62	51.25±1.83	51.94±4.84	45.31±4.71	44.78±5.43
Sperm agglutination(%)		9.43±3.11	8.2±1.53	8.49±1.38	7.11±2.25	8.93±3.02	12.22±4.34
Round cells count		5.04±1.84	6.9±1.05	5.61±0.96	3.83±1.47	5.27±1.18	6.33±2.58

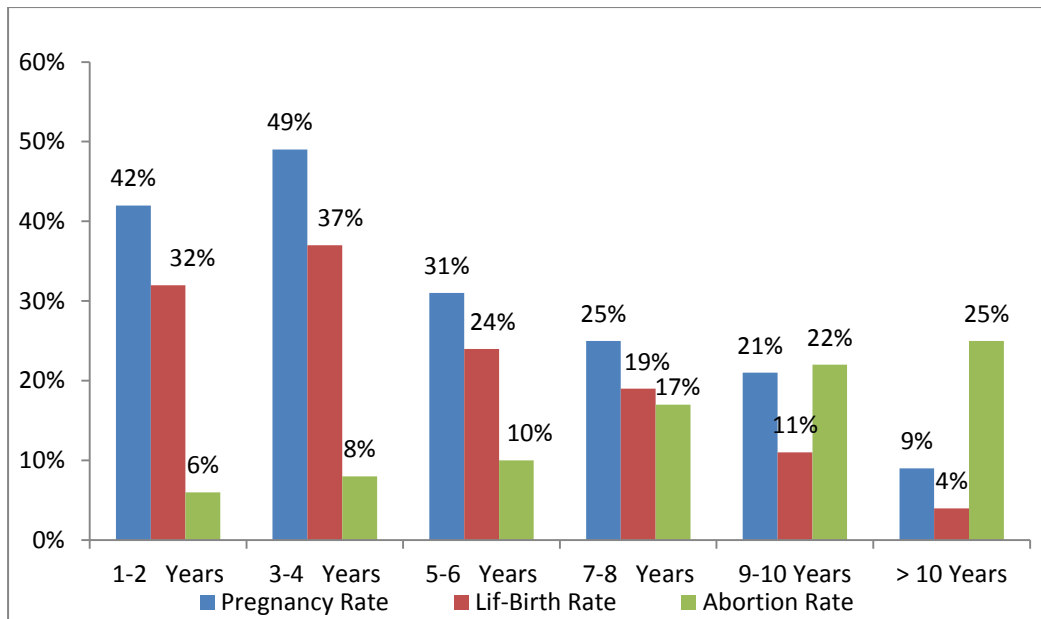


Figure 2: Pregnancy, life-birth and abortion rates, after IUI, among infertile males according to duration of infertility.

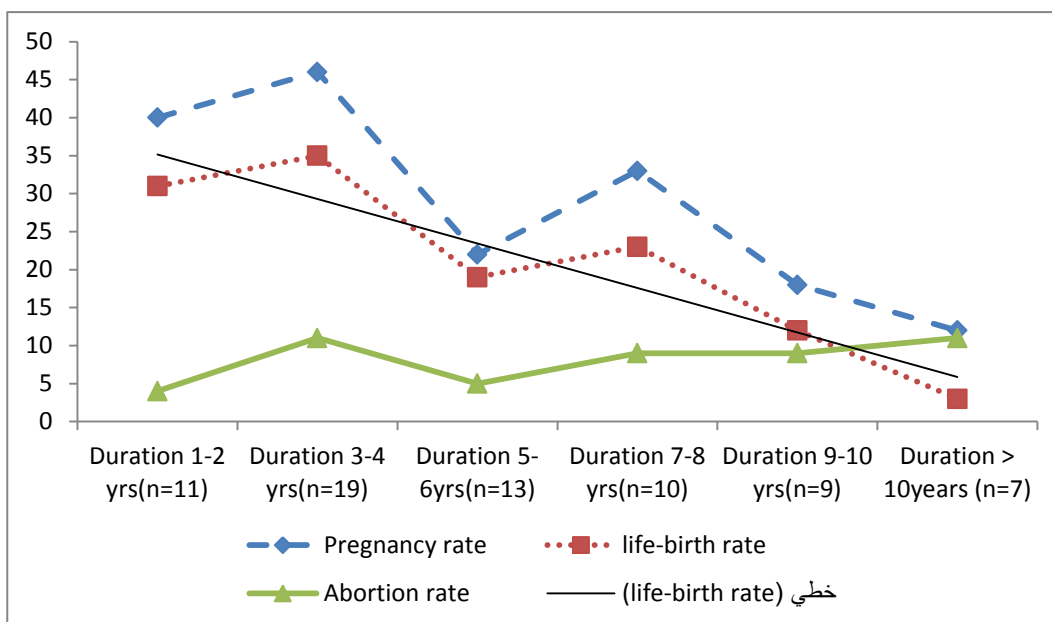


Figure 3: The linear life-birth rate among infertile couple treated by intrauterine insemination due to male factor infertility Yemini infertile couples

Discussion

The results of this study showed that the secondary infertility was more than three times as the primary infertility. This is in a good agreement with that results published by another researchers^[11, 12]. This was in disagreement with the results of this study because the couples who

involved in this study, had visited us asking for IUI, which means that they had no intense causes of infertility which made the IUI not a choice of treatment. Factors cause secondary infertility are less severe than those cause primary male infertility which can result from a variety of conditions included hypothalamo-pituitary

disorders, systemic disorders, chronic illnesses, nutritional deficiencies and congenital disorders^[13, 14]. A multicenter study reported that chromosomal abnormalities are common in infertile men mostly those with primary infertility, with an incidence of 5.8% as compared to an incidence of 0.5% in the fertile population^[15].

A relatively high incidence of asthenozoospermia could be observed in the immunologically infertile males^[16], because antisperm antibodies may be sustained and enhanced through bacterial or viral infections^[3]. subsequently they may severely alter spermatogenesis^[17]. The different causes of male infertility support the results of this study because the causes of primary infertility are more intense in their effects than that of the secondary infertility, and need more sophisticated ways of ART other than IUI^[11]. In infertile males with secondary infertility in addition to the previous causes, varicose veins and number of environmental factors including high temperature, inflammatory factors, social habits, drugs, radiation therapy and xenobiotics (pesticides, insecticides) had been shown to have negative impact on testicular function but had been implicated in the decline of sperm quality^[18].

The groups of the infertile males with history of infertility of 3-4 years duration are largest groups who attended medical services, in contrast infertile males with history of infertility ≥ 10 years were the smallest group. As the duration of infertility increases, the couples become less interested to seek the medical services. Besides, the psychological factors (depression and hopelessness) play a major role in these cases^[1].

Intra-uterine insemination has been practiced widely as an empirical

treatment for male factor infertility and as a mean to bypass defects in sperm-cervical mucus interaction^[19]. In the present study IUI was performed for 152 couples with mild male factor infertility. Studying the results of this study, the positive IUI outcome was observed in groups who had post-activation sperm parameters of more sperm progressive motility percentage grade (A) and grade (B) and higher percentage of normal sperm morphology as well as less sperm concentration. The sperm quality that is necessary for successful IUI is lower than the WHO threshold values. IUI is an effective therapy for male factor infertility when initial sperm motility is $\geq 30\%$ and the total motile sperm count is ≥ 5 million, when the initial values are lower IUI has little chance of success^[20]. An average total motile sperm count of 5 million may be a useful threshold value for decision about treating a couple with IUI or IVF^[21]. The final post-washed sperm count used for IUI may be considered predictive of the success for pregnancy and allow couples to be informed of the chances of success. Pregnancy rates, were significantly higher among couples with more than (14%) normal sperm morphology than among those of sperm morphology was less than (14%) normal sperm morphology^[1, 22]. The greatest enthusiasm supports IUI is when combined with controlled ovarian hyperstimulation (COH) that increases the number of oocytes ready for fertilization. IUI combined with superovulation may increase monthly probability of pregnancy approximately four times compared to that following IUI timed by LH surge^[23]. According to the largest available clinical studies, IUI in stimulated cycles with conventional doses of gonadotropin, induce pregnancy in (10-15%) of cases with better results in couples with normal sperm parameters

^[24]. The use of an ovulation induction agent, clomiphene citrate, human chorionic gonadotropin (hCG) or human menopausal gonadotropin (HMG), increases the success rate of IUI by 10% ^[3].

