Epidemiology and Health Related Quality of Life in Infertile Females

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Abstract

Background: Female infertility is a growing problem. Numerous risk factors are incriminated. Also infertility has many effects on the individual. Its effect on the Health related quality of life (HRQOL) among Egyptian females has not been sufficiently studied.

Aim: This study aimed to study epidemiology and identify the main risk factors associated with infertility among Egyptian females and assess the health related quality of life among these patients including physical, psychological and social domains

Subjects and Methods: A Case control study was conducted on females attending outpatient clinic at two tertiary hospitals in Cairo. An interview questionnaire was designed and administered. 468 cases (infertile) and 450 (fertile) controls were interviewed. Data was analyzed using SPSS program version18.

Results: Significant risk factors for infertility included age at marriage more than 30, BMI more than 30, alcohol intake, exposure to X-ray, radiotherapy, lead, domestic pesticides, chemicals, history of congenital malformation, family history of hereditary disease, abnormal pattern of menstruation. 12.4% of the cases had poor or very poor HRQOL in comparison to 3.1% of the controls. Cases showed lower scores than controls in all three domains of QOL.

Conclusions: There are numerous risk factors affecting infertility in the Egyptian society, many of which are preventable. Infertility and its related health conditions have a negative effect on all domains of HRQOL. **Recommendations:** Care should be taken to avoid the risk factors. Infertile females should be offered suitable supportive measures as counseling and patient centered care throughout their course of treatment.

Key words: female infertility, risk factors, health related quality of life

Introduction

Infertility is defined as the inability to conceive or to bring pregnancy to term after one year of continuous marital life, [(1)] .The origin of infertility is due to male or female factors; the causes are multiple. Female factors account for 40% of infertility. Male factors account for 40% of infertility. Male and female factors combined cause 10% of fertility. The etiology is unknown in 10 % of cases [(2).] Although estimates of the prevalence of infertility are not very accurate and vary from region to region, approximately 8-10% of couples experience some form of infertility problem [(3).] While the prevalence of primary infertility is 2.5%, being higher among women under 30 years than older ages, the incidence of secondary infertility (7.9%) increases with advanced age[(4).] These figures, however, may rise in the near future as increasing

numbers of women decide to delay having children till an age when natural female fertility is in decline[5].

The number of couples treated for infertility has risen significantly in recent decades. This is often attributed to increased diagnosis and by the availability of assisted reproductive technologies, but there are indications that the actual incidence rate of infertility is rising too[6]. There are many risk factors which affect female fertility. They include: increased age, tobacco smoking, alcohol use, being underweight, excessive exercise and caffeine intake[7]. A growing body of scientific evidence is encouraging infertility patients and practitioners to pay more attention to the impacts of environmental chemicals on reproductive health [6]. Environmental risk factors are numerous and include heavy metals, chemical agent, radiation, and so on, [8, 9] Many of these are preventable risk factors.

The desire to have children should be considered as a normal need that should be met [5]. Patients who pursue treatment for infertility often find themselves involved in a stressful and emotionally draining quest for a child. Many studies demonstrate that infertile patients commonly experience feelings of depression, isolation, anxiety, grief and inadequacy[10]. In Egypt this is further aggravated by social pressure from spouse or other relatives is another factor which could worsen the quality of life for infertile couples[11].

This study aims to identify the main risk factors associated with infertility among Egyptian females and to measure the healthcare related quality of life among this group, in an attempt to identify problems facing this group of patients in order to aid in providing more suitable care for them in the future.

Methodology

Methods and study population: A Case - Control study was carried out. Four hundred and eighty infertile females from two tertiary care hospitals were interviewed. 468 were included in the study. Infertility was defined as failure of conception for a period of at least one year of continuous marital life. Four hundred and sixty fertile females from the same two tertiary care hospitals were interviewed from antenatal care & family planning clinics. 450 females were included in the study. Exclusion criteria for controls included having previously received treatment for infertility. Cases and controls were matched for social class.

