

Personal & Environmental Risk Factors of Missed Miscarriage among Women Attending Ain -Shams University Maternity Hospital, Cairo, Egypt

¹Habiba S. Abd Elsalam, ²Ghada O. Wassif, ³Ebtihal M. Eltaieb, ³Yasser M. Ali Abou Talib

¹Family Medicine Specialist, Elobour Family Medicine Center, ²Department of Community, Environmental & Occupational Medicine, ³Department of Obstetrics & Gynecology, Faculty of Medicine, Ain Shams University

Received: January, 2019 Accepted: March, 2019

Abstract

Background: In recent years, the incidence of missed miscarriage tended to increase; its prevalence becomes more than 3% of all pregnancies. Although chromosomal abnormalities are implicated in approximately 50% of all spontaneous miscarriages, the remaining 50% may be preventable and related to environmental factors. **Objectives:** To determine the risk factors for missed miscarriage among women attending the emergency room and outpatient clinic at Ain-Shams University Maternity hospital. **Method:** A Case control study was carried out among 130 women with normal pregnancies “Controls” and 130 cases of missed miscarriage. Data were collected using a structured interviewed questionnaire. Anthropometric measurements were performed, and Ultrasonography was done to all participants to confirm the diagnosis of missed abortion. **Results:** Age, Hypercoagulation of blood, DM, PCO, Practicing physical exercise, using mobile phone for long time and fast food are independent significant predictors for missed miscarriage in the studied pregnant women. **Conclusion:** Missed Abortion is linked to many modifiable risk factors which could be easily prevented and hence decrease maternal morbidity & mortality; the researchers recommend further work to confirm these findings in other study populations.

Key words: *Missed miscarriage – Risk factors – Environmental – Lifestyle – Cairo - Egypt*

Corresponding author: Dr Ghada Osama Wassif E-mail: ghada_wassif@yahoo.com

Introduction:

Miscarriage or Spontaneous abortion is the spontaneous termination of pregnancy before 20 weeks of gestation or delivery of a fetus weighing 500 grams or less (a non-viable fetus), after which fetal death is known as a stillbirth.¹ Miscarriage is one of the most common complications of pregnancy. It is estimated that more than 20% of pregnancies terminate in miscarriage but the figures may actually be much higher since many early miscarriages are undiagnosed and are taken as unusually heavy periods. A miscarriage occurring

before 12 weeks of pregnancy is known as early miscarriage, while one occurring between 12 and 20 weeks of pregnancy is called late miscarriage⁽²⁾. Miscarriages are categorized as threatened, inevitable, incomplete, complete, or missed, and can be further classified as sporadic or recurrent (≥ 3 occurrences)⁽³⁾.

Missed miscarriage (silent miscarriage) is defined as an in utero death of the embryo or fetus before the 20 week of gestation with retained conception products, the fetal death occurs with no uterine activity to

evict the products of conception and it can happen in the first or second trimester, though it usually happens in the first trimester.⁴ In recent years, the incidence of missed miscarriage tended to increase; the prevalence of missed miscarriage becomes more than 3% of all pregnancies.⁵ Based on missed miscarriage statistics, about 17% to 22% is the over-all risk of missed miscarriage from all miscarriages. Miscarriage occurs due to many different causes, some of them known and others unknown, Most missed miscarriages are caused by chromosomal abnormalities in the fetus, which do not allow the pregnancy to develop however, there is a possible Risk factors may increase the incidence of missed miscarriage related to personal factors, life style, environmental factors and miscellaneous factors.⁶ Although chromosomal abnormalities are implicated in approximately 50.0% of all spontaneous miscarriages, the remaining 50.0% may be preventable and related to environmental factors.⁷

In Egypt, missed miscarriage is a widespread and serious clinical situation which not only affects the woman's health but also has great influence on population quality. Previous researches focused primarily on the management of missed miscarriage from the clinical point of view, Very few researches; which are all carried out abroad studied some of the risk factors related to missed miscarriage. In this study; all risk factors "Maternal and Environmental" have been studied in women attending the emergency room and outpatient clinic at Ain Shams Maternity hospital in an attempt to provide a clue for prevention of such situation in pregnant mothers and decrease its related morbidity and mortality.

Objectives: To determine the Personal and Environmental risk factors for Missed miscarriage among women attending the

emergency room and outpatient clinic at Ain-Shams University Maternity hospital.