The timing of insemination in IUI programmes in relation to other major events around ovulation or most probably ovulation itself has been suggested as the most important variable affecting the success of this treatment ^[25]. In addition timing of insemination, number of insemination per cycle may influence the ultimate pregnancy ^[23]. To maximize the chance of success of IUI, the timing of insemination needs to be closely related to the time of ovulation, ovulation occurred at a mean time of (27.3) hour from onset of LH surge ^[26]. The normal physiological activity of the reproductive organs gradually decreases with advancing age due to irreversible abnormal physiological changes in the testes that affect the fertilization potential of human spermatozoa. Semen quality, frequency of ejaculation and sperm functions gradually decrease with advancing age. Moreover, the spermatozoa from older men have increased incidence of abnormalities and many children born from older men have an increased chance of abnormalities ^[27].

With increment duration of infertility, the infertile males become less interested in seeking the medical services. Depression and hopelessness play a major role in those cases. An increment in the duration of infertility to more than 10 years results in reduction in the testicular blood supply especially in the older infertile males and this affects the normal physiology of the testes and epididymis which results in marked elevation of the serum FSH and LH levels ^[28]. Furthermore there is an increase in the number of pathological spermatozoa

which linked to an increase in both age and duration of infertility ^[19]. Therefore, in this study least positive IUI with 10 years duration of infertility and age ≥ 50 years. The success of IUI is very strongly tied to precise adherence to established methods for everything from preparing the sperms to inseminating the lady. The factors that may influence the results of IUI, age of the couples and duration of infertility, final post-activation sperm parameters, method of preparing the semen, type and composition of the culture media, COH protocols, timing of IUI and accurate selection of couples for IUI with experience of the physician in performing the insemination. In 2010, a study of pregnancy rates performed at infertility centers; it was found that unsuccessful outcomes often were attributed to physician error and a lack of familiarity with procedure ^[25].

Conclusion

Present study shows a negative relationship between the duration of infertility and outcome of ART include pregnancy and live-birth rates. That is in a good agreement with that study published by Glazener et al in 2000 ^[29]. The researcher of the present work conclude that by increase in the duration of infertility the outcome of assisted reproductive techniques –IUI in infertile male will decrease markedly.

Recommendations

Study the hormonal imbalance in patient with male factor infertility that could be appeared in late inability to achieve pregnancy. Improve the cultural fertility educations of couples whose cannot be parents within 2 years regular unprotected intercourse and prepare patients psychologically with regard to the duration of infertility more than 8 years before their

involvement in the ART.

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SUJMS

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Interferon-gamma release assay versus tuberculin test in diagnosis of latent tuberculosis

infection among healthcare workers, Sana'a city-Yemen

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Abstract

Background: Latent tuberculosis infection (LTBI) is the presence of *Mycobacterium tuberculosis* in the body without evidence of tuberculosis (TB) disease. Healthcare workers (HCWs) are at occupational risk of contracting & transmitting TB. Therefore, identifying of persons with LTBI is an essential TB prevention & control strategy. **The aim of this study was** to evaluate the performance of interferon-gamma release assay (IGRA) in diagnosis of LTBI among HCWs, in comparison to tuberculin skin test (TST); as well as identifying risk factors for test positivity.

Methods: A cross-sectional study was conducted in 2015 on 90 HCWs tested with TST and IGRA. All Participants were subjected to a questionnaire to assess their risk factors. Differences between categorical variables were analyzed by χ^2 . Kappa coefficient used to detect the agreement between TST and IGRA. Also, accuracy of both tests was calculated.

Results: Of the 90 HCWs; 54.4% were females and 45.6% were males with an age ranged between 20-60 years. The participants were classified as 38.9% nurses, 34.4% physicians, 16.7% technicians and 10% were administrators. The highest prevalence of LTBI was found in female 14.3% & 28.6% by TST and IGRA, respectively. In general, the positivity by both tests increased with increasing age. 27.8% of HCWs were Bacille Calmette-Guérin (BCG) vaccinated and most of the positivity occurs among vaccinated HCWs. The crude prevalence for LTBI was 12.2% by TST and 20% by IGRA; overall agreement between TST and IGRA results was poor ($k=0.39$).

Conclusion: Most HCWs with LTBI were females, nurses, older age, BCG vaccinated and in a group of profession of close contact with TB patients'. The higher positivity was found by IGRA than by TST with poor agreement between them. Superior specificity was observed with IGRA; whereas TST had a higher sensitivity.

Keywords: Latent tuberculosis infection, Healthcare workers, IFN- γ release assay, tuberculin skin test.

Introduction

Tuberculosis (TB) is a serious public health problem that is responsible for about 1.7 million deaths each year. The current trends suggest that TB will still be among the 10 leading causes of global disease burden in the year 2020; with an estimation that one-third of the world's population latently

infected with TB¹, and therefore potentially at future risk of developing active disease. Latent tuberculosis infection (LTBI) is considered to be given when the immunological tests are positive and active TB is ruled out by way of X-ray bronchoalveolar lavage or sputum-smear microscopy².

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Working in healthcare is a well-known risk factor for TB. Even in countries with low TB incidence, the risk of TB in healthcare workers (HCWs) is elevated for a wide range of tasks in healthcare, and the prevention of nosocomial infection of HCW remains as a challenge ³. Improvement of diagnostic methods for LTBI is an important step towards the goal of tuberculosis elimination, as laid out by the WHO Stop TB strategy ⁴. In Yemen, the identification of LTBI relies on the tuberculin skin test (TST) which is based on a type IV delayed hypersensitivity reaction that occurs when those infected with *Mycobacterium tuberculosis* (*M.tuberculosis*) are exposed intradermally to standardized mycobacterial antigenic components. The immune response to *M.tuberculosis* is highly dependent upon interferon-gamma (IFN- γ) production by macrophage and antigen-specific T cells ^{2, 5}. However, TST has many limitations in terms of its potential and the cross-reactivity with the other strains of mycobacteria and antigens present in Bacille Calmette-Guérin (BCG) vaccination ⁶. Recently, interferon gamma release assays (IGRAs) have provided an additional tool to identify suspected cases of TB. As with TST, IGRAs measure the cell-mediated immune response to antigens specific for *M.tuberculosis*, therefore, both TST and IGRAs do not measure the presence of viable *M.tuberculosis* but merely the immunological footprints left behind by recent infection ⁷.

Aims of the study

The primary objective of this study was to assess the performance of IGRA in diagnosis of LTBI in comparison to TST among HCWs in Sana'a, Yemen. Secondly, to identify the risk of infection associated with TST and IGRA positivity among these HCWs.

Subjects and methods

A cross-sectional study of 90 HCWs was carried out in the Typical Police Hospital, Al-Thawra Hospital and the National TB Center in Sana'a city from January to March 2015. Variables were collected at the individual levels included sex, age, occupation. Each participant in this study was examined for the presence of BCG scar. All individuals were informed of the nature of the study and agreed to participate.

About 5 ml of blood were collected from each participant and serum were separated and stored at -20 °C for later analysis by DRG IFN- γ ELISA kit; which is a solid phase enzyme amplified sensitivity immunoassay performed on micro titer plate. The TST was performed by injecting of 0.1 ml of tuberculin into the skin in the lower part of the arm of each participant. The test was read within 48-72 hours, according to manufacture information. TST induration ≥ 10 mm was used as a cutoff point ⁸.

SPSS software for windows, version 20 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis. The chi square (χ^2) test was used to compare the

frequencies of positive test results among different groups of study recruits. Results were reported as odd ratios (OR) with confidence intervals (CI). Statistical significance was set to p-value <0.05. Test concordance was calculated using chance corrected proportional agreement rate; kappa (κ)

Results

This study included 90 HCWs; 54.4% were females and 45.6% were males. The participants' age ranged between 20-60 years. Most of the selected individuals were in age group 30-39 years (31.1%), followed by age group 20-29 years (28.9%) while age group 50-60 years were only 13.3%.

coefficients, with $\kappa > 0.75$ defined as excellent agreement, $\kappa < 0.4$ as poor agreement, and κ between 0.4 and 0.75 as fair to good agreement⁹. Additionally, sensitivity, specificity, false positive and negative, positive predictive values (PPV) and negative predictive values (NPV) were calculated

The distribution of HCWs according to profession in our study; 38.9% was nurses, followed by physicians (34.4%), technician (16.7%) and administrators (10%). Of the 90 HCWs only 25 (27.8 %) have been vaccinated against TB (Table 1).