Sampling method: Convenience sample method was used. Data was collected on the three days which the infertility clinic worked weekly for 12 month. Any suitable subject for cases or controls was included in study. Fertile females undergoing previous therapy for infertility were not included in the study.

Study tools: After reviewing relevant references, an interview questionnaire from several questionnaires including short form 36 (SF 36), World health organization quality of life scale (WHOQOL) scale and scales from other related studies [12, 13, 14, 15, 16] was developed. It contained personal data as age, age at marriage, occupation, special habits, and residence, risk factors related to infertility as caffeine intake, smoking, medical history, gynecological and obstetric history, hereditary diseases and congenital malformations, exposure to environmental factors such as : occupational exposure, exposure to lead

and pesticides, past history for disease and any medication received.
Health related quality of life: Data about the three main domains for quality of life: physical, psychological and social domains, was collected. Each domain consisted of 20 parameters. Physical domain included complaining of abdominal pain, backache, dysmenorrhea, amenorrhea, etc... Psychological domain included both satisfaction and depression factors. Social domain included interference with job duties, relations with friends and relatives, and financial troubles.

Ethical considerations: Approval for carrying out the research was obtained from hospital administration. Patients were informed about the nature of the research and an informed consent was taken during the interview. Privacy for all information related to the patients has been confirmed.

Data management and analysis
All the collected data was coded and introduced into an IBM compatible personal computer using the SPSS-version 18 Data entry for windows.
The score of each domain of HRQol was calculated by summation of the scores of each parameter in the domain and dividing the result by 20; a mean of the individual parameter scores in the corresponding domain. This gave a score ranging from 1 to 5, where 1 was the least score (meaning worst quality of life) and 5 was the maximum score (meaning best quality of life). Thus each subject had three scores; one for the physical, psychological and social domains.
Suitable statistical tests were chosen according the nature of the data including chi square, independent t test, Cronbach test of reliability.

Results

Part I: Risk factors for infertility
Sixty two percent of the infertile females and 34% of the fertile females were aged less than 30. 11% of the infertile group married at age more than 30 in comparison to 2.4% of the fertile group. About 50% of the infertile group were married for less than 5 years whereas about 50% of the fertile group were married for 5 to less than 15 years. There was no significant difference between both groups as regards place of residence, education and employment (table 1).

The infertile group showed a higher BMI. Alcohol drinking was a significant risk factor for infertility. There was no significant difference between the two groups concerning other lifestyle risk factors in the study like smoking or caffeine intake (table 2). Environmental risk factors showing a statistically significant difference included exposure to x-ray, radiotherapy, lead, domestic pesticides, and chemicals (table 3). Table four shows medical characteristics among the studied females. Infertile females showed a significantly higher percent having history of congenital malformations, family history for hereditary disease, and abnormal pattern of menstruation (table 4).

Part II: Health Related Quality of life
The alpha cronbach's test for validity was done on the part of the questionnaire concerning HRQOL. It had a high value of 91.5. This indicates that the scale is coherent and reliable (table 5).

The distribution of the different levels of HRQOL among the study group 12.4% of the cases had either poor or very poor HRQOL in comparison to 3.1% of the controls. Still 7.7% of cases considered themselves to have excellent HRQOL in comparison to 2.0% of controls. Ficsher exact test was significant, (figure one). The independent sample t- test that was done to compare between QOL domains between cases and controls, (table 6). Cases showed lower scores than controls in all three domains of QOL, especially the psychological domain (figure 2).

Discussion

Risk factors for infertility are numerous. They could be divided into sociodemographic risk factors, lifestyle risk factors, environmental risk factors and medical risk factors. Of the life style risk factors showing a significant difference between the two study groups were: age, age at marriage, BMI 30 or more and alcohol intake.

Sociodemographic and lifestyle risk factors

Age at marriage was more in consistence with previous studies than age of the female at the time of the study. The age of infertile females in this study was less than the fertile females, whereas age at marriage was higher in infertile females than in the fertile females. Most of the infertile females (62%) were less than 30 years old in comparison to 34% of the fertile females at the time of the study. Examining age at marriage therefore is more relevant, 11% of infertile females got married at age 30 or more in comparison to only 2.4% of the fertile females.