Method

A hospital based analytical case control study was carried out at Emergency Room and outpatient clinic at Ain Shams University Maternity hospital located in Abbassia square in Cairo, Cases were women who diagnosed as missed Miscarriage based on Missed Miscarriage case definition provided that all participants were incident cases; A missed miscarriage is usually diagnosed during a routine checkup when the blood B hCG fails to increase as expected or when on ultrasound there is either no embryo (blighted ovum) or when there is an embryo or fetus with a crown rump length of more than 5 mm without cardiac activity.⁸ Controls were Women with current normal pregnancy (have +ve fetal life with Ultrasound), Controls have been selected from Antenatal care outpatient clinic. The researcher selected healthy controls were in the 3rd trimester in order to be sure that there is a negligible chance of missed miscarriage occurrence as it occurs in the 1st or 2nd trimester only (before 20 weeks of gestation).¹ Participating women were included according to a presettled inclusion and exclusion criteria, *Inclusion criteria were:* Women with regular menstrual cycles and sure of their last menstrual period (Naegele's rule), Singleton pregnancy and women with Intrauterine pregnancy who agrees to participate were included in the study. *Exclusion criteria* were all women with Molar pregnancy, incomplete miscarriage. The sample size of this study was divided into two groups: Group sample sizes of 130 women with normal pregnancies "Controls" and 130 case of missed miscarriage .The calculated sample size achieve 80% power to detect an odds

Table (1): Comparison between cases of missed miscarriage and controls regarding Sociodemographic characteristics and special habits of medical importance:

Variables	Cases (n=130)		Controls (n=130)		t-test	P-value	Odds ratio	95% CI	
	Mean	± SD	Mean	± SD					
Age	29.63	6.33	27.26	5.41	3.24	0.001*			
Duration of marriage (years)	8.27	6.04	5.51	3.59	4.48	<0.001*			
BMI	28.22	5.17	28.25	4.75	0.05	0.96			
	N	%	N	%	Chi square	P-value	Odds ratio	95% CI	
Level of education	Illiterate	12	9.2%	19	14.6%	1.39	0.24	-	-
	Read and Write	27	20.8%	32	24.6%				
	Basic Education	11	8.5%	14	10.8%				
	Qualified Average	61	46.9%	37	28.5%				
	High Qualified	19	14.6%	28	21.5%				
Working status	not working	114	87.7%	110	84.6%	0.52	0.47	0.77	0.38 – 1.57
	Working	16	12.3%	20	15.4%				
Residence	Rural	38	29.2%	28	21.5%	2.03	0.15	1.51	0.86 – 2.64
	Urban	92	70.8%	102	78.5%				
Smoking	No	125	96.2%	130	100.0%	5.10	0.06	-	-
	Yes	5	3.8%	0	.0%	FE (≠)			
Taking sedatives	No	125	96.2%	130	100.0%	5.10	0.06	-	-
	Yes	5	3.8%	0	.0%	FE (≠)			
Consanguinity	No	79	60.8%	91	70.0%	2.45	0.12	1.51	0.90 – 2.52
	Yes	51	39.2%	39	30.0%				
Premarital investigations	No	100	76.9%	68	52.3%	17.23	<0.001*	0.33	0.19 – 0.56
	Yes	30	23.1%	62	47.7%				

* Statistically significant at P<0.05

(≠) Fisher Exact test was used as (20%) of the cells or more have expected count less than 5

ratio in the group proportions of 3.0. The significance level of the test was targeted at 0.05. Data was collected using interview questionnaire which was adopted from different studies^{9,10}; the questionnaire consisted of four main sections which are: Sociodemographic data and special habits of medical importance, Reproductive history, Medical history and Environmental and Behavioral factors. The designed interview questionnaire was pilot tested on 10% of the sample size prior to data collection, necessary modifications were carried out on the questionnaire and data obtained from the pilot study was excluded from the study. Anthropometric assessment in the form of Weight, height and BMI (Kg/m²) were performed for all participating women, In addition to that;

significant ultrasound findings was recorded to diagnose missed miscarriage cases.

The collected data were revised, coded, tabulated and introduced to personal computer then finally analyzed using statistical package for social sciences (IBM SPSS Version 20). Differences were considered significant at p-value less than or equal to 0.05.