Table 1: Description of the study population

Variables	No.
<u>Sex</u>	
Male	41(45.6%)
Female	49 (54.4%)
<u>Age group (years)</u>	
20-29	26 (28.9%)
30-39	28 (31.1%)
40-49	24 (26.7%)
50-60	12 (13.3%)
<u>Profession</u>	
Administrator	09 (10%)
Technician	15 (16.7%)
Physician	31 (34.4%)
Nurse	35 (38.9%)
<u>BCG vaccination</u>	
NO	65 (72.2%)
Yes	25 (27.8%)
Total	90 (100%)

The higher positive rate was found in female 14.3% and 28.6% by TST & IGRA, respectively. The age specific rates were highly varied for

different age groups (ranged from 7.7-16.7% by TST and from 3.8-50% by IGRA). Generally, both tests tended to have higher positive results with

increasing age.

As regard profession, the highest rate of TST positive occurred among nurses (14.3%) followed by physicians (12.9%) however, the highest rate by IGRA occurred among technicians and administrators (33.3%). Among the vaccinated HCWs; the positivity of IGRA (56%) was higher than those with

TST (36%). Similarly, the positive results (6.2%) by IGRA were higher than that by TST (3.1%) among unvaccinated HCWs. Moreover, most of the positivity results 81.8% by TST and 77.8% by IGRA were found among vaccinated HCWs (Table 2).

Table 2: Prevalence of LTBI among health care workers using IGRA and TST

Variables	TST Positivity No.	IGRA Positivity No.
<u>Sex (n)</u>		
Male (41)	4 (9.8%)	4 (9.8%)
Female (49)	7(14.3%)	14(28.6%)
<u>Age group (years) (n)</u>		
20-29 (26)	2 (7.7%)	1(3.8%)
30-39 (28)	3 (10.7%)	5(17.8%)
40-49 (24)	4 (16.7%)	6(25%)
50-60 (12)	2 (16.7%)	6(50%)
<u>Profession (n)</u>		
Administrator (9)	1 (11.1%)	3(33.3%)
Technician (15)	1 (6.7%)	5(33.3%)
Physician (31)	4 (12.9%)	4(12.9%)
Nurse (35)	5 (14.3%)	6(17.1%)
<u>BCG vaccination (n)</u>		
NO (65)	2 (3.1%)	4 (6.2%)
Yes (25)	9 (36%)	14 (56%)
Total	11 (12.2%)	18 (20%)

The association of TST and IGRA with risk factors summarized in Table 3. When sex was considered, there was association of positivity with female in which associated OR is equal 1.54 & 3.7 times by TST and IGRA, respectively; being significant ($p=0.02$) only in IGRA. When the positive results

of both tests were analyzed using age group, the significant association was obtained only for a positive IGRA with the oldest group ($p=0.005$). As an indicator of experience, the highest positivity by TST and IGRA found in the older age group; 16.7% & 33.3% (OR=1.96 & 4.0), respectively; being

significant ($p=0.011$) only in IGRA. As regard BCG vaccination, the positivity of both tests among vaccinated HCW

was higher than among unvaccinated and the difference was statistically significant ($p= 0.000$) by both tests.

Table 3: Risk factors of latent tuberculosis infection among health care workers

Character	TST				IGRA			
	OR	CI	χ^2	P	OR	CI	χ^2	P
<u>Sex (n)</u>								
Male (41)	Ref				Ref			
Female (49)	1.54	0.42-5.69	0.43	0.37	3.7	1.1-12.33	4.94	0.023
<u>Age group (years)</u>								
(N)								
20-29 (26)	Ref				Ref			
30-39(28)	0.81	0.15-3.79	0.09	0.76	0.82	0.22-2.9	0.12	0.73
40-49(24)	1.7	0.4-7.4	0.6	0.43	1.5	0.43-5.2	0.51	0.47
50-60(12)	1.5	0.2-9.5	0.25	0.61	5.5	1.3-2.4	7.8	0.005
<u>Profession (n)</u>								
Administrator(9)	Ref							
Technician(15)	0.46	0.02-4.1	0.52	0.47	2.4	0.6-9.5	2.0	0.15
Physician(31)	1.1	0.24-4.7	0.02	0.88	0.48	0.12-1.8	1.5	0.22
Nurse (35)	1.4	0.3-5.65	0.23	0.63	0.74	0.22-2.5	0.29	0.58
<u>BCG vaccination (n)</u>								
Negative(65)	Ref				Ref			
Positive (25)	0.56	.011-.287	18.2	0.00	.052	0.014-.186	28.0	0.00

OR: odds ratio ≥ 1 at risk; CI: Confidence intervals; χ^2 : Chi-square ≥ 3.9 (significant); P: Probability value ≤ 0.05 (significant)

Total concordant results of the two tests were 83.3%, predominantly in those with negative results 90.7%, however, only 9.3% were positive by both tests. The total discordant results between the two tests occurred in 16.7%

of the HCWs, most of them as a combination of TSTnegative/IGRA positive 73.3%; while the combination of TSTpositive/IGRAnegative was only 26.7%. Overall agreement between the assays was poor ($k= 0.39$, Table 4).

Table 4: Overall agreement between TST & IGRA

Concordant results (75, 83.3%)	Positive results (7, 9.3%) Negative results (68, 90.7 %)
Discordant results (15, 16.7%)	TST neg./IGRA pos. (11, 73.3%) VS TST pos./IGRA neg. (4, 26.7%)
<i>k</i>	0.39

κ : kappa coefficients; κ : $\kappa > 0.75$ defined as excellent agreement, $\kappa < 0.4$ as poor agreement, and κ between 0.4 and 0.75 as fair to good agreement

Estimation of the accuracy of the tests for diagnosis of LTBI are shown in Table 5. As regard TST test,

the sensitivity, specificity, were 63.6%, 86%, while for IGRA 38.8%, 94.4%, respectively.

Table 5: The accuracy of TST and IGRA

Test	Sensitivity	Specificity	False pos.	False neg.	PPV	NPV
TST	63.6%	86%	13.9%	36.4%	38.9%	94.4%
IGRA	38.9%	94.4%	5.5%	61%	63.6%	86.1%

PPV: positive predictive values, NPV: negative predictive values

Discussion

This study investigated the performance of IGRA for a diagnosis of LTBI in comparison to TST ($\geq 10\text{mm}$) among HCWs. We found that the crude prevalence of LTBI in HCWs by TST was 12.2% while by IGRA was 20%. Our results were comparable to previous studies^{10, 11} in Europe and Saudi Arabia that reported the prevalence of LTBI among HCWs by TST to be 12.8% and 11%, respectively and among French HCWs by IGRA being 22.2%¹². In addition, the prevalence of LTBI among HCWs in our study is higher than that of general population in Yemen (2-4%)¹³. Our result was confirmed by many studies¹⁴⁻¹⁶ which suggest that nosocomial transmission of TB is an important occupational problem among HCWs. On the other hand, lower rate of IGRA (7.2%) was reported by a study in a hospital for pulmonary diseases in Germany¹⁷. Females had a higher rate of TST and IGRA positive results (14.3% & 28.6%, respectively) but the association was only significant with IGRA ($p=0.023$, Table 2). Our result is similar to previous studies in which females showed a higher prevalence of LTBI than males¹⁸⁻²⁰. While other studies showed the prevalence of LTBI not to be associated with sex^{11, 16, 21}. As regard the age, our results showed an association between age and the positive results of both tests, however the association was only significant by IGRA ($p=0.005$). This was in agreement

with a study reporting higher positive results with increasing age¹⁶. Moreover, German and Japanese studies showed the association between age and LTBI with IGRA but not with TST^{17, 22, 23}. The immunologic interpretation of this observation is not clear; however, it may be due difficulties to apply the tuberculin correctly into the aging skin or by decreasing mobility of T lymphocytes to the forearm²². In accordance with our results, a German study using QuantiFERON-TB Gold In tube assay reported that the lowest prevalence in HCWs occurred among younger age group¹⁷.