It is known that female fertility decreases with age. In theWHO report byRutstein and Shah [17] it was shown that the percent of secondary infertility increased by age in Egypt. A review on historical data done by Eijekmans et al [18] has shown that natural fertility decreases by age. The authors studied six natural fertility populations. They showed that at the age of 20 only less than 3% were infertile (had last baby at this age reflecting infertility following). This number increased slowly till the age of 41 where 50% of females were infertile (had last baby) and it approached 100% by the age 50. Thus delaying age of marriage is an important risk factor for infertility, which is increasing in most communities.

Obesity is a risk factor for infertility as shown by many authors [19,20, 21 22]. Zain and Norman, [23] reported obesity contributes to anovulation and menstrual irregularities, reduced conception rate and a reduced response to fertility treatment. It also increases miscarriage and contributes to maternal and perinatal complication. Homan et al [22] and Zain and Norman[23] also reported that female fertility may be enhanced by losing weight. In this study obesity (BMI > 30) was found to be a significant risk factor also. The importance of this fact is that obesity is increasing worldwide and in Egypt too. Also physicians asking females with infertility to lose weight before treatment; which is usually time consuming, expose them to another factor for decreased fertility, which is increasing age. Females may choose to accept the risks of obesity and continue treatment. Taking into consideration more than 74% of Egyptian females aged above 15 are overweight or obese [24] this could become a problem which could engulf many of the limited resources; if a percentage of these females needed infertility treatment.

Alcohol has numerous effects on fertility in females, but the question which has not been settled is what amount of alcohol is required to affect female fertility, [19, 20, 21, 22]. Romero et al [25] found alcohol intake to be insignificant as a risk factor for infertility. Five cases reported alcohol drinking in this study and they were all infertile. . The infertile cases could have been more honest than the fertile ones, as they face a problem. But still the fact that alcohol is forbidden in Islam may have caused this low reporting rate. Furthermore alcohol intake could be stigmatizing and so people on alcohol are reluctant in admitting their situation.

The sociodemographic and lifestyle risk factors that did not show statistical difference included residence either urban or rural, educational level, being employed, taking caffeine, smoking either passive or active, waterpipe smoking, taking drugs and practicing an adequate amount of exercise. On the other hand several studies have confirmed a positive relationship between smoking and infertility [20, 21, 22].

Environmental Risk Factors

Exposure to environmental risk factors was expected to be generally low. These risk factors have been studied at occupational levels and have been found to have a role in infertility [26]. The question is do they have a similar role at lower levels of exposure. Namely the risk factors meant are exposure to pesticides, lead, and chemicals. Our homes are now full of objects containing lead like paints, batteries, electronics, ceramics, printing, and PVC (polyvinylchloride) plastic [27]. Also our homes are full of objects containing chemicals as toluene (in inks, cosmetics, glues), formaldehyde (in plywood, dyes, cosmetics, and rubber) and glycol ethers (in electronics, inks, dyes, varnish, paint, cosmetics)[27]. These are some examples, there are many others. Insecticides are used regularly in many homes. Biological monitoring would give more accurate data about these risk factors and existing dose response relationships would be made clear. Significant environmental risk factors between the two groups were exposure to x-ray, radiotherapy, lead, domestic pesticides and chemicals. Insignificant risk factors included exposure to chemotherapy and radioactive materials,

Repeated exposure to radiation, ranging from simple x-rays to radiotherapy, has been shown to contribute to a wide array of ovarian problems [28]. The effect of ionizing radiation depends on the interaction between four factors: dose rate, time period of exposure and total dose of exposure and the organ exposed, [29]. Both exposure to x-ray and exposure to radiotherapy were significant risk factors for infertility in our study. X-ray use is wide spread and precautions should be taken for patients anticipating childbirth in the future. The risk factor was positive in this study. It is known that radiotherapy and chemotherapy affect fertility. It is now the trend in most cancer therapies to save fertility. Enhancements in cancer treatment have now allowed more children with cancer to survive to adulthood and so face problems with infertility. Romero et al [25] found no significance for either in their study. His case control study probably did not recruit enough patients to thoroughly study these rare risk factors. In our study radiotherapy was positive and chemotherapy was negative as a risk factor for infertility. Only one case had been exposed to chemotherapy

which is not enough of course for comparison.

