



Original Article

Prevalence and factors associated with pregnancy loss among physicians in King Abdul-Aziz University Hospital, Saudi Arabia

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ABSTRACT

Objective: Medical profession is a stressful occupation as it carries potential risk for pregnancy outcome. There is lack of researches regarding the pregnancy loss among physicians working in hospitals in Saudi Arabia. The current study aims at estimating the prevalence and factors associated with pregnancy loss among female physicians working at King Abdul-Aziz University Hospital in Jeddah, September, 2015.

Materials and methods: A cross sectional study has been conducted, which included all the female physicians working at King Abdul-Aziz University Hospital in Jeddah by filling a self-administered online questionnaire.

Results: Out of all responding physicians (n = 92), the majority were Saudis (93.5%), who were mostly married (89.1%) and rest were either divorced (8.7%) or widowed (2.2%). Seventeen female physicians had pregnancy loss before (18.5%) with a total of 25 losses, which were mostly occurred during first trimester, especially while working as residents (40%), the average monthly working hours in the first pregnancy loss was (median; IQR, 160, 110–198 h). No statistically significant difference could be detected regarding the variation in pregnancy losses according to nationality marital status nor specialty. **Conclusion:** Most of the pregnancy losses in physicians occurred in first trimester during residency with a relatively longer monthly working hours. Further researches are needed on a larger sample and wider scale with inclusion of other pertinent factors to enable judging on the independent relationship of pregnancy loss and medical profession.

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Introduction

Spontaneous pregnancy loss is surprisingly common worldwide, where approximately 15% of all clinically recognized pregnancies end by spontaneous loss. Spontaneous pregnancy loss may be emotionally and physically demanding for couples particularly when recurrent losses are faced. The habitual pregnancy loss is also referred as the recurrent pregnancy loss and defined as three consecutive pregnancy losses prior to twenty weeks from last menstrual period [1]. Out of this percentage, 12% were recurrent with more than two consecutive pregnancy losses [2]. Lok et al. [3] reported that almost 50% of women, who experience pregnancy loss suffer from some sort of psychological morbidity following

weeks or months of loss. Mostly, elevated anxiety, depressive symptoms, and even major depressive disorder had been reported in 10–50% after pregnancy loss. These psychological symptoms may last up to 6 months or 1 year after pregnancy loss [3]. Moreover, pregnancy loss can be physically and emotionally distressing for couples, especially when faced with recurrent losses [1]. Although, the etiological factors of pregnancy loss recognized, included uterine malformations and parental balanced chromosomal rearrangements. There have been many other factors suggested to be the possible risk factors [4]. Among these possible factors, life stress and insufficient social support during pregnancy were claimed to be related with spontaneous pregnancy loss [5].

In this respect, work stress had been identified as a remarkable risk factor that may affect pregnancy outcome [6]. There is a trend that female doctors usually carry on working during pregnancy, even though their profession puts a significant physical and emotional burden on them [7]. To explore the relationship between medical profession and pregnancy outcome in female physicians,

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reviewed literature revealed controversial results. For example, Phelan involved 2000 female doctors in the US and observed that there was no difference between reproductive disorders of female doctors and those of the general female population [8]. Cole et al. found a higher rate of preterm births among female physicians compared with the general female population [9].

In Saudi Arabia, although risk factors of spontaneous pregnancy loss had been studied among Saudi females in general population [10], but there is a lack of studies about it among female physicians. Therefore, the current study attempted to find out the possible impact of the medical profession on pregnancy loss in female physicians.

Rationale

The researcher decided to carry out this research due to personal pregnancy loss experience and it was repeated twice in the same year during the usual working hours. Up to the researcher's knowledge, such great loss had no explanation and exact answers were not well established or reached by professional physicians in Saudi Arabia, particularly in Jeddah. This triggered the researcher to look for clear answers regarding pregnancy loss and its associated factors among working female physicians.

Objectives of the study

This research aims at reducing pregnancy loss and its consequences in female physicians by analyzing the following objectives:

- To estimate the prevalence of pregnancy loss among female physicians working at King Abdul-Aziz University Hospital in Jeddah, 2015.
- To determine factors associated with pregnancy loss among female physicians working at King Abdul-Aziz University Hospital in Jeddah, 2015.

Contribution of the study

This research is expected to provide an evidence for the extent of pregnancy loss among female physicians. Also, it explores possible demographic and professional factors associated with pregnancy loss duties for female physicians.