Surprisingly, in our study profession was not associated with both assays. Nurses had the higher positivity with TST (14.3 %), while technicians and administrators had the higher positivity (33.3 %) with IGRA without any significant. In agreement with our result, Torres *et al.*²¹ did not find any association of profession with positivity of TST nor IGRA. However, other studies reported that the nurses are at high risk of developing TB than other HCWs due to possibility of nosocomial transmission^{3, 15, 24-26}.

Regarding BCG vaccination, most of positivity of both assay; 23 (92%) of participants were BCG vaccinated. The significant association of positive LTBI with the previous BCG vaccination ($p=0.000$) in our results are consistent with many works that reported people with

BCG vaccination to have a higher prevalence of LTBI^{6, 21, 23, 25,27-29}. A study reported that 20-25% of those receiving school-age BCG boosters would have a persistently positive TST at least 10 years later³⁰, and the repeated BCG vaccination increased the probability of TST results higher than 10 mm²¹. Importantly, the declining of TST over years after vaccination cannot be measured accurately as a result of different types of BCG strains that administered and genetic variability of the individual³¹.

On comparing both TST & IGRA, our results found the higher positivity of LTBI among vaccinated HCWs were 56% by IGRA as compared to 36% by TST. Recently, a study reported that a recent BCG vaccination or a repeated BCG vaccination in general decreased the probability of IGRAs positive and they suggest that this may be due to a protective effect of BCG vaccination²¹. However, in our study we did not have data about the number of doses nor time of BCG vaccination. Overall agreement between TST and IGRA was poor ($k=0.39$) which is in agreement with several studies^{32, 14, 23, 33}. In contrast, other studies showed good to excellent agreement between the two assays^{23, 34-35}. An earlier study by Pttumartly *et al.* using quantification assay showed a correlation between quantitative IGRA and the size of skin test indurations³⁶. Another study suggests that a positive QFT-GIT

result may be a better indicator of LTBI than a positive TST result³⁷. According to this, quantifying the IFN- γ response may predict the future risk of developing TB.

Concerning discordant results the proportion of TSTnegative/IGRA positive is more than TSTpositive/IGRAnegative (11 vs. 4) of all HCWs tested. Our findings are consistent with a number of studies^{12, 21} which reported that the overall positivity of LTBI by IGRAs is higher than that by TST. Nienhouse *et al.* suggested that these combinations partly explained by decreasing sensitivity of the TST with age and the BCG vaccination²³. Although our study and other studies found that the prevalence of LTBI by both methods was statistically significance with BCG vaccination, however, there was no clear trend that TSTpositive/IGRAsnegative discordant result, increased with an increasing proportion of BCG-vaccination³⁸. Interestingly, one study conducted in a city with a high TB incidence, high LTBI prevalence and where BCG is routinely administered, reported that the discordance between the two assay was high (24%), and BCG did not account for this discordance. Another study suggested that TSTpositive/IGRA negative results might be explained by resolved or old TB infection³⁹. However, other previous studies observed that only the combination of TSTpositive/IGRAnegative

HCW develop active TB ^{27, 40}. In addition, discrepancies encountered in our study might be due to the natural host variability and the different assay conditions.

In this study, we also assess the accuracy of the positivity of both tests in terms of sensitivity, specificity, NPV and PPV. Importantly, for any new test to replace the TST should show a higher specificity, especially in subjects with confounding factors, such as BCG vaccination, and at least a similar sensitivity. Our result showed that the specificity of IGRA (94.4%) was higher than that of TST (86%); however, its sensitivity (38.8%) was lower than that of TST (63.6%). This finding is consistent with many studies that compared TST and IGRA and reported the specificity of IGRA to be higher than that of TST ⁴¹⁻⁴³. As we know the immune response to TB is complex and the decreased specificity is due to the non-specific immune response to a heterogeneity mixture of antigens that are present in the mycobacterial cell wall ⁴⁴, as well as due to BCG vaccination based on purified protein derivative ⁴⁵. False positive of TST was 13.9% and 5.5% for IGRA while false negative 36.4%, 61%, respectively. False positive reactivity may be explained due to tuberculin strains such as BCG, inter-observer variability in reading ³³, while the under laying immunosuppression may lead to false negative results. In our study, NPV of TST (94.4%) was higher than that of IGRA

(86.1%) while the PPV of IGRA (63.3%) is higher than that of TST (38.9%). Unfortunately, the lack of gold standard diagnosis method for LTBI makes the determination of accuracy for IGRA and TST difficult. However, an alternative way to evaluate the sensitivity in this context is through comparison of the risk of developing active tuberculosis in subjects with an increased risk of progression from LTBI to active TB ⁴⁶.

Conclusion

A High positivity rate of LTBI was found by IGRA than by TST among HCW in Sana'a city, Yemen. IGRA results are more associated with risk factors than TST. TST and IGRA were significantly influenced by previous BCG vaccination, with poor overall agreement between the two assays. IGRA had a superior specificity than TST; whereas TST had a higher sensitivity.

Recommendations

Additional studies are needed with quantities estimation of IGRA in line with study of progression disease.

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Emergency Cesarean Hysterectomy Among Women attending to Obstetric Unit in Al-Thowrah Hospital, Sana'a City, Yemen

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Abstract

Background: Peripartum hysterectomy is a major operation and is invariably performed in the presence of life threatening hemorrhage during or immediately after abdominal or vaginal deliveries.

Aim: To determine the incidence and indication of cesarean hysterectomy, among women attending to the obstetric unit in Al-Thowrah modern general hospital, Sana'a City, Yemen.

Methods: A total of 60 women cesarean underwent hysterectomy were enrolled in the study. Data were collected from labor registers, theater records, patient cases notes, ward registers and intensive care unit records.

Results: During the period of study there were 60 cesarean hysterectomy and 54500 deliveries, representing an incidence rate of 1.1 cases per 1000. Vaginal delivery was the most common mode of delivery (83.3%)

followed by a cesarean section (16.7%), and cesarean hysterectomy (0.11%). Most of the women with cesarean hysterectomy were in the age group of 30-39 years (56.7%), 23.3% of women were older than 40 years, and the least were at age group less than 30 years (20%).

The majority of women were grand multipara (80%) while 16.7% were multipara and only two women (3.3%) were primigravida. Cesarean hysterectomy was performed in two-thirds of women at the gestational age of 37 weeks or more and in one third at the gestational age of less than 37 weeks.

The most common indication for cesarean hysterectomy was rupture uterus (58.3%), massive hemorrhage due to the placenta (15%). Placenta previa, uterine atony, and placenta adherent were indicated in 11.7%, 8.3%, 6.7%, respectively.

There were 53 stillbirths and 7 alive birth. The most common causes of death were placental abruption, ruptured uterus, and prematurity. There was 10 maternal death (16.7%) due to DIC in 6 women as a complication of massive hemorrhage and acute renal failure in 4 patients.

There were 42 maternal complications. These were due to shock (bleeding) in 14, DIC in ten, anemia in eight, acute renal failure in seven, and ureteric ligation in three.

Conclusion: The incidence of cesarean hysterectomy was very high, and the most common causes were found to be due to rupture uterus and PPH due to uterine atony and abruption placenta and placenta previa. The maternal mortality rate was found to be very high and the prenatal mortality rate also was very high.

Keywords: Cesarean hysterectomy, Placenta previa, uterine atony, placenta adherent, Rupture uterus.

Introduction

Peripartum hysterectomy has been described as catastrophic procedure and is often performed in acute life threatening emergency¹. The difficulty

associated with the procedure is not necessarily the surgical technique but is the support of such ill patients. These difficulties are more pronounced in developing countries when

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institution are inadequately founded, facilities are lacking and patients are present in the hospital very late where pathology is advanced².