Sources of lead around us are numerous; [27]) and even our urban air contains lead of increasing levels [26], Exposure to lead is reported to be related to infertility[26, 30] and cause miscarriage [27]. In our study 27 cases reported exposure to lead versus 9 controls. This difference was significant, but the controls could have ignored their exposure to lead as it may seem unimportant to them. Documenting increased levels of lead by blood test would give more reliable results. Herz – Piccioto [31] found a dose response relation between blood level of lead and risk for spontaneous abortion even at levels much lower than in some occupational exposures.

Pesticides are known to have numerous health effects. They are directly related to increase in levels of cancers, endocrine disruption, cognitive dysfunctions, infertility and sterility, kidney failure, respiratory disorders and skin irritation. Moreover, occupational exposure to pesticides has been better known for its adverse effects on fertility than domestic use. Other authors found residential exposure to have a role in spontaneous abortion especially if exposure happened early in pregnancy, [26]. Domestic use of pesticides was positive as a risk factor in this study. Some of the cases even used insecticides daily. Romero et al [25] in Mexico found exposure to insecticides to be insignificant in a study similar to this study. Measuring levels of active substances in blood would be more accurate.

Romero and his colleagues [25] found no effect for exposure to glues and solvents in non occupational settings on infertility. Occupational exposure to solvents like formaldehyde in wood industries was found to be related to infertility and spontaneous abortion[32, 33]. Exposure to petrochemicals was also found to be related to spontaneous abortion [34]. Exposure to dry cleaning chemicals has also been reported to be related to infertility[27]. Also occupational exposure in the heath care sector to anaesthetic gases was found to be related to spontaneous abortion and congenital defects [26]. Antineoplastic drug exposure in nurses and those exposed to them in pharmaceutical industries were found to be related to spontaneous abortion. Other chemicals causing environmental pollution appear to act as endocrine disruptors, disturbing the endocrinal balance, although data is still not conclusive [26].

Exposure to chemicals in the form of dry cleaning, paints, dyes, labs, cosmetics, glues, solvents, acetone, benzene was positive as a risk factor in this study. But care should be taken in interpreting these results because of recall bias. Also studies measuring levels of active substances in blood would be more accurate in identifying true relations.

Medical risk factors (Medical conditions, medications and family history)

Many medical conditions and their treatment, a couple's degree of consanguinity, family history of disease and other medical conditions can affect fertility[20].

Significant medical risk factors included, history of the having a congenital malformation, familial history of hereditary disease, and abnormal pattern of menstruation.

Insignificant medical risk factors included history of chronic disease, having hereditary disease, family history

of congenital disease, history of repeated abortion in the subject or female relatives, history of consanguinity and delayed menarche.

With respect to history of congenital malformation: all those who had congenital malformation were cases; none of the controls reported having congenital malformation. There was a significant difference between cases and controls. Five out of 11 of cases had a uterine anomaly. Saleh and Shawky, who conducted a study in Egypt, found an association between PCOs (polycystic ovary) and uterine anomalies in infertile patients. They suggested a genetic rather than a developmental defect to play a role in the development of both [35]. Chan et al found the prevalence of uterine anomalies to be 8 % in infertile women. In this study the prevalence of uterine anomalies as reported by the patients was only 1%. The difference could be due to the fact that many of our patients still needed workup to identify the cause of infertility. On the other hand the family history of congenital anomaly showed no significant difference. It may be that the cause of the congenital malformation affected the fertility of the subject, and this cause was not inherited in the family.

History of hereditary disease in the study subjects was not significant but it was significant in family history. Examples of hereditary diseases included mental retardation, thalassemia and diabetes. These are known for their relation to infertility [37]. Numerous genes are now being studied for their relation to galactosemia, endometriosis, leiomyomas and polycystic ovarian disease[37].