A verbal informed consent was obtained from each participant prior to data collection which addresses the confidentiality of data obtained and assuring that participation in the study is completely voluntary; The protocol was submitted for ethical committee board approval and it was approved as an exempted research, In addition to that;

Table (2): Comparison between cases of missed miscarriage and controls regarding reproductive history:

Variables	Cases (n=130)		Controls (n=130)		Chi square	P-value	Odds ratio	95% CI	
	N	%	N	%					
Number of pregnancies (Gravidity)	No	19	14.6%	14	10.8%	12.32	<0.001*	-	-
	Once	11	8.5%	39	30.0%				
	Twice	19	14.6%	39	30.0%				
	three or more	81	62.3%	38	29.2%				
Number of labor (Parity)	No	55	43.0%	17	13.1%	6.09	0.01*	-	-
	Once	19	14.8%	46	35.4%				
	Twice	20	15.6%	38	29.2%				
	three or more	34	26.6%	29	22.3%				
Type of last labor	CS	44	55.0%	50	43.1%	2.69	0.10	1.61	0.91 – 2.86
	Vaginal	36	45.0%	66	56.9%				
Previous miscarriage	No	43	33.1%	102	78.5%	54.28	<0.001*	7.37	4.23 – 12.84
	Yes	87	66.9%	28	21.5%				
Number of previous miscarriage	Once	29	33.3%	21	75.0%	14.96	<0.001*	6.00	2.29 – 15.74
	recurrent	58	66.7%	7	25.0%				
Period of previous miscarriage	first trimester	67	77.0%	28	100.0%	7.79	0.01*	-	-
	second trimester	20	23.0%	0	.0%				
Type of previous miscarriage	Missed	63	72.4%	7	25.0%	19.99	<0.001*	7.88	2.97 – 20.90
	Normal	24	27.6%	21	75.0%				
D & C after previous miscarriage	No	31	35.6%	21	75.0%	13.25	<0.001*	5.42	2.07 – 14.17
	Yes	56	64.4%	7	25.0%				
Medical intervention after previous miscarriage	No	65	74.7%	24	85.7%	1.47	0.23	2.03	0.63 – 6.50
	Yes	22	25.3%	4	14.3%				

* Statistically significant at $P < 0.05$

administrative approval from the Maternity hospital manager, Ain Shams university was obtained.

Results

Regarding Sociodemographic characteristics and special habits of medical importance of the studied participants, the Current study findings showed that there was a statistically significant difference between cases of missed miscarriage and controls as regard Age, duration of marriage and premarital investigations ($P < 0.05$) where the mean age and the mean duration of marriage was higher in cases than in controls. In contrast to that history of premarital investigation was higher in controls than cases.

However, There was a statistically insignificant difference between cases and controls as regard BMI, level of education, working status, residence, smoking, taking sedatives and consanguinity ($P > 0.05$) (Table 1)

Concerning Reproductive history of the studied participants; there was a statistically significant difference between cases and controls as regard Gravidity, Parity, previous miscarriage, number of previous miscarriages, period of miscarriage, type of miscarriage and D&C after miscarriage ($P < 0.05$). Where the gravidity, previous miscarriage, previous miscarriage in the second trimester, previous missed miscarriage and previous D&C was higher in cases than controls. In

Table (3): Comparison between cases of missed miscarriage and controls regarding medical history:

Variables	Cases (n=130)		Controls (n=130)		Chi square	P-value	Odds ratio	95% CI
	N	%	N	%				
Heart disease	No	114 87.7%	130 100.0%		17.05	<0.001*	-	-
	Yes	16 12.3%	0 .0%					
HTN	No	110 84.6%	124 95.4%		8.38	0.004*	3.76	1.46 – 9.69
	Yes	20 15.4%	6 4.6%					
DM	No	113 86.9%	130 100.0%		18.19	<0.001*	-	-
	Yes	17 13.1%	0 .0%					
Hyper-coagulation of blood	No	67 51.5%	130 100.0%		83.15	<0.001*	-	-
	Yes	63 48.5%	0 .0%					
Immune disease	No	126 96.9%	129 99.2%		1.84 FE(≠)	0.37	4.10	0.45 – 37.15
	Yes	4 3.1%	1 0.8%					
Pelvic operation	No	84 64.6%	91 70.0%		0.86	0.36	1.28	0.76 – 2.15
	Yes	46 35.4%	39 30.0%					
PCO	No	103 79.2%	127 97.7%		21.70	<0.001*	11.10	3.27 – 37.62
	Yes	27 20.8%	3 2.3%					

* Statistically significant at P<0.05

≠ Fisher Exact test was used as (20%) of the cells or more have expected count less than 5

Table (4): Comparison between cases of missed miscarriage and controls regarding Behavioral Factors:

Variables	Cases (n=130)		Controls (n=130)		t-test	P-value	Odds ratio	95% CI
	Mean	± SD	Mean	± SD				
Duration of physical exercise (min per day)	33.04	13.46	32.22	11.57	0.38	0.70		
	N	%	N	%	Chi square	P value	Odds ratio	95% CI
Physical exercises	No	79 60.8%	42 32.3%		21.16	<0.001*	0.31	0.19 – 0.51
	Yes	51 39.2%	88 67.7%					
Type of PE	Swimming	6 11.8%	11 12.5%		0.02	0.90	0.93	0.32 – 2.70
	Walking	45 88.2%	77 87.5%					
Frequency of PE per week	Once	4 7.8%	0 .0%		4.86 FE≠	0.03*	-	-
	Twice	6 11.8%	9 10.2%					
	≥ 3	41 80.4%	79 89.8%					
Good ventilation in house	No	24 18.5%	21 16.2%		0.24	0.62	0.85	0.45 – 1.62
	Yes	106 81.5%	109 83.8%					
Exposure to continuous noise	No	77 59.2%	107 82.3%		16.73	<0.001*	3.20	1.81 – 5.66
	Yes	53 40.8%	23 17.7%					
Fast food	No	93 71.5%	127 97.7%		34.16	<0.001*	16.84	5.04 – 56.29
	Yes	37 28.5%	3 2.3%					
Drink coffee	No	94 72.3%	112 86.2%		7.57	0.01*	2.38	1.27 – 4.47
	Yes	36 27.7%	18 13.8%					
Number of cups per day	<2	22 61.1%	15 83.3%		2.75	0.10	3.18	0.78 – 13.02
	2-5	14 38.9%	3 16.7%					

* Statistically significant at P<0.05

≠ Fisher Exact test was used as (20%) of the cells or more have expected count less than 5

Table (5): Comparison between cases of missed miscarriage and controls regarding Environmental factors:

Variables	Cases (n=130)		Controls (n=130)		Chi square	P-value	Odds ratio	95% CI	
	N	%	N	%					
Exposure to environmental toxins	No	111	85.4%	114	87.7%	0.30	0.59	1.22	0.60 – 2.49
	Yes	19	14.6%	16	12.3%				
Family stress	No	65	50.0%	114	87.7%	43.06	<0.001*	7.13	3.81 – 13.33
	Yes	65	50.0%	16	12.3%				
Job stress	No	115	88.5%	130	100.0%	15.92	<0.001*	-	-
	Yes	15	11.5%	0	.0%				
Physical trauma	No	116	89.2%	128	98.5%	9.59	0.002*	7.72	1.72 – 34.71
	Yes	14	10.8%	2	1.5%				
Psychological trauma	No	89	68.5%	125	96.2%	34.23	<0.001*	11.52	4.28 – 30.30
	Yes	41	31.5%	5	3.8%				
Passive smoking	No	45	34.6%	65	50.0%	6.30	0.01*	1.89	1.15 – 3.11
	Yes	85	65.4%	65	50.0%				
Duration of exposure to passive smoking	<2	38	44.7%	53	81.5%	21.10	<0.001*	-	-
	2-3	31	36.5%	7	10.8%				
	>3	16	18.8%	5	7.7%				
Exposure to radiation during pregnancy	No	126	96.9%	130	100.0%	4.06	0.12	-	-
	Yes	4	3.1%	0	.0%				
Using mobile for long time >50 min (11)	No	62	47.7%	104	80.0%	29.39	<0.001*	4.39	2.53 – 7.61
	Yes	68	52.3%	26	20.0%				
Duration of using mobile in years	<4	25	36.8%	25	96.2%	28.61	<0.001*	-	-
	4-6	37	54.4%	1	3.8%				
	>6	6	8.8%	0	.0%				

* Statistically significant at P<0.05

≠ Fisher Exact test was used as (20%) of the cells or more have expected count less than 5

contrast the no of labors (parity) was higher in controls than cases. However, There was a statistically insignificant difference between cases and controls as regard type of the last labor and history of medical intervention after last miscarriage (P>0.05) (Table 2)

Regarding Medical history of the studied participants; that there was a statistically significant difference between cases and controls as regard presence of heart disease, hypertension, diabetes, hyper coagulability of blood and PCO (P<0.05), where HTN, DM, Hyper coagulation of blood and PCO were higher in cases than controls. However, there was a statistically insignificant difference between cases and controls as regard presence of immune

disease and history of pelvic operation (P>0.05) (Table 3)

Concerning Behavioral risk factors in the studied participants; there was a statistically significant difference between cases and controls as regard frequency of practicing physical exercise per week, where there was higher percentage of controls than cases who reported practicing physical exercise three or more times per week. However, There was a statistically insignificant difference between cases and controls as regard duration of physical exercise (minutes per day), type of physical exercise (P>0.05). In addition to that, that there was a statistically significant difference between cases and controls as regard consuming fast food, drinking coffee (P<0.05) where a higher

percentage of missed miscarriage cases than controls reported consumption of fast

food frequently, drinking coffee. However,

Table (6) Logistic regression analysis for risk factors of missed miscarriage:

	B	Wald	Sig.	Odds ratio	95% C.I. for odds ratio	
					Lower	Upper
Age	.198	32.748	.000*	1.219	1.139	1.304
Previous miscarriage	.423	.749	.387	1.526	.586	3.976
Hyper Coagulation of Blood	5.616	16.329	.000*	274.679	18.027	4185.367
HTN	.293	.141	.708	1.341	.290	6.208
DM	2.669	3.745	.053*	14.424	.967	215.258
PCO	1.450	3.785	.052*	4.261	.989	18.353
Physical Exercise	-1.622	11.688	.001*	.198	.078	.501
Passive smoking	-.089	.033	.856	.915	.352	2.380
Using Mobile phone	1.539	9.859	.002*	4.661	1.783	12.183
Fast Food	1.954	6.274	.012*	7.055	1.530	32.543
Coffee	.079	.024	.877	1.082	.400	2.927
Family stress	.869	3.081	.079	2.385	.904	6.297

* Statistically significant at $P < 0.05$

There was a statistically insignificant difference between cases and controls as regard number of cups of coffee consumed per day ($P > 0.05$) (Table 4).

Concerning Environmental risk factors in the studied participants; there was a statistically significant difference between cases and controls as regard Exposure to passive smoking, Duration of exposure to passive smoking and using mobile for long time > 50 min and Duration of using mobile ($P < 0.05$); where there was higher percentage of missed miscarriage cases than controls who reported exposure to passive smoking, use of mobile phones > 50 minutes, using mobile phones for long duration. In addition to that, that there was a statistically significant difference between cases and controls as regard exposure to continuous noise, exposure to family & job stress, exposure to physical and psychological trauma ($P < 0.05$) where a higher percentage of missed miscarriage cases than controls reported exposure to family & job stress, exposure to physical and psychological trauma. However, There was a statistically insignificant difference

between cases and controls as regard history of exposure to radiation during pregnancy, history of exposure to environmental toxins and good ventilation in house during pregnancy ($P > 0.05$) (Table 5).

Multivariate logistic regression analysis showed that; Age, Hyper coagulation of blood, DM, PCO, Practicing physical exercise, using mobile phone for long time and fast food are independent significant predictors for missed miscarriage in the studied pregnant women ($P < 0.05$) (Table 6).

Discussion:

Several factors have been correlated with higher miscarriage rates, but whether they cause miscarriages is debated. Regarding Sociodemographic characteristics of study participants the mean age in cases was significantly higher than controls, This finding could be explained by the fact that advanced maternal age is associated with higher incidence of missed miscarriage The current study agrees with *Gleicher et al., 2011*¹² who stated that the age of the

mother is a significant risk factor for missed miscarriage and miscarriage rates increase steadily with the age, with more substantial increases after age 35. Branch *et al.*, 2010¹³ explained this finding by stating that the increasing maternal age affects ovarian function and increases rates of aneuploidy in association with older oocytes and increased missed miscarriage rate. Concerning relationship between active smoking among studied women and the occurrence of missed miscarriage, the present study didn't find a statistically significant relationship between them in addition to that none of the interviewed women whether cases or controls admitted active smoking, Lis, *et al.*, 2015¹⁴ mentioned that Tobacco (cigarette) smokers have an increased risk of missed miscarriage, this finding was not easy to be studied in the present study due to differences between eastern and western cultures. The present study couldn't find association between pre-pregnancy BMI and missed miscarriage. This point should be subjected to further research as the relationship between obesity and missed miscarriage in participants had to be adequately investigated by cohort study. This finding contradicts with Vinter *et al.*, 2012¹⁵ who mentioned that obesity may increase the general risk of miscarriage. Concerning history of Polycystic ovarian disease in the studied women, the current study showed that there polycystic ovarian disease is significantly higher in missed miscarriage cases than healthy controls. This finding is further supported by a study carried out by Boomsma *et al.*, 2008¹⁶ who stated that polycystic ovarian syndrome, may increase the rate of miscarriage.