The incidence of cesarean hysterectomy is 8.3 per 1000 cesarean³. Even today 8-10% of maternal mortality in developing countries directly occur due to massive obstetrical hemorrhage⁴. Maternal mortality in Yemen still unacceptably high, the majority of these deaths occur in poor illiterate women who make little use of modern obstetric care has therefore been proposed as a major necessity in the reduction of maternal mortality⁵. The indication for peripartum hysterectomy includes uterine atony unresponsive to conservative measures, previous cesarean birth, laceration of major vessels, abnormal placentation, cervical dysplasia, or carcinoma in situ^{6,7}. Vaginal birth after cesarean, primary and repeat cesarean deliveries and multiple births are independently associated with an increased risk for peripartum hysterectomy⁷. The association between placenta previa accrete and prior cesarean sections was confirmed, and the incidence of the placenta accrete increased as the number of previous cesarean sections increased. The patient with antepartum hemorrhage due to placenta previa, who had a previous cesarean section should be considered at high risk for developing placenta accrete^{3,8}. The combination of high parity, cesarean section, prior cesarean delivery, current placenta previa and oxytocin use for uterine stimulation were among the risk factors for uterine atony and should alert the obstetrician that an emergency peripartum hysterectomy may needed^{3,9}. Risks of the cesarean hysterectomy include increased operative time, blood loss, increased rate of infection, and higher contaminated incidence of damage to

bladder and ureters than in non-gravid hysterectomy or cesarean section alone¹⁰. In addition, the cervix is not easily identified in a labored uterus and may not be completely excised at the time of cesarean hysterectomy.

Aim of the study:

to identify the incidence and indications of cesarean hysterectomy among women attended to the obstetric unit in Al-Thowrah modern general hospital, Sana, a city, Yemen.

Subjects and methods

This is descriptive cross-sectional study was done among patients who had a cesarean hysterectomy at Al-Thowrah modern general hospital (TMGH) from January 2009 to December 2013. This study carried out in TMGH, The hospital is the largest public and referral center in Yemen, and it receives all obstetric emergency cases referred from different locations. The department of obstetrics and gynecology has all facilities that serves the patients including blood bank, laboratory and a well expert staff. The obstetric unit which was the core of our collected data and information, this unit consists of the antenatal ward, post-natal ward, Operation Theater of Gynecology ward and labor room which contains four delivery beds and eight beds for post-delivery observation, and the dark room contains two beds and qualified operation room for complicated cases. The data were collected from the patients' files using checklist. The demographic characteristics, incidence, indications and outcomes of hysterectomy, peripartum complications, the parity, causes of cesarean hysterectomy, Type of hysterectomy, Causes of maternal mortality, and fetal mortality were evaluated.

Peripartum hysterectomy is the

surgical removal of the uterus at the time of a planned or unplanned cesarean delivery or in the immediate postpartum period. Maternal age in years from age 16 years up to 45 years. Parity is the number of deliveries the mother had before. Gestational age is the duration of pregnancy in weeks 24 to 40.

A total hysterectomy is the surgical removal of the uterine corpus with its cervix. Subtotal hysterectomy is the surgical amputation of the uterine corpus from its cervical stump. Rupture uterus is a tear involves layer or all layers of the uterus. Abruptio placenta is the separation of a normally implanted placenta from its site of implantation. Placenta previa is the abnormal implantation of the placenta in the lower uterine segment either over or near the internal os of the cervix. Uterine atony: is he inability of the uterine myometrium to contract effectively after delivery. Placenta accrete is the placenta villi attached to the myometrium. Placenta percreta is the placenta villi penetrate through the entire layer of the myometrium. Maternal mortality is the death of any women dying due to cause whilst pregnant or within 42 days after termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes. Maternal morbidity is the complication that developed in the patient who underwent cesarean hysterectomy as hemorrhage, DIC, acute renal failure, shock, paralytic ileus, intestinal obstruction, ligation of ureter and anemia. Data was analyzed

by using SPSS version 19 for frequency and cross tabulation.

Results

There were 54,500 deliveries, 45375 normal vaginal deliveries, 9125 cesarean deliveries and 60 emergency cesarean hysterectomies, representing an incidence rate of 1.1 cases per 1000. (Table-1).

The age of the patients ranged from (16-45 years). The highest percentage of cesarean hysterectomy was found among the age group 30-39 years 34 patient (56.7%), then in age group 40yrs or more, there were 14 patients (23.3%), followed by age group 20-29 yrs. 10 patients (16.7%), the lowest percentage was in age group <20years 2 patient(3.3%), (Table-2).

Most cases of cesarean hysterectomy were found among grand multipara (5 and more) 48 patients (80%), there were 2 patients primigravida (3.3%) had a cesarean hysterectomy due to improper use of oxytocin and obstructed labor (Table-3).

The majority of patient 40 (66.7%) who had cesarean hysterectomy were pregnant ≥ 37 weeks, while a minority 20 patients (33.3%).who underwent a cesarean hysterectomy at gestational age<37 weeks (Table -4).

Figure 1 shows that 14 cases (23.3%) of patient of cesarean hysterectomy suffered from shock, and 10 cases (16.7%) suffered from DIC, and 7cases (11.7%) suffered from acute renal failure and 8 cases (13.3%) suffered from anemia and finally 3 cases (5%) complicated by ureteric ligation during operation,18 cases (30%) passed without complication.

Table 1: Distribution of modes of delivery among women (No=54,500).

Mode of delivery	F	%
• Cesarean section	9125	16.7
• Cesarean hysterectomy	60	0.11
• Vaginal delivery	45500	83.3
Total	54,500	100

Table 2: Distribution of cesarean hysterectomy according to age (No=60).

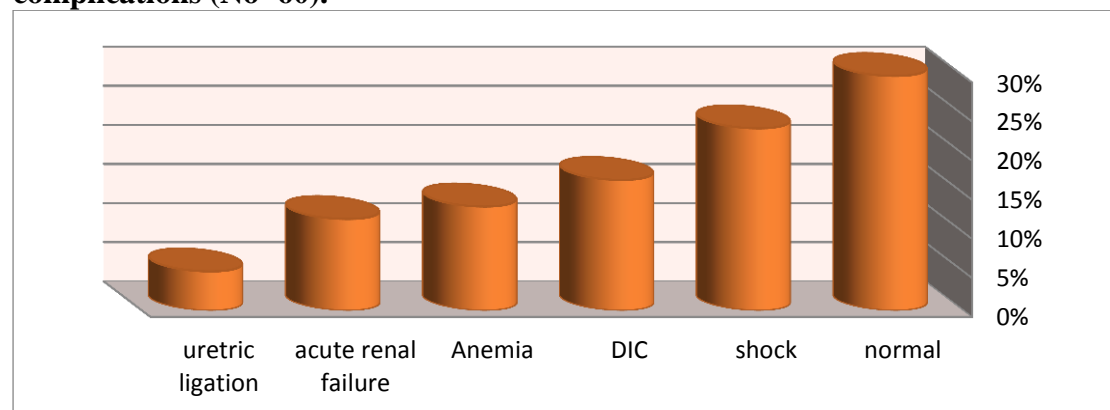
Age group	F	%
• <20 years	2	3.3
• 20-29 years	10	16.7
• 30-39 years	34	56.7
• 40 years	14	23.3
Total	60	100

Table 3: Distribution of cesarean hysterectomy according to parity. (No=60).

Parity	F	%
• Primigravida	2	3.3
• 2-4	10	16.7
• ≥ 5	48	80
Total	60	100

Table 4: Distribution of cesarean hysterectomy according to gestational age (No=60).

Gestational age	F	%
• < 37 weeks	20	33.3
• ≥ 37 weeks	40	66.7
Total	60	100

Figure 1: Distribution of cesarean hysterectomy according to maternal complications (No=60).

The most common causes of cesarean hysterectomy was rupture uterus 35 patients (58.3%), followed by abruption placenta 9 patients (15%), then placenta previa 7 patients (11.7%) and uterine atony 5 patients (8.3%), then placenta adherent 4 patients (6.7%), (Table-5).

Thirty-one women (51.7%) had a total abdominal hysterectomy; whereas as 29 women (48.3%) had a subtotal hysterectomy (Table -6).

As regard to fetal outcome this study

Table-5: Causes of cesarean hysterectomy (No=60).

revealed that the stillbirth was reported in 53 (88.3%), (Table 7).