Literature review

Female physicians are believed to be at higher risk due to factors related to the nature of their profession such as working for long hours in a stressful job, despite of its possible importance, there is no enough evidence from researches about the impact of medical profession on pregnancy outcome [11]. In USA, a study was carried out to explore pregnancy outcome among residents in obstetrics and gynecology departments in 2003. It has been observed that although female house officers continued to work for more than 80 h weekly during pregnancy, still they had good pregnancy outcome. It can be attributed to the institutional policies, which allow paid maternity leave usually 4–8 weeks, in addition to planned time off before delivery [12].

In USA, a qualitative study was conducted in 2009, where five otolaryngology residents, who gave birth during residency were interviewed, out of them one had pregnancy loss. As a whole, work load and altered schedule were acknowledged as main source of stress. It has also been claimed that maternity leave and flexible shifts could help in avoiding such adverse event [9].

Earlier in USA, a study was carried out in 1991, where the prevalence of pregnancy loss among the female physicians was

compared with the female partners of male physicians. Only the induced pregnancy loss was higher among the female physicians, but there was no statistically significant difference in the prevalence of spontaneous pregnancy loss. It was found that medical profession has no adverse impact on pregnancy outcome [13]. In Hungary, it has been evaluated through a nationwide study conducted in 2014 that the causality between medical profession and the development of reproductive disorders is mediated by burnout, which is an important risk factor for high-risk pregnancies and pregnancy loss. It has been suggested that the improvements in working conditions and prevention of burnout in female doctors are essential for reducing the likelihood of pregnancy loss among physicians [7].

Behbehani et al. used a web-based questionnaire, which was sent to 190 residents in both medical and surgical departments in North America, the results were compared with 3767 pregnant women of similar age. The prevalence of pregnancy loss was higher among residents (11.8%) compared to the control group (4.2%). Higher number of on-calls per month had significant influence on pregnancy and increased the pregnancy complications including pregnancy loss. Also, complications were significantly higher in female surgical residents, who worked for more than 8 h per week in the operation room as compared to female residents, who worked less than 8 h per week [14]. However, this study is criticized by depending on web based non-random selection of respondents.

In Saudi Arabia, the review of published literature revealed that only one case control study was carried out in Riyadh in 1994 about risk factors for spontaneous pregnancy loss at King Khalid University Hospital. The identified risks for spontaneous pregnancy loss included older age of menarche, husband's age older than 50 years, blood-related husbands, family history and previous pregnancy loss, increased consumption of daily caffeine, abdominal trauma, and fever during pregnancy [10]. Nevertheless, no previous study was carried out in Saudi Arabia to explore other potential factors related to medical profession that could possibly be related to pregnancy loss in female physicians.

Material and methods

A cross-sectional descriptive study design has been implemented. The study was conducted in King Abdul-Aziz University Hospital, which is a teaching hospital with a total capacity of more than 1000 beds. It covers major specialties such as general surgery, internal medicine, obstetrics & gynecology and pediatrics. Almost 30% of the female physicians are working in the hospital, who have duties and responsibilities equivalent to their male counterparts.

Study population

All female physicians working at King Abdul-Aziz University Hospital during the study period were considered eligible for inclusion in the study. According to the data obtained from the human resources administration, the total number of working female physicians was 186. Female physicians in the reproductive age, who were either currently married, divorced or widowed and had personal emails registered with their respective departments were included in the study. The female physicians, who were single and married but had no pregnancy ever, were excluded. The minimum sample size to achieve the study objective was 126 female physicians, excluding the menopausal women from the survey to justify the biasness in the study about early pregnancy or pregnancy loss. The list of recruited female physicians was obtained from the human resource manager, and online questionnaires were given to female physicians only through HR. This procedure was adopted to ensure that the recruited cases were female physicians only.

Sample size

Raosoft web site was used to calculate the sample size. As no accurate figure could be obtained about incidence of pregnancy loss in Saudi women, the prevalence was substituted in the equation by 50% to obtain the largest sample size. The population of the study was 186 physicians, an error of 5% and a confidence level of 95% was considered for the interpretation of results. The sample of the study included 126 physicians.

Data collection tool

A self-administered online questionnaire was constructed by the researcher and approved by three consultants. The questionnaire covered the socio-demographic status; such as age, nationality, degree, department and specialty. Also, it included other variables possibly related to pregnancy loss, such as night duties, number of working hours, number of on-calls per month, previous pregnancy loss and parity.

Data collection technique

The questionnaire was submitted to each department secretary, who redistributed it to the female physicians working at each department through emails. The submission of the filled questionnaire was online linked directly to the researchers' email.