There are numerous causes of abnormal menstruation. These include polycystic ovarian disease, hyperprolactinemia, dysfunctional uterine bleeding, ovarian cysts, fibroids and so on. Any of these could lead to infertility[38]. This risk factor was found to be positive in 41.9% of cases versus 13.1% in controls. This is important as care should be given to females with history of irregular menstruation in order to avoid other modifiable risk factors for infertility.

Abnormal age at onset of menarche is a risk factor for several diseases later in life, but the effect on infertility is unknown [39]. Delayed menarche was insignificant as a risk factor infertility in this study. Guldbrandsen et al, found a relation between delayed menarche and increased time to pregnancy beyond one year[39]. Sadrezadah et al found a relation between delayed menarche and PCO disease [40]. Authors also found a relation between premature ovarian failure and early age at menarche[39] [41]. The relation between early age at menarche and infertility was insignificant in this study.

Spontaneous abortion is estimated to be between 15 – 20%,[42]. In our study the percentage of history of repeated abortion was found to be 15.4% in cases and 14% in controls with no significant difference between the two groups.

The degree of consanguinity has been reported to affect fertility, [20]. In this study there was no significant difference. There were nearly an equal number of consanguineous marriages in each study group (21.4% cases versus 23.6% controls). A study in Jordan also found no effect of consanguinity on fertility, although the rates of still births and infant mortality were higher among consanguineous marriages[43]. It may be that their role is more important in inheritance of disease more than causing infertility.

Health related Quality of life

Reliability of the scale

Alpha Cronbach test for reliability was done for the section of the questionnaire on health related quality of life. Its value was found to be 0.915. This indicates that this section is coherent and the questions generally measure the same item which is health related quality of life by 91.5%.

Distribution of study group according to level of HRQOL**.**

12.4% of the cases seeking infertility treatment had either poor or very poor HRQOL in comparison to 3.1% of the controls. Still 7.7% of cases considered themselves to have excellent HRQOL in comparison to 2.0% of controls. Ficsher exact test was significant. Fardiazar et al [(44)] had similar results; around 16% had poor or very poor HRQOL and 8% had excellent HRQOL. 40% of cases had good health and 36.1 % had fair or intermediate health.

These results thus can imply that not all infertile women have poorer HRQOL. There are though some subgroups who do, and they need to be identified to provide suitable supportive measures.

Comparison of the different domains of quality of life

Comparison of the different domains of quality of life between cases and controls showed the cases had lower scores in all three domains. This is in accordance withDrosdzol A,and Skrzypulec [(45)] who also found a decrease in all QOL domains in their study conducted in Poland. This result was also found by Fekkes et al[(46)] in Netherlands and Valsangkar et al [(47)] in India, and Charandabi et al [(48)] in Iran.

But on the other hand , when the subjects were asked to give a score to their whole QOL, the cases had a mean of 3.24±0.88, and controls had a mean of 3.25±0.55. There was no significant difference between the two groups. Ragni et al, [5] also found no difference between his cases and the general population in his study. These results could be interpreted as follows. The different domains of quality of life reflect the point of view of scholars and researchers. Thus the questions postulated by them to reflect the HRQOL did show lower scores for cases than controls. But when we asked the cases and controls to evaluate their total HRQOL, there was no big difference between the two groups. Kalkhoran et al, [49] found similar results where they found anxiety and depression to be higher among infertile women but life satisfaction did not show much difference between the two groups. This could reflect the fact that having children is not that important to have a good quality of life as many of the cases may believe. Or in other words, those who have children also have other problems which affect their quality of life making it not as good as infertile females may anticipate. The higher standard deviation in the cases could be due to the personal variations among subjects in dealing with infertility. Some persons have irrational parenthood beliefs where they believe their whole happiness is centered on parenthood. Other cases are quite serene and calm on the subject. Fardiazar et al, [44], found that irrational parenthood beliefs were related to worse scores on HRQOL.