Regarding reproductive history of studied women, this study found that there was significantly higher percentage of cases who reported gravidity only which ended with more subsequent number of

miscarriages more than healthy controls. This finding was supported by Royal College of Obstetricians and Gynecologists, 2007¹⁷ who stated that there is a higher risk of miscarriage among the couples that have suffered a previous one, Women who have had a previous miscarriage have a 25 percent chance of future miscarriage. The present study found also that a significantly higher percentage of cases reported that they performed previous D&C procedures more than healthy controls. The current study finding is in agreement with Allison and Schust 2009¹⁸ who explained this by stating that D&C following miscarriage may cause Asherman's syndrome which is an acquired condition due to the presence of post-traumatic intrauterine adhesions which results from destruction of large areas of endometrium by curettage, partly or completely obliterating the uterine cavity and usually if pregnancy follows, the amount of remaining endometrium may be insufficient to support the pregnancy, and miscarriage may ensue. Our results found that there is a there is a statistically significant difference between cases and controls as regard performing premarital investigation ($P < 0.05$), where history of premarital investigation was higher in controls than cases. The results of our study also agree with Al Kindi *et al.*, 2012¹⁹ who stated that A lot of things can be anticipated by conducting premarital screening.

Concerning medical history in the studied women, the present study found that cases had significantly higher co morbid conditions than controls such as heart diseases, hypertension, Diabetes and hypercoagulability of blood. The present study agrees with Ramin *et al.*, 2010²⁰ who stated that Women with diabetes mellitus have a significantly higher risk of pregnancy loss and embryopathies

compared with healthy women, indicating that a tight control of glucose and/or insulin is essential for proper embryo development. In addition to that the current study is in concordance with *Cunningham et al., 2010*²¹ who found that some genetic disorders of blood coagulation may increase the risk of both arterial and venous thrombosis, and increase the risk of missed miscarriage. The current study showed that autoimmune disease is not significantly associated with the risk of missed miscarriage. This finding contradicts with the finding of *Gleicher et al., 2011*¹² who has suggested that autoimmune disease may cause genetic abnormalities in embryos which in turn may lead to missed miscarriage. This disagreement may be due to the fact that autoimmune diseases were not prevalent in the studied sample of women in order to be adequately studied, further studies should be entailed to prove or disprove this association. *Concerning Environmental and Lifestyle factors associated with missed miscarriage*, this study found that cases were significantly exposed to passive smoking more than healthy controls, in addition to that the current study succeeded to find a statistically significant association between long duration of exposure to passive smoking and missed miscarriage. This finding agrees with *Rogers, 2009*²² who stated that exposure to passive smoking and its substances like nicotine and carbon monoxide, is associated with a number of serious complications during pregnancy as increased rates of spontaneous abortion, preterm birth, placental abruption, growth restriction, premature rupture of membranes, missed miscarriage and stillbirth.

The present study also revealed that there is a statistically significant association between exposure to mobile phones for long duration > 50min and higher incidence

of missed miscarriage in cases more than healthy controls. This finding was further confirmed and explained by *Parazzini et al., 2010*²³ who have reported increased risk of spontaneous miscarriage and congenital malformations on exposure to Electromagnetic fields of mobiles that produce biological stress and free radicals, which can make a susceptible population prone to congenital malformations, tissue and cell damages.

The current study also found that controls who practice regular physical exercise 3 times per week for 30 min (e.g. walking) had decreased risk of missed miscarriage. These results agreed with *American College of Obstetricians and Gynecologists, 2015*²⁴ who mentioned that exercise had been shown to benefit most women (*protective factor*). Regular physical activity during pregnancy improves or maintains physical fitness, helps with weight management, reduces the risk of gestational diabetes in obese women, and enhances psychologic well-being. An exercise program that leads to an eventual goal of moderate-intensity exercise for at least 20–30 minutes per day on most or all days of the week should be developed with the patient and adjusted as medically indicated. However; exercise should be practiced with caution in terms of duration and intensity and duration as *Madsen, et al 2007* mentioned that women shouldn't exercise more than 7h/week especially in the first 18 weeks of pregnancy as it may increase the risk of missed miscarriage.

The present study revealed that exposure to coffee drinking has been shown to significantly increase the risk of missed miscarriage, this finding is confirmed by a study carried out by *Madsen et al., (2007)*²⁵ who stated that Caffeine consumption has been correlated to miscarriage rates, at least at higher levels

of intake. On contrast to that; Another prospective cohort study carried out by Savitz *et al.*, 2009²⁶ found that light or moderate caffeine consumption (up to 300 mg per day which equal 3 cups per day) had no effect on pregnancy or miscarriage rates.