Study variables

The dependent and independent variables were considered for the study to analyze the results. The dependent variable was pregnancy loss. Independent variables were age, nationality, specialty, type of work (clinical and nonclinical), number of working hours, number of monthly on-calls and emergency shifts.

Data entry and analysis

A personal computer was used for data coding and entry. SPSS version 20.0 was used for the data analysis and a *p*-value of <0.05 was adopted for statistical significance. For summarizing data, mean and standard deviations were used for quantitative variables, while the frequency and percentages were used for qualitative variables. Chi-square test was used for testing significance of the variation in categorical outcome. Fisher exact test was used when requirements were violated such as when cells with expected value less than 5% exceed 20%. *P*-value <0.05 was considered as the standard level of significance.

Pilot study/pretesting

A pilot study was conducted on 10% of the calculated sample size in one of the ministry of health general hospitals to test the tool (Maternal and Child hospital), where no necessary changes were made.

Ethical considerations

Research committee approval was obtained from Joint program of family medicine and community. Higher authority, local and departmental approval from King Abdul-Aziz University Hospital was obtained. Response of the physicians to the sent questionnaire was considered as a consent to be enrolled in the study. It was ensured that all the collected data will be kept confidential and it will not be disclosed except for the study purpose.

Results

Out of all requested physicians (*n* = 126), 92 physicians responded making a response rate of 73%. Table 1 showed that the overwhelming majorities of the respondent physicians were Saudis (93.5%), and most of them were married (89.1%), and the rest were either divorced (8.9%) or widowed (2.2%). Their age ranged between 24 and 60 years old with a mean of 38.8 ± 10.9 years. Almost one third of the respondent physicians (31.5%) were obstetricians, followed by 16.3% family physicians and 13% pediatricians. Only one physician reported that she was specialized in emergency medicine and another one as ophthalmologist.

History of pregnancy loss

Fig. 1 demonstrated that 17 (18.5%) of the respondent physicians encountered pregnancy loss before. Out of them, there were 13 (14.1%), who lost pregnancy once, while two of them (2.2%) lost more than two pregnancies. The total number of pregnancies experienced by the respondent physicians (*n* = 92) accounted for 258, and the total number of pregnancy losses was 25 forming 9.7% of all pregnancies. Fig. 1 further showed that the majority of these losses occurred in the first trimester 22 (8.5%), while only 3 (1.2%) occurred in the second trimester.

Most of the pregnancy losses occurred in physicians while they were in their residency (40%), and the rest occurred while they were students, interns or specialists (Fig. 2). As shown in Table 2, the first pregnancy loss occurred while the pregnant physicians were working for an average monthly working hours of 160 h with Inter Quartile Range (IQR) (110–180 h), and three weekly on calls with IQR (0–3 on calls). The physicians, who experienced second pregnancy loss indicated that they were working for less number of monthly working hours [median, IQR; 140 (111–140) hours] but more weekly on calls [median, IQR; 4 (4–4) hours] occurred when the pregnancy loss occurred. A further lower number of monthly working hours were observed in the third pregnancy loss [median, IQR; 124 (111–123)], as well as lower number of weekly on calls [median, IQR; 2 (0–2) times weekly].

Characteristics of the respondents possibly associated with pregnancy loss

To explore characteristics of the respondent physicians that could possibly influence likelihood of pregnancy loss, Table 2 further

Table 1
Characteristics of the study group (*n* = 92).

Characteristics	No.	%
Nationality		
Saudi	86	93.5
Non Saudi	6	6.5
Marital status:		
Married	82	89.1
Divorced	8	8.7
Widowed	2	2.2
Age (mean \pm SD)	38.8 ± 10.9 years	
Specialty		
Obstetrics and Gynecology	29	31.5
Family medicine	15	16.3
Pediatrics	12	13.0
Radiology	9	9.8
Medicine	7	7.6
Otolaryngology	7	7.6
Surgery	6	6.5
Basic science	5	5.4
Emergency medicine	1	1.1
Ophthalmology	1	1.1