The maternal death during and after operation were 10 cases (16.7%), the most common cause was disseminated intravascular coagulation (DIC) 6 cases (0.10%), followed by acute renal failure 4 cases (0.07%), (Table 8).

Causes	F	%
• Rupture uterus	35	58.3
• Abruptio placenta	9	15
• Placenta previa	7	11.7
• Uterine atony	5	8.3
• Placenta adherent	4	6.7
Total	60	100

Table 6: Type of hysterectomy (No=60).

Type of hysterectomy	F	%
• Subtotal hysterectomy	29	48.3
• Total hysterectomy	31	51.7
Total	60	100

Table 7: Fetal outcome (No=60).

Fetal outcome	F	%
• Alive	7	11.7
• Stillbirth	53	88.3
Total	60	100

Table 8: Causes of maternal mortality (No=10).

Cause of death	F	%
• DIC	6	60
• Acute renal failure	4	40
Total	10	100

Discussion

During the period of study, there were 54500 deliveries and 60 cesarean hysterectomies, representing an incidence rate of 1.1 cases per 1000. The rate is higher than that of the earlier studies conducted by Yamani Zamzami at king Abdull Aziz Hospital in Sudia Arabia where 17 hysterectomies among 34379 deliveries were reported from 1991-2002 with a rate of 0.5 per 1000 deliveries¹¹. El-Jallad MF¹² at the princess Badeea Hospital in Jordan identified 61 cesarean hysterectomies among 70252 deliveries between 1994-2002 giving a rate of 0.87 per 1000 deliveries, whereas Smith J described 14 cesarean hysterectomies in 50000 deliveries from 1988-2003 giving a rate of 0.36 per 1000 deliveries¹³. At Sveti –Duh general hospital¹⁴, Zagreb,

Croatia, Habek D and Becarevic R reported 17 cesarean hysterectomies among 21659 deliveries from 1990-2003 giving a rate of 0.078%. At Winthrop University Hospital, Mineola, New York, Kastner ES, Figueroa R, Garry D, Maulik D, reported 48 cesarean hysterectomies among 34241 deliveries from 1991-1997 giving a rate of 1.4 per 1000 deliveries¹⁵. Syed N at Lalla-Ded hospital in Kashmir, India, describes 146 cesarean hysterectomies among 55599 deliveries from 2001-2002 giving a rate of 2.6 per 1000 deliveries which are higher than that in our study¹⁶.

This study shows that, up to 56.7% of women with cesarean hysterectomy were in age group 30-39 years, 23.3% of 40 years of age or greater, 16.7% of age group 20-29 years, and finally

3.3% of <20 years. Similar trends were observed by Syed Nasser Ahmed, reported that up to 60% of patients undergoing hysterectomy were in age group of 30-34 years, followed by 42% of 35-39 years. Selo-Ojeme DO and co-workers in their study in Royal-free hospital, Pond Street, London UK (1993-2003), reported that mean age was 37 years 75%, followed by 29

undergoing cesarean hysterectomy belonged to para 3 or above and 3% performed for primipara¹⁶. Habek and co-workers described that most hysterectomies were carried out in multipara 70.5% and 29% in primipara¹⁴. Barclay in 1975 showed that 82.65% of patients undergoing cesarean hysterectomy were para 2 or greater¹⁸. Our study results runs in conformity. In this study the most common cause of cesarean hysterectomies was rupture uterus 58.3% followed by abruption placenta 15%, placenta previa 11.7%, uterine atony 8.3% and placenta accrete/percreta 8.3%. Syed Nasser A¹⁶ reported that uterine rupture was the most common cause of cesarean hysterectomy 58.3% which is consistent with our study. Faheem Z in his study reported that 27.9% of cesarean hysterectomy was done for uterine rupture¹². Yucel O, Ozdemir I, Yucel N, and Somunkiran A in their study reported that 35% of cesarean hysterectomies were carried out for rupture uterus¹⁷.

Two study by Mc-Mahon 1996 and Miller 1997 and their colleague's, they reported that 10-20% of women complicated with rupture uterus underwent hysterectomies¹⁹. At Osijek clinical Hospital in Croatia, there was one study reported that 11.7% of hysterectomies were performed due to rupture uterus¹⁴. The rate of uterine rupture in these studies was between 10-35% which is lower than that figure

years⁸. This study shows that 80% of cesarean hysterectomy was performed for a patient with para 5 or more, followed by 16.7% for para 2-4, and 3.3% performed for primipara. Yamani Zamzami 1991-2002 in his study show that high parity was identified as a risk factor and 17.6% was performed for primipara^{8,11,17}. Syed Nasser Ahmed reported 64% of patients

reported in our study (58.3%). The explanation of higher rate of uterine rupture in the present study could be due to most patients are poor illiterate, low socioeconomic status, high parity, the trial of labor at home with a traditional method with or without previous deliveries, no antenatal care and transfer patient to hospital at late stage especially from a rural area. This study shows that 15% of patients complicated by antepartum hemorrhage were due to abruption placenta underwent a cesarean hysterectomy. This incidence rate is slightly higher than incidence rate in a study carried out by Syed N¹⁶ at Lalla-Ded hospital in Kashmir for 2 years period reported that 12% of patients complicated by abruption placenta underwent a cesarean hysterectomy. Also, this study shows that 11.7% of women complicated by antepartum hemorrhage due to placenta previa underwent a cesarean hysterectomy. Syed N¹⁶ reported 25% of cesarean hysterectomy was due to placenta previa.

At Winthrop University Hospital, Kastner and co-workers¹⁵ in their study reported that 25% of cesarean hysterectomies were indicated for placenta previa. Another study in Croatia¹⁴ showed that 33% of hysterectomies were performed due to placenta previa. A lower rate of placenta previa was reported in our study. From this study, we found that 8.3% of women complicated by

hemorrhage due to uterine atony ended by cesarean hysterectomy. Yamani Z¹¹ in his study in Saudi Arabia reported that 64.7% of hysterectomies were carried out due to uterine atony. Another study¹³ reported that 28% of hysterectomies were carried out due to uterine atony. Study of Faheem Z¹², showed that 21.3% of cesarean hysterectomy was indicated for uterine atony. Syed N reported 21% of cesarean hysterectomy were performed due to uterine atony¹⁶. Another study was done in New York at Winthrop-University hospital, and this study reported that 29.8% of cesarean hysterectomies were carried out due to uterine atony¹⁵. All incidence rates in these studies are higher than incidence rate in our study. This study show that 6.7% of cesarean hysterectomy had been done due to placenta\percreta. Faheem Z¹² reported that morbidly adherent placenta accreta \percreta was the most common indication for cesarean hysterectomy (47.5%). Yamani Z¹¹ reported 35.3% of morbid adherent placenta was the common indication for cesarean hysterectomy. Smith j described 28% of hysterectomies was performed for placenta accrete¹³.

At Stony Brook University hospital, New York, Bakshi S, Meyer BA²⁰ (1990-1995) reported that placenta accrete was identified as a risk factor for peripartum hysterectomy. At the hospital in Chojnice²¹, the study was performed from 1992 to 2002 reported that placenta accrete was the most common indication of cesarean hysterectomy and had an incidence of 48.4%. Yucel O and Co-workers¹⁷ in their study reported that 29% of cesarean hysterectomy was done due to placenta accrete. Other study done at Osijek clinical hospital in Croatia¹⁴, reported that about 33% of cesarean hysterectomies had been done due to placenta percreta. The incidence rate in