The current study also revealed that cases had significant increased risk of missed miscarriage due to consuming fast foods during pregnancy. This finding agree with Endrikat *et al.*, 2010²⁷ who stated that there is list of certain foods as 'fast foods' should be avoided for pregnant women, The reason is that these foods are regarded as having a higher risk of containing the bacteria such as salmonella that can cause food poisoning and *Listeria monocytogenes* which if transmitted to unborn baby it can lead to extremely serious complications including miscarriage, premature labour, or stillbirth. The current study mentioned that cases had significant increased risk of missed miscarriage due to their exposure to family, job stress and exposure to psychological trauma. These finding is in agreement with *National Institute of Occupational Safety and Health (NIOSH) (2008)*²⁸ who stated that there is adverse influence of job stress on a woman's reproductive health including infertility, menstrual disorders, lower conception rates, spontaneous miscarriage, and low birth weight. In addition to that Kicia *et al.*, 2015²⁹ found that a two-fold increase in miscarriage rate was found in women with a history of exposure to psychological stress (e.g. financial or marital problems, death, divorce, physical and nonphysical abuse inflicted on a woman by her partner and loss of social support).

The current study revealed also that exposure to physical trauma during pregnancy was significantly higher in missed miscarriage cases than healthy

controls. The present study agrees with Cunningham *et al.*, 2005³⁰ who Stated that a major abdominal trauma can precipitate miscarriage.

Study limitations

Recall bias was the main limitation due to the use of case control study; however the interviewer tried to ask participants more than one time if they fail to recall any exposure.

This study couldn't find association between some risk factors which were previously reported as causes of missed miscarriage such as smoking, alcohol consumption and use of addictive drugs due to two main reasons, under reporting by study participants due cultural issues or inadequate sample size. Studying the relationship between these exposures (as they are rare exposures in our community are better to be studied by cohort study design to prove or disprove their relationship with missed miscarriage.

Conclusions and recommendations:

In conclusion, passive smoking, a sedentary lifestyle, exposure to electromagnetic field of mobiles, stress, fast food consumption, heavy consumption of coffee, Psychological and physical trauma during pregnancy are modifiable risk factors for missed miscarriage. Most of these risk factors are related to pregnant women lifestyle and surrounding environment and thus we recommend the following to prevent the occurrence of such condition that eventually affects women's health; Pregnant women should be encourage practicing light to moderate physical exercise during pregnancy e.g. Walking for 30 minutes 5 days per week to maintain healthy body balance, Encourage doing premarital investigations, Avoid causes of psychological and family stress

and promote emotional wellbeing, Decrease using a mobile phone and computer for long time (not more than 50 minutes per day), Reduce exposure to active and passive smoking might help women in early pregnancy (or planning a pregnancy) reduce their risk of missed miscarriage, Good control of diabetes, hypertension, heart diseases, PCO, Avoid exposure to physical trauma, Avoid high caffeine intake during pregnancy (not more than 300 mg per day or 3 cups per day), Eat a balanced diet. Include more fruits, vegetables and whole grains & Avoid unhealthy diet (fast foods, processed and fatty foods, To avoid or minimize the risk of maternal thrombosis, prophylactic maternal heparin should be maintained at least up to 6 weeks postpartum.

References:

1. Chayachinda C, Manopchai T, Moalee B and Alissara S (2012) Septic abortion: A 5-year experience at siriraj hospital. *J Med Assoc thai*;95(3):307-12.
2. American Pregnancy Association (2017). Miscarriage: Signs, Symptoms, Treatment and Prevention, available at: <http://americanpregnancy.org/pregnancy-complications/miscarriage/>
3. American College of Obstetricians and Gynecologists (2010): Medical management of abortion. *Practice Bulletin No. 26*, April.
4. Zegiri F, Pacarada M, Kongjeli N, Zegiri V and Kongjeli G (2010): missed abortion and application of misoprostol. *Med Arch*;64(3):151-53.
5. SuShiLi (2010): Managements of Missed Abortion. Available at: <http://www.m.dissertationtopic.net/doc/117900>.
6. Branch D.W., Gibson M & Silver R.M. (2010): Clinical practice. recurrent miscarriage. *The New England Journal of Medicine*; 363(18): 1740-1747.
7. Stephenson M and Kutteh W (2007): Evaluation and management of recurrent early pregnancy loss. *Clin Obstet Gynecol*; 50:132–145.
8. Salamanca A, Fernandez-Salmeron E, Beltran E, Mendoza N, Florido J, Mozas J (2013): Early embryonic morphology sonographically assessed and its correlation with yolk sac in missed abortion. *Arch Gynecol Obstet*; 287: 139–142.
9. Zhang X, Li J, Gu Y, Zhao Y (2011): A pilot study on environmental and behavioral factors related to missed abortion; *Medical Association*, 305(8): 808-13.
10. Eum KD, Li J, Lee HE, Kim SS, Paek D, Siegrist J, et al. (2007): Psychometric properties of the Korean version of the effort-reward imbalance questionnaire: a study in a petrochemical company. *Int Arch Occup Environ Health*; 08:653–661.
11. Volkow ND, Tomasi D, Wang GJ, Vaska P, Fowler JS, Telang F, et al. (2012): Effects of cell phone radiofrequency signal exposure on brain glucose metabolism. *JAMA*; 305(8): 808-813.
12. Gleicher N, Weghofer A, Barad DH (2011): Do chromosomally abnormal pregnancies really preclude autoimmune etiologies of spontaneous miscarriages?. *Autoimmunity Reviews* 10 (6): 361–3
13. Branch D.W., Gibson M & Silver R.M. (2010): Clinical practice. recurrent miscarriage. *The New England Journal of Medicine*; 363(18): 1740-1747.
14. Lis R, Rowhani-Rahbar A, Manhart LE (2015): Mycoplasma genitalium Infection and Female Reproductive Tract Disease: A Meta-Analysis. *Clinical Infectious Diseases*; 61: 418–26
15. Vinter CA, Tanving MH, Damm P, Naver KV, Andersen LL, Liest S and Renault KM (2012): Obese pregnant women and complications in relation to pregnancy and birth. *Ugeskr Laeger*; 174(16):1079-1082.
16. Boomsma CM, Fauser BC, Macklon NS (2008): Pregnancy complications in women with polycystic ovary syndrome. *Seminars in reproductive medicine* 26 (1): 72–84.
17. Royal College of Obstetricians and Gynaecologists (2007): Long-term consequences of polycystic ovarian syndrome.
18. Allison JL and Schust DJ (2009): Recurrent first trimester pregnancy loss: revised definitions and novel causes. *Curr*

Opin Endocrinol Diabetes Obes; 16(6): 446-50.

19. Al Kindi R and Al Rujaiabi S (2012): Knowledge and attitude of University students towards premarital screening program. *Oman Med J*; 27:291–296.

20. Ramin N, Thieme R, Fischer S, Schindler M, Schmidt T, Fischer B and Navarrete SA (2010): Maternal diabetes impairs gastrulation and insulin and IGF-1 resaptor expression in rabbit blastocysts. *Endocrinology*; 151: 4158-67.

21. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ and Spong CY (2010): *Abortion: Williams Obstetrics, 23rd edition*, Prentice-hall International Inc., McGraw-Hill companies; (9): 215-34.

22. Rogers JM (2009): Tobacco and pregnancy. *Reprod Toxicol*; 28(2): 152-60.

23. Parazzini F, Chiaffarino F, Chatenoud L, Cipriani S, Ricci E, Chiantera V, et al. (2010): Exposure to video display terminals and risk of small-for-gestational-age birth. *J Environ Health*; 72(6):24–7.

24. American College of Obstetricians and Gynecologists (2015). *Physical Activity and Exercise During Pregnancy and the Postpartum Period*; available at: [https://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Physical-Activity-and-](https://www.acog.org/Resources-And-Publications/Committee-Opinions/Committee-on-Obstetric-Practice/Physical-Activity-and-Exercise-During-Pregnancy-and-the-Postpartum-Period)

Exercise-During-Pregnancy-and-the Postpartum-Period

25. Madsen M, Jørgensen T, Jensen ML, Juhl M, Olsen J, Andersen PK, Nybo Andersen AM (2007): Leisure time physical exercise during pregnancy and the risk of miscarriage: A study within the Danish National Birth Cohort. *BJOG* 114 (11): 1419–26.

26. Savitz DA, Chan RL, Herring AH, Howards PP, Hartmann KE (2008): Caffeine and Miscarriage Risk. *Epidemiology* 19 (1): 55–62.

27. Endrikat S, Gallagher D, Pouillot R (2010): A comparative risk assessment for *Listeria monocytogenes* in prepackaged versus retail-sliced deli meat; *Journal of Food Protection*, 73(4): 612-619.

28. National Institute of Occupational Safety and Health (NIOSH) (2008): Working with stress. Publication number 114; Available at: <http://www.cdc.gov/niosh/docs/video/stress1.html>

29. Kicia M, Skurzak A, Wiktor K, Iwanowicz-Palus G & Wiktor H (2015): Anxiety and stress in miscarriage. *Pol J Public Health*. 125: 162–165.

30. Cunningham FG, Leveno KJ, Bloom SL, Hawth JC, Gilstrap L and Wenstron KD (2005): *Williams Obstetrics; 22nd edition*. MC Graw-Hill, New York. CH9 (Abortion): 231-51.