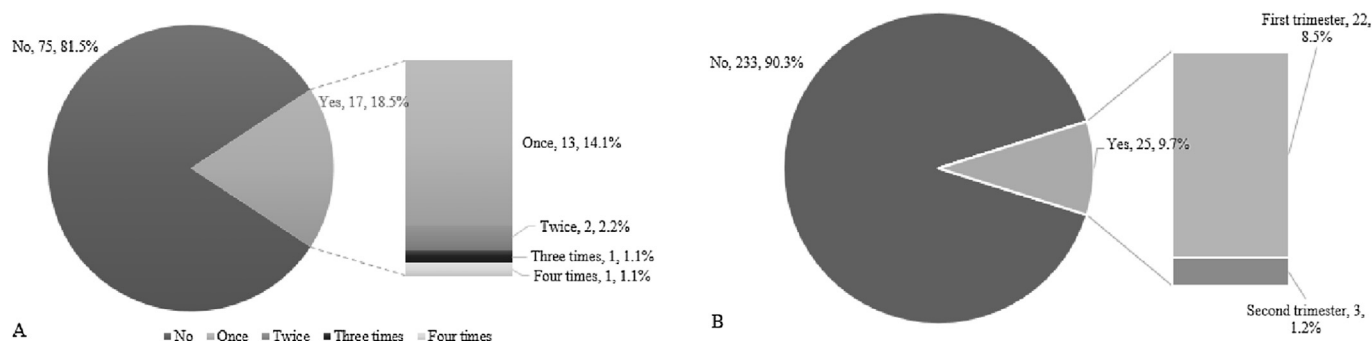


Fig. 1. Frequency of previous pregnancy loss among respondent physicians and Distribution of pregnancy losses according to prenatal stages.

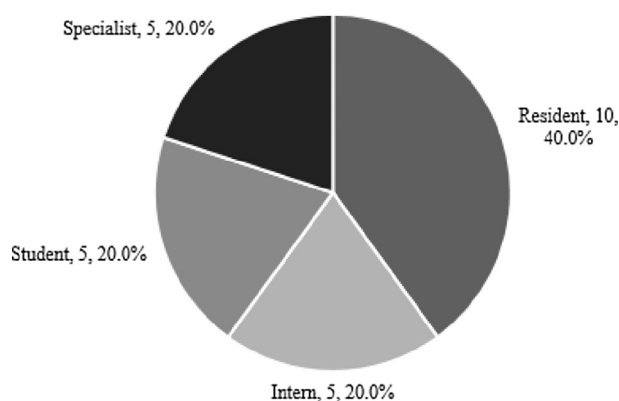


Fig. 2. Type of work when pregnancy loss occurred in physicians.

demonstrated that although the non-Saudi physicians had higher frequency of pregnancy loss (33.3%) than the Saudis (17.4%), this difference is not statistically significant $p > 0.05$. Despite of the observed differences between the frequencies of pregnancy loss according to marital status, the pregnancy loss was higher among widowed. According to specialty, it was highest among internal medicine

physicians. However, it was not possible to run tests for statistical significance due to small numbers in most of the subcategories.

Discussion

Medical profession is a stressful occupation and this stress could affect negatively on the pregnancy outcome among pregnant physicians [11]. Different results have been observed through the review of previous literature. For example, in North America the prevalence of pregnancy loss in physicians was low (11.8%) [14], while among Hungarian physicians, the prevalence reached up to 20.8% [7]. In the current study, 18.5% of the physicians reported that they had already suffered from pregnancy loss. Pregnancy loss among physicians was discussed in researches from different perspectives to investigate whether it differs from that in the general population, and if the medical profession has direct or indirect impact on pregnancy loss. In USA, the prevalence of pregnancy loss among physicians was found to be higher than the general population. It was attributed to the frequent on calls, and long working hours in the operation room among surgical female residents [14]. In the present study, the average number of weekly on calls was three in the first pregnancy loss, and reached up to four in the second pregnancy loss, which is considerably higher.

Table 2

Working hours and duties when pregnancy loss occurred and Differences in the history of pregnancy losses according to characteristics of the respondent physicians.

Characteristics	Monthly working hours median (IQR)		Number of weekly on calls median (IQR)		Number of weekly ER shifts median (IQR)	
First pregnancy loss	160 (110–198)		3 (0–5)		0 (0–3)	
Second pregnancy loss	140 (111–140)		4 (4–4)		0 (0–0)	
Third pregnancy loss	124 (111–123)		2 (0–2)		0 (0–0)	
Characteristics	Positive history of pregnancy loss				X ²	p
	No		Yes			
	No	%	No	%		
Nationality					Fisher	0.306
Saudi	71	82.6%	15	17.4%		
Non Saudi	4	66.7%	2	33.3%		
Marital status						NA
Married	67	81.7%	15	18.3%		
Divorced	7	87.5%	1	12.5%		
Widowed	1	50.0%	1	50.0%		
Specialty						NA
Medicine	4	57.1%	3	42.9%		
Pediatric	8	66.7%	4	33.3%		
Obs/Gyn	28	96.6%	1	3.4%		
Surgery	4	66.7%	2	33.3%		
Ophthalmology	1	100.0%	0	0.0%		
ENT	5	71.4%	2	28.6%		
ER	1	100.0%	0	0.0%		
Radiology	14	13.9%	19	10.6%		
Family medicine	13	86.7%	2	13.3%		
Basic science	3	60.0%	2	40.0%		