these studies is higher than incidence rate in our study. This study shows 51.7% of patients underwent a total hysterectomy and subtotal hysterectomy was performed in 48.3%. Faheem Z¹² reported that 64% underwent a total hysterectomy and 36% were subtotal hysterectomies. Ozedmir I and co-workers¹⁷ reported that about 70.5% of hysterectomies were total and 29.4% were subtotal hysterectomies. Yamani Z¹¹ in his study reported that total hysterectomy was performed in 53% and subtotal hysterectomies were performed in 47%. One study at Osijek hospital in Croatia¹⁴ reported that 94% of hysterectomies were total and 5.8% of hysterectomies were subtotal. Our study runs in confirmatory. During the period of this study, the prenatal mortality was very high, there were 53 (88.3%) stillbirth, and most causes of death due to abruption placenta, rupture uterus and prematurity. Faheem Z¹² in his study reported that 7 (11.5%) cases of stillbirth and 4 (6.6%) cases of early neonatal deaths. Sayed N reported 43% of prenatal mortality in his study¹⁶. In Abant Izzet Baysal University, Turkey, one study reported that among 34 cases underwent cesarean hysterectomy, there were 6 (17.8%) stillbirth and 2 (5.8%) early neonatal death¹⁷. Becarevic R, Habet D¹⁴, in their study reported that among 17 cases of cesarean hysterectomy there was only 1 (5.8%) stillbirth. Other study^{22,23} showed that the prenatal mortality rate associated with abruption placenta was 12%. But in most reports²⁴, prenatal mortality in 25% of cases was associated with abruption placenta. Reports by Anarth and Co-workers²⁵ described that about 40% of prenatal death due to prematurity. During the period of this study, the most common complication of cesarean hysterectomy was shock (23.3%), disseminated DIC (16.7%),

acute renal failure (11.7%), anemia (3%), ureteric ligation (5%) and 30% of a patient discharged in good condition. In USA²⁶ hemorrhage remains the third most common cause of maternal mortality and morbidity. In Saudi Arabia at King Abdull Aziz hospital¹¹ one study 1991-2002 reported that 53% of patients developed DIC and 6% had bilateral ureteric ligation after cesarean hysterectomy. Other study done in Sveti Duh, General hospital, Zagreb¹⁴ 1995-2003 reported that 25% of patients complicated by shock after cesarean hysterectomy.

This study shows that maternal death during and after cesarean hysterectomies were 10 cases (16.7%) which was very high because most of these patients present to hospital very late where pathology is advanced and facilities are lacking institutions are inadequately founded, facilities are lacking, lacking workers who identifying high-risk pregnancies and their timely referral, most patients presented to the hospital in advanced stage due to the improper mechanism of referral to a higher hospital and lacking qualified and specialist surgeons.

Causes of death were respectively due to DIC 60%, acute renal failure 40%. Faheem Z¹² and Syed N¹⁶ reported that 3% of maternal mortality during their study period. In the USA the maternal mortality after cesarean hysterectomy was very low, there were 3 studies in California and Massachu²⁷ sets were reported that the rate is 3.2 per 100.000 (1 in 310). Yucel O, and Co-workers¹⁴ reported that in their study, the rate of maternal mortality following cesarean hysterectomy were 5.9%. Several studies show that no maternal mortality after cesarean hysterectomy^{11,15,21}.

Conclusion

This study shows a high incidence of

cesarean hysterectomy due to conservative surgery as ligation of internal iliac or uterine arteries or B-Lynch Brace suture not performed to stop bleeding. Uterine rupture still is the leading cause and the main indication for cesarean hysterectomy, high parity, current placenta previa, uterine atony, accidental hemorrhage and placental adherent are identified as risk factors for cesarean hysterectomy and should alert the obstetrician that an emergency cesarean hysterectomy may need. The prenatal mortality is very high due to abruption placenta, uterine rupture, and prematurity.

Recommendations

Improvement in ANC services and identifies high-risk cases and their reference to appropriate referral hospitals. Reevaluated our ANC and delivery services with a view to cover an area that lacks such services and improved the available.

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Consanguinity Is Strongly Associated with Fetal Congenital Anencephaly

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Abstract

Background: Anencephaly is a type of neural tube defect characterized by abnormal development of the brain and the bones of the skull. **Aims:** to investigate the association between consanguinity and anencephaly which is the most severe form of neural tube defects and to assess the magnitude of the problem. **Methods:** A case-control study was conducted between January and December 2014, all women with anencephaly that were admitted to the obstetric department of al Thawra General hospital, Sana'a, were enrolled in this study. The subjects were divided into study (n = 72) and control groups (n=25). **Results:** From a total of 11283 deliveries, 97 women were having anencephaly giving the overall incidence as 8.5/1000 births. We found significant number (74.2%) of these affected women had consanguineous marriage (95% CI 62.5-83.7; p = 0.0001). The first cousin union was present in (68%). Compared with control, the study cases were characterized by poverty, low education, absence of antenatal care, and mostly from rural setting. **Conclusion:** Consanguineous marriage is common in our societies and strongly associated with fetal congenital anomalies particularly anencephaly.

Key words: Consanguinity, Marriage types, Neural tube defects (NTDs),

Introduction

Consanguineous marriages refer to union contracted between biologically related couples¹. Consanguinity is traditionally favored in most of the Eastern Mediterranean region, south Asia and African countries especially in the Muslim populations^{2,3}. It is reported that the overall consanguinity rates in such communities collectively account for 20-50%^{4,1}.

The rate in Yemen is 40-44.7%⁵ and similar to Qatar and Oman, the rates are increasing in the current generation¹. In these countries

inbreeding is popular and frequently respected practice¹ because the religious, social and cultural factors are still playing in favoring consanguineous union¹. It is well known that offspring of consanguineous marriages are at increased risk for rare recessive syndrome, congenital malformation and fetal, infant and child morbidity and mortality⁶⁻⁷.

The detrimental health effects associated with consanguinity are caused by the expression of recessive genes inherited from a common ancestors which probably applies to rare single gene

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conditions as well as to multigenes disorders with multifactorial inheritance ^{8,9}. Many different types of genetic disorders have been reported to be more common among consanguineous progeny such as neural tube defects (NTD) ^{10,8} including anencephaly which represents the most severe form of NTD ¹¹⁻¹².

Aim of the study:

The aim of this study was to examine the association between consanguinity and anencephaly and to assess the magnitude of the problem.

Subjects and Methods

It was a case-control study of women with anencephalic fetuses who admitted to the delivery room for termination of pregnancy between January and December 2014 in the department of obstetrics and gynecology, Al Thawra General Hospital, Sana'a, Yemen. This study was performed according to the principles of Helsinki declaration and was approved by the hospital ethics committee. A total of 97 women diagnosed as having anencephalic fetuses were enrolled in this study. They were divided into 2 groups: those with consanguineous marriages (n=72) were assigned as the study group and the remaining cases (n=25) with non-consanguineous marriage as a control group. The control group was selected non-randomly as woman who had non-consanguineous marriage and delivered anencephalic baby was selected as control. None was excluded from the study. The diagnosis of anencephaly was based on clinical background and ultrasonography.

A standard questionnaire was prepared that included all maternal demographics and clinical data such as maternal age, parity, gestational age, location, socioeconomic status, level of education, antenatal care, folic acid supplementation, previous history of congenital anomalies, family history of congenital malformation, level of consanguinity, drug taking and co morbidity such as DM. In addition, pregnancy complication, methods of termination, and the outcome were assessed. The questionnaire was administered through personal interview with the patients after explaining the aim and methods of the study and reassured that confidentiality is preserved. The informed consent was obtained from each participant and the questionnaire was filled by doctor in-charge. Associated malformation was considered when anencephaly associated with one or more other anomalies not included in NTDs proved by neonatologist. Polyhydramnios was defined as ultrasound estimation of amniotic fluid index >25 cm. We defined the first cousins and closer as double – first cousins (in which all grandparents are shared) and first cousins in which the couple are parallel or cross cousin of either paternal or maternal descent. Distant relatives were defined as the members of the couple were relative but not with first degree relations, for example they were first cousin once removed, second cousin once removed etc. The data were analyzed using SPSS software (SPSS.Inc,Chicago,IL) version 21. The differences between the groups were calculated using t-test for parametric and Mann- Whitney-

test for non-parametric data. Odd ratio and 95% confidence interval were calculated as appropriate. A *p* value of <0.05 is considered significant.

Results

A total of 11283 deliveries were occurred. Of these, 97 women having anencephaly. Seventy-two women (74.2%) with anencephaly had consanguineous marriage and 25 women (25.8%) had no consanguineous marriage. The notable findings was that women who had consanguineous marriages were significantly more frequent

from rural areas (73.6%), non-educated (33.3%), having low socioeconomic states (55.6%), and had no antenatal care (61.1%). The differences were statistically significant between the two groups ($p < 0.05$). None of both groups was on folic acid supplementation in periconceptional period. Analysis of the levels of consanguinity among the study group revealed that (68 %) of them, the marriage was contracted between the first cousins whereas the remaining (32 %) were with distant relatives ($p < 0.0001$) (Table 1).