Conclusions and recommendations:

There are numerous risk factors in the Egyptian society that could affect female fertility. Many of these are preventable. Infertility has negative effects on the

quality of life of affected females in separate domains but the total quality of life was not affected although patients may think so. It is recommended that the preventable risk factors be avoided. It is also recommended that more precise environmental studies measuring different exposures in relation to infertility be carried out. It is also recommended that special supportive care and counseling be provided for this sensitive group of patients.

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Table 1: Distribution of demographic and social characteristics of the study population (n = 918)

		Infertile females N = 468		Fertile females N = 450		p value
		N	%	N	%	
Age:	< 30 30 – 39 ≥ 40	290 155 23	(62) (33) (4.9)	161 212 77	(34) (47) (17)	<0.01
Age at marriage:	< 20 20 – 29 ≥ 30	142 274 52	(30) (59) (11)	162 277 11	(36) (61.6) (2.4)	<0.01
Duration of marriage	< 5 years 5 – 14 years ≥ 15 years	246 200 22	(52.6) (42.7) (4.7)	86 223 11	(19.1) (49.6) (31.3)	<0.01
Place of residence	Urban Rural	367 101	(784) (21.6)	348 102	(77.3) (22.7)	N.S.
Education	Undergraduate Graduate and postgraduate	401 67	(85.7) (14.3)	365 85	(81.1) (18.9)	N.S.
Employment:	works doesn't work	153 314	(32.8) (67.2)	156 294	(34.7) (65.3)	N.S.

N.S. = not significant

Table 2: Distribution of Lifestyle Risk Factors among the study sample

	Infertile females N = 468		Fertile females N = 450		
	N	%	N	%	p value
BMI < 30 ≥ 30	 366 102	 (78.2) (21.8)	 421 29	 (93.6) (6.4)	 <0.01
Caffeine (any daily intake)	312	(66.7)	299	(66.4)	N.S.
Smoking Active Passive Water pipe	 6 283 3	 (1.3) (60.5) (0.6)	 3 255 0	 (0.7) (56.6) (0.0)	 N.S. N.S. N.S.
Alcohol (any intake)	5	(1.1)	0	(0.0)	<0.01
*Inadequate practice of exercise:	353	(75.5)	325	(72.3)	N.S.

*Adequate amount of exercise was defined as doing exercise at least 3 times a week for 20 minutes or more.
N.S. = not significant

Table 3: Distribution of the environmental risk factors among the study population

	Infertile females N = 468		Fertile females N = 450		
	N	%	N	%	p value
Exposure to x-ray	49	(10.5)	3	(0.7)	<0.01
Exposure to radiotherapy (3 cases had occupational exposure)	46	(9.8)	4	(0.9)	<0.01
Exposure to radioactive materials	1	(0.2)	1	(0.2)	N.S.
Exposure to chemotherapy	1	(0.2)	0	(0)	N.S.
Exposure to lead	27	(5.8)	9	(2.0)	<0.05
Exposure to domestic pesticides	147	(31.4)	96	(21.3)	<0.01
Exposure to chemicals:	42	(9.0)	15	(3.3)	<0.01

N.S. = not significant

Table 4: Distribution of medical characteristics among the study population, n=918

	Infertile females n = 468		Fertile females n = 450		p value
	n	%	n	%	
Chronic disease:	86	(18.4)	100	(22.2)	N.S.
Regular medication use :	42	(9.0)	60	(13.3)	<0.05
Contraceptive use:	83	(17.73)	330	(73.3)	<0.01
History of hereditary disease	9	(9.1)	2	(0.4)	N.S.
Family history for hereditary disease	10	(2.14)	5	(1.1)	<0.01
History of congenital malformation	11	(2.4)	0	(0.0)	<0.01
Family history of congenital malformation	6	(1.3)	10	(2.2)	N.S.
History of repeated abortion in self or female relatives:	72	(15.4)	63	(14)	N.S.
History of consanguinity :	100	(21.4)	106	(23.6)	N.S.
Menstrual history; Delayed menarche Abnormal pattern of menstruation	34 196	(7.3) (41.9)	47 59	(10.4) (13.1)	N.S. <0.01

N.S. = not significant

Table 5 : Reliability of the quality of life scale

60	N of Items
0.915	Cronbach's Alpha

Table 6: Comparison of different domains of quality of life among infertile and fertile females