On the same line, most of the reported pregnancy loss among the physicians occurred while they were in their residency, which was characterized by a relatively longer working hours and less sleeping hours [15]. This claim was supported by Gabbe et al. [12], where it has been assumed that the modification of the condensed work schedule, paid maternity leave and planned time off before delivery could reduce adverse pregnancy outcome among residents [12]. Most of the pregnancy losses occur in the first trimester due to various reasons including chromosomal abnormalities, and other less likely reasons, such as uncontrolled diabetes, obesity and old-aged mothers [16]. In the present findings, majority of the pregnancy losses occurred in the first trimester. In this respect, one of the controversial measures for treatment of threatened pregnancy loss is bed rest [17], which is not always applicable for on-duty physicians.

The current study showed that 40% of pregnancy losses in physicians occurred during the residency period. In this respect, Behbehani and Tulandi addressed that pregnancy during residency carry a higher rate of adverse outcome than average. This argument was attributed to the relatively longer operating hours and having more on calls per month. Pregnant residents are more likely to have hypertension complicating pregnancy, and pregnancy loss than a cohort of pregnant women of similar age [14]. These arguments were also supported by the findings of the study that most of the pregnancy losses occurred in the residency period, and the average number of monthly working hours was 160 h in the first pregnancy loss. Working in residency period could also have an impact on the pregnancy outcome. Apart from the assumed impact of medical profession, there are other factors related to pregnancy loss in the Saudi community, which were not included in the current study. For example, Al-Ansary et al. [10] carried out a case control study in King Khalid University Hospital in Riyadh in 1995 and found that marriage with first blood husband is a significant risk factor for spontaneous pregnancy loss in Saudi women [10].

Takeuchi et al. [18] conducted a study to investigate the association between long working hours during pregnancy and pregnancy complications among female physicians. The results revealed that long working hours during the first trimester of pregnancy resulted in threatened abortion and pre-term birth of infants. Another study examining the occupational hazards revealed that performing surgery in absence of proper scavenger system and long working hours cause preterm birth among the female physicians [19]. Physically stressful work during pregnancy is associated with increased risk of pre-term delivery. This is more common in jobs that require combination of tasks with physical efforts; like female physicians. However, the risk can be minimized by taking preventive measure on physically demanding work in initial 20 weeks of gestation period [20]. A study conducted by Mook-Kanamori et al. [21] investigated the impact of maternal physical characteristics and lifestyle on first trimester fetal adaptations and post-natal consequences. The results showed that physical activities and lifestyle habits have been associated with early fetal growth. The increased risk of adverse birth outcomes has been associated with restriction of first trimester fetal growth [21].

Prevalence of pregnancy loss among female physicians working in King Abdul-Aziz University Hospital was 18.3%. Most of the cases occurred in the first trimester, during residency, while working for longer monthly hours. However, no statistically significant association was found between pregnancy loss and age, nationality, marital status, specialty, number of emergency shifts and number of on-calls. Due to relatively small number of respondents from some specialties, it was not possible to compare the frequency of pregnancy loss in physicians according to their specialty. Future studies must consider the female physicians according to their specialty by considering relatively larger sample size to obtain efficient outcomes.

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Conflict of interest

The authors declare no conflict of interest.