Table 1: Distribution of demographic data among the case and control groups

Demographic data	Case n=72	Control n=25	P-value
Age (year)	31.9±0.22	32±0.32	0.08
Parity			
• 1	7(9.7)	3 (12)	0.7
• 2-4	47(65.3)	14 (56)	0.4
• >5	18(25)	8 (32)	0.4
Gestational age (weeks)	35.7±3.3	36.1±3.9	0.6
Location			
• Rural	53(73.6)	9 (36)	0.008
• Urban	19(26.4)	16 (64)	0.0012
Socio-economic status			
• Low	40(55.6)	6 (24)	0.008
• Middle	22 (30.5)	11 (44)	0.2
• High	10(13.9)	8 (32)	0.05
Education			
• Primary school	22(30.5)	3(12)	0.06
• Secondary school	21(22.1)	14(56)	0.01
• University	3(4.1)	6 (24)	0.008
• None	24(33.3)	-	0.02
Consanguinity level			
• First cousin	49 (68)	-	
• Distant relative	23 (32)	-	
Hx of congenital anomaly	2 (2.8)	(4)	0.7
Antenatal Care			
• Yes	28 (38.9)	21 (84)	0.000
• No	44 (61.1)	4 (16)	0.0004

The data are present as mean± SD or n (%)

Frequency of consanguinity among all women delivered in the hospital during the study period was (11.6%). Odds of exposure in anencephaly was 2.88, odds of exposure in non- anencephaly was 0.12467 and the odds ratio (OR) =

23.1; 95% CI 14.6003 to 36.5491, $p < 0.0001$.

The proportion of consanguinity among case was 0.074 (7.4%) and the proportion of consanguinity among control group was 0.12(12%). (Table 2).

Table 2: Distribution of consanguinity among women with anencephaly

Consanguinity	Anencephaly		Total
	Yes	No	
• Yes	72	1240	1312
• No	25	9946	9971
Total	97	11186	11283

Eighteen cases (25 %) of the study group had additional congenital anomalies unrelated to neural tube defects versus 3 % of the control group.

Pregnancy complications recorded in the study and control groups were anemia (31.9% versus 20 %; $p=0.02$) and polyhydramnios (23.6% versus 16%; $p=0.4$).

Five cases (6.9%) of the study group had cesarean delivery versus two cases (8%) of the control

group. The indications for cesarean section in the study cases were prolonged pregnancy in four cases and contracted pelvis in one case (2.9%).

In the control group the recent scar was the indication in two cases. Female sex was preponderance in both groups. Description of the management and outcomes are shown in table 3.

Table 3: Distribution of clinical data among the case and control groups

Clinical data :(mean± SD/ n (%))	Case (n=72)	Control (n =25)	P-value
Associated anomalies			
• Club feet	4(5.5)		
• Cleft palate± cleft lips	6(8.3)	1 (4)	0.4
• Gastrointestinal	8(11.1)	2 (8)	0.6
• Anemia	23(31.9)	5 (20)	0.02
• Polyhydramnios	17(23.6)	11 (16)	0.4
Mode of termination			
• Spontaneous	29 (40.2)	9 (36)	0.6
• Induced	38 (52.8)	12 (48)	0.1
• Cesarean	5(6.9)	2 (8)	0.8
Fetal out come			
• Alive	37 (51.3)	12 (48)	0.7
• Stillbirth	35 (48.7)	13 (52)	0.9
Sex			
• Male	28 (38.9)	11 (44)	0.9
• Female	44(61.1)	14 (56)	0.6

Odds of exposure in anencephaly =72/25= 2.8; Odds of exposure in non- anencephaly =1240/9946 = 0.12467. Odds of anencephaly in consanguinity = 72/1240 = 0.058; Odds of anencephaly in non-consanguinity = 25/9946 = 0.0025.

Odds ratio (OR)= 2.88/0.12467=23.1; 95% CI 14.6003 to 36.5491, p < 0.0001.

Discussion

Consanguinity is common and continues to be preferred in Yemen due to social, cultural and economic reasons. A Consanguineous marriage is of genetic importance since close relatives have a greater chance of carrying the same alleles than do unrelated couples¹³. The results of our study showed that the babies whose mothers had consanguineous marriage were 23 times more likely to have anencephaly compared to their counterparts. A study on Pakistani population reported 21% consanguinity in couples with children affected with congenital anomalies¹⁴. It is reported that among Arabs and other Middle East countries, due to consanguinity there are adverse reproductive outcomes and

increase in rates of congenital malformations including NTDs¹⁵. In the present study it is found that the most common form of consanguineous marriage was between the first cousins (68%).According to Bittle A H (2001), it is predicted for these cases to have 12.5% of their genes in common that is equivalent to inbreeding coefficient of $F \geq 0.0625$ ¹⁶. This finding suggests that anencephaly and close relative marriage is strongly associated, similar to other study findings¹⁷⁻¹⁹. The marriage is mostly family decision and arranged linked to significant advantages of consolidation their power and structure. Under such circumstances of long unbroken history of inbreeding among repeated generations, there is evidence that the cumulative level

may be significantly higher than the value calculated for a single generation¹⁰.

This might explain the presence of anencephaly among consanguineous couples with distant relatives in the present study. The data on the present study confirm the previous studies reported that the highest rates of marriage to close relatives are consistently common in more traditional rural areas and among the poorest and less educated society²⁰.

Likewise, the female preponderance in our sample is in line with the previous reports²¹⁻²² though this association is recently debated²³. The proportion of anencephaly recorded in this study is comparable to that reported in other neighboring countries such as Saudi Arabia and Iran (<1/1000 births)^{1,11}. It is expected for the birth rate of anencephaly to decline with the introduction of prenatal ultrasonography in which the condition can be easily identified as early as 12-13 week in 100% of cases²⁴. Unfortunately, the failure to achieve prenatal care was noted in the majority of cases with the resultant of late diagnosis and therefore, the possibility of unnecessary surgical intervention. The central role of the obstetricians in such lethal and untreatable condition relies on the recognition of the risk factors for example consanguinity and thus providing preconception counseling to minimize the couples' risks of having affected offspring⁸. The only other feasible option is an early detection of anencephaly so as the early interruption of pregnancy can be achieved safely. Certainly, owing to the fact that consanguinity is long – held

traditional trend in the Arab and Muslim societies and the major shift in the practice is hardly predicted in the foreseeable future, the rising public awareness on its hazard and the possible preventive measures for congenital disorders may enhance the access to the appropriate preconception and premarital counseling services⁸. However, this study suggest that increasing of the public awareness of the potential hazards of birth defect particularly NTDs and the importance of periconceptional counseling of the close relative couples could result in substantial response. Such practice is cost saving compared to the cost of providing surgeries, physical therapy, and continuous care and rehabilitation for children with spina bifida. Moreover, as NTDs is life –long disabilities it is often invisible in our country because the surveillance system for birth defects is lacking as the number of pregnancies terminated due to diagnosis of NTDs is not recorded. It is therefore our suggestion that NTDs need to count, as simply counting is the first step in the analysis and prevention.

This study has some limitations. First, it is of small sample size thus, it is likely that the findings may not representative of the general population. More studies on this issue are considered priority to help understand the magnitude of the problem and therefore, planning for the appropriate preventive measures. Second, although the participants had no diabetes mellitus, were not obese or under anti-convulsant medications, we could not control for other factors shared with

consanguinity for example malnutrition. These data however showed that consanguinity was strongly associated with anencephaly, but we could not confirm that it is completely independent of those attributable factors.

Conclusion

Our study indicates that the consanguineous marriages between the first cousins was significantly high. Both close and distant unions were strongly associated with anencephaly. Less educated people are less aware of the risk associated with consanguinity and therefore less aware of the antenatal care benefits.

Recommendations

The public education along with providing the appropriate facilities for preconception and premarital counseling are stressed issue that must be addressed promptly.

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