	Infertile females (n=468)		Fertile females (n = 450)		t-test	p value	95% C.I. of the difference
	mean	S.D.	mean	S.D.			
Physical Domain	3.77	0.58	4.151	0.47	10.73	<0.001	-0.44 – -0.30
Psychological domain	2.97	0.60	3.70	0.28	23.66	<0.001	-0.78 - -0.66
Social Domain	3.78	0.51	4.12	0.17	13.66	<0.001	-0.39 - -0.29
Total QOL	3.24	0.88	3.25	0.55	0.064	N.S.	-0.98 - 0.85

Independent sample T- test was done to compare between QOL domains between cases and controls. Cases showed lower scores than controls in all three domains of QOL.

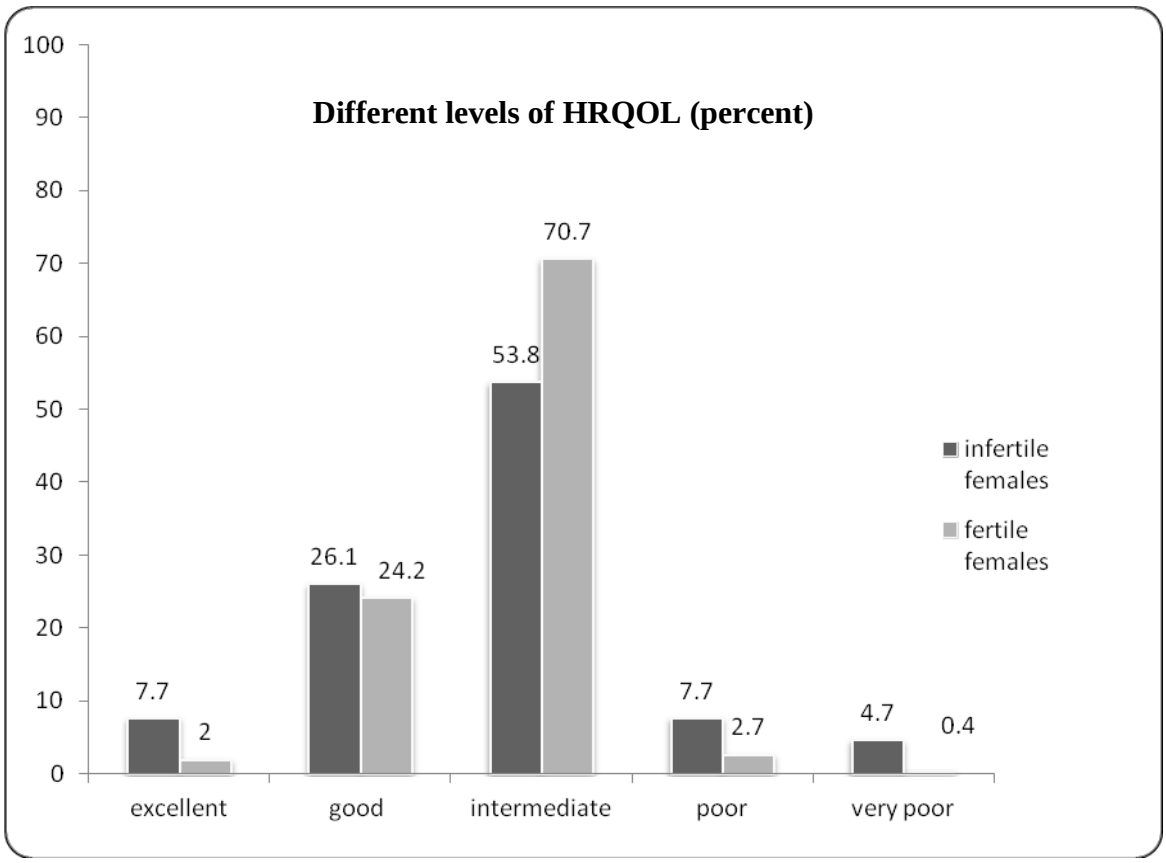

Figure 1: Distribution of the different levels of HRQOL among the study group

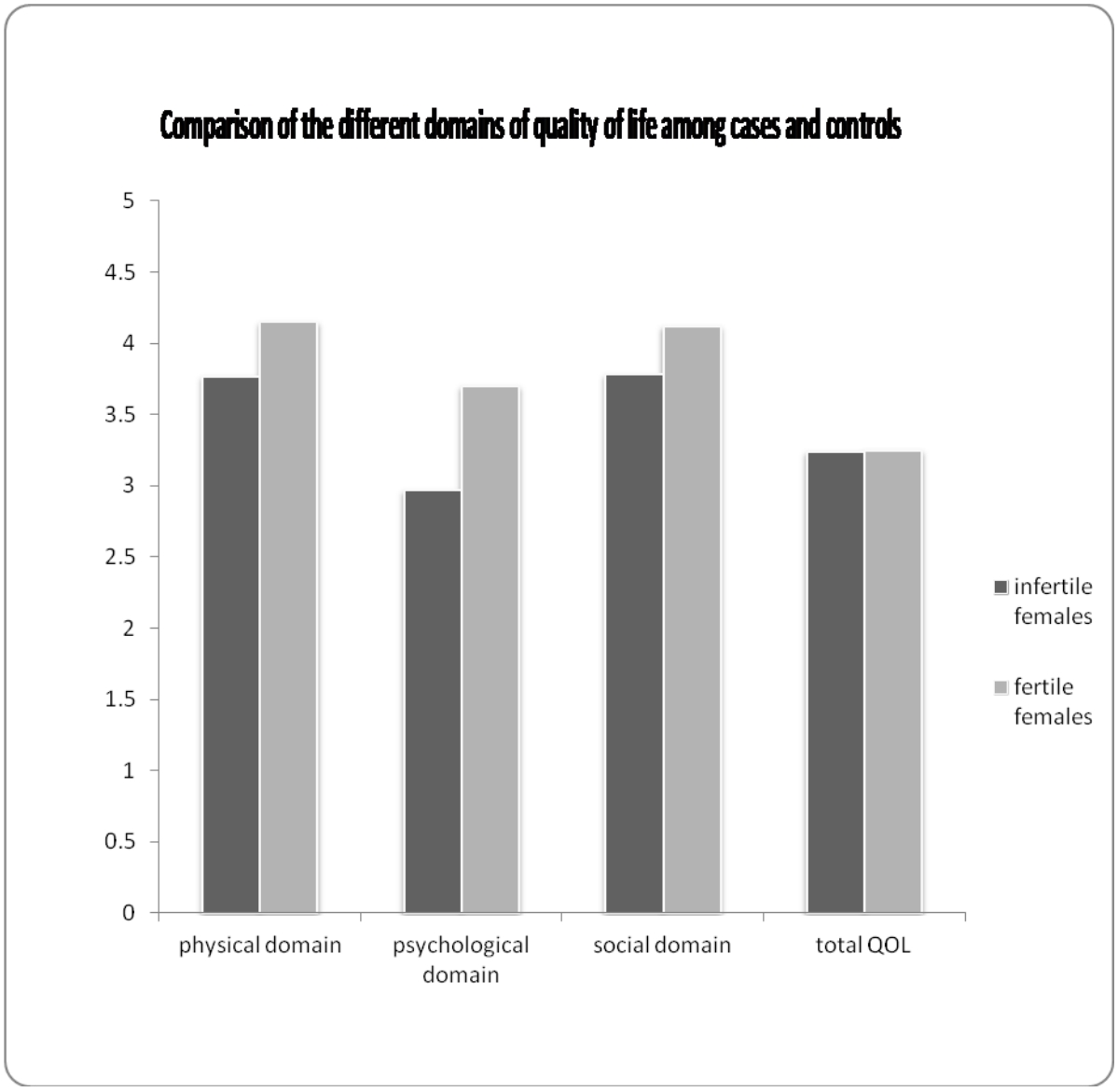

Figure 2: Comparison between the different domains of quality of life