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References

- [1] Ford HB, Schust DJ. Recurrent pregnancy loss: etiology, diagnosis, and therapy. *Rev Obstet Gynecol* 2009;2:76–83.
- [2] Beaman KD, Ntrivalas E, Mallers TM, Jaiswal MK, Kwak-Kim J, Gilman-Sachs A. Immune etiology of recurrent pregnancy loss and its diagnosis. *Am J Reprod Immunol* 2012;319–25. <https://doi.org/10.1111/j.1600-0897.2012.01118.x>.
- [3] Lok IH, Neugebauer R. Psychological morbidity following miscarriage. *Best Pract Res Clin Obstet Gynaecol* 2007;229–47. <https://doi.org/10.1016/j.bpobgyn.2006.11.007>.
- [4] Garcia-Enguidanos A, Calle ME, Valero J, Luna S, Dominguez-Rojas V. Risk factors in miscarriage: a review. *Eur J Obstet Gynecol Reprod Biol* 2002;2: 111–9.
- [5] Wainstock T, Lerner-Geva L, Glasser S, Shoham-Vardi I, Anteby EY. Prenatal stress and risk of spontaneous abortion. *Psychosom Med* 2013;3:228–35. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23362503>5Cnhttp://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00006842-201304000-00002.
- [6] Sheiner E, Sheiner EK, Potashnik G, Carel R, Shoham-Vardi I. The relationship between occupational psychological stress and female fertility. *Occup Med (Chic Ill)* 2003;4:265–9.
- [7] Györfy Z, Dweik D, Girasek E. Reproductive health and burn-out among female physicians: nationwide, representative study from Hungary. *BMC Womens Health* 2014;1:121. <https://doi.org/10.1186/1472-6874-14-121>.
- [8] Phelan ST. Pregnancy during residency: II. Obstetric complications. *Obstet Gynecol* 1988;(3 Pt 1):431–6.
- [9] Cole S, Arnold M, Sanderson A, Cupp C. Pregnancy during otolaryngology residency: experience and recommendations. *Am Surg* 2009;5:411–5.
- [10] Al-Ansary LA, Oni G, Babay ZA. Risk factors for spontaneous abortion among Saudi women. *J Community Health* 1995;6:491–500. <https://doi.org/10.1007/bf02277065>.
- [11] Quansah R, Gissler M, Jaakkola JJK. Work as a physician and adverse pregnancy outcomes: a Finnish nationwide population-based registry study. *Eur J Epidemiol* 2009;9:531–6. <https://doi.org/10.1007/s10654-009-9369-0>.
- [12] Gabbe SG, Morgan MA, Power ML, Schulkin J, Williams SB. Duty hours and pregnancy outcome among residents in obstetrics and gynecology. *Obstet Gynecol* 2003;5:948–51. <https://doi.org/10.1097/00006250-200311000-00012>.
- [13] Klebanoff MA, Shiono PH, Rhoads GG. Spontaneous and induced abortion among resident physicians. *JAMA* 1991;21:2821–5. <https://doi.org/10.1001/jama.1991.03460210067031>.
- [14] Behbehani S, Tulandi T. Obstetrical complications in pregnant medical and resident residents. *J Obstet Gynaecol Can* 2015;1:25–31. [https://doi.org/10.1016/s1701-2163\(15\)30359-5](https://doi.org/10.1016/s1701-2163(15)30359-5).
- [15] Defoe DM, Power ML, Holzman GB, Carpentieri A, Schulkin J. Long hours and little sleep: work schedules of residents in obstetrics and gynecology. *Obstet Gynecol* 2001;6:1015–8. <https://doi.org/10.1097/00006250-200106000-00028>.
- [16] Zhang HK, Luo FW, Geng Q, Li J, Liu QZ, Chen WB, et al. Analysis of fetal chromosomal karyotype and etiology in 252 cases of early spontaneous abortion. *Zhonghua yi xue yi chuan xue za zhi= Zhonghua yixue yichuanxue zazhi. Chin J Med Genet* 2011;5:575–8.
- [17] Jurkovic D, Overton C, Bender-Atik R. Diagnosis and management of first trimester miscarriage. *BMJ* 2013 Jun19;2. f3676–f3676. Available from: <http://www.bmj.com/cgi/doi/10.1136/bmj.f3676>.
- [18] Takeuchi M, Rahman M, Ishiguro A, Nomura K. Long working hours and pregnancy complications: women physicians survey in Japan. *BMC Pregnancy Childbirth* 2014;14:245.
- [19] Shirangi A, Fritsch L, Holman CDAJ. Associations of unscavenged anesthetic gases and long working hours with preterm delivery in female veterinarians. *Obstet Gynecol* 2009;113:1008–17.
- [20] Van Beukering MD, van Melick MJ, Mol BW, Frings-Dresen MH, Hulshof CT. Physically demanding work and preterm delivery: a systematic review and meta-analysis. *Int Arch Occup Environ Health* 2014;87:809–34.
- [21] Mook-Kanamori DO, Steegers EA, Eilers PH, Raat H, Hofman A, Jaddoe VW. Risk factors and outcomes associated with first-trimester fetal growth restriction. *JAMA* 2010 Feb;303:527–34.