*Available online at* www.scholarsresearchlibrary.com

Scholars Research Library

**Der Pharmacia Lettre, 2016, 8 (1):348-353**
***(http://scholarsresearchlibrary.com/archive.html)***

Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

# Menstrual-reproductive and socio-demographic factors of secondary infertile and fertile women in Zahedan: A case-control study in southeastern Iran

**Hossein Ansari[1], Fatemeh Azarkish[3], Shahindokht Navabi Rigi[1], Rohollah Rouhandeh[1] and Younes Mohammadi[2]**

[1]*Health Promotion Research Center, Zahedan University of Medical Sciences, Zahedan, Iran*
[2]*Department of Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran*
[3]*Iranshahr University of Medical Sciences, Iranshahr, Iran*

---

**ABSTRACT**

*Secondary infertility may have severe complications for the involved couples, especially for the women. It thought menstrual-reproductive factors could influence the fertility status of the couples. This study was aimed to comparison the socio-demographic and menstrual-reproductive factors between secondary infertile and fertile women in southeastern Iran. In this case-control study, 125 secondary infertile women as case group and 140 fertile women as control group were investigated in 2015. The subjects were selected from the fertility clinics and private office of the gynecologists in Zahedan, southeast of Iran. A structured questionnaire including reproductive history and socio-demographic variables was used to data collection. The data were analyzed in Stata.12 software using Chi-square and multiple logistic regression with Hosmer & Lemeshow method. The mean age of marriage, age at first pregnancy and age at first menarche in secondary infertile women was more than in fertile women, but only the difference of age at first menarche (P=0.0001) were statistically significant. Multiple logistic regression model showed that the secondary infertile women were more likely to have had the first conception in older age (OR = 1.71, CI=1.12-5.3) and irregular menses (OR=3.91, CI= 1.5-6.7). The main finding of this study is that obstetric events contribute approximately equally to secondary infertility in Zahedan. Socio-demographic and menstrual-reproductive factors not only influence the obstetric events, but directly effect on fertility via other paths. However, health promotion to improvement of menstrual-reproductive and high quality counseling of women at risk are likely to decrease secondary infertility.*

**Key words**: Women, Secondary infertility, Infertility, Menstrual-reproductive

---

## INTRODUCTION

Secondary Infertility (SI) refers to infertile couples who have conceived at least once before. This implies that women with SI do not necessarily have a living child [1]. The problem can have severe outcomes for the couples involved, especially for the women. Although the SI is not life-threatening, but if a woman cannot produce a live child in a formal merger with a man, she will often be told to leave and/or is stigmatized in the community [2-5]. Some of the consequences of primary and secondary infertility are including: societal repercussions, personal suffering, psychological disorders, sexual dysfunctions and marital dissonance [6-9]. It should be noted that both primary and secondary infertility can influence the life style of the involved families, especially in developing countries [10-11].

The incidence of female infertility is rising [12)], so that the primary or secondary infertility occurs in almost 15% of all women around the world [13]. Some studies have shown that about 25% of all couples are involved with infertility in developing countries [13] and the infertility in women consists one third of infertility among all infertile pairs [14]. The Center for Disease Control (CDC) has reported that 11% of couples in USA go on to experience SI [15]. The previous studies conducted in Iran estimated the current primary infertility and the prevalence of lifetime primary infertility to be 3.4% and 24.9%, respectively [16]. Another study showed the prevalence of primary infertility to be 20.2% in Iran [17], but on the other hand, a new study in Iran estimated the primary and secondary infertility among women to be 26.1% and 1.7%, respectively [18].

The previous studies have reported several determinants for infertility that awareness about them could help to management the infertile couples' life. A study conducted in Rwanda showed that the lack of prenatal care in the last pregnancy, the first pregnancy before the age of 21 years, a history of unwanted pregnancy, a pregnancy with other than current partner, an adverse pregnancy outcome, stillbirth, postpartum infection and curettage could be as risk factors for SI in women [19].However, the other researches in this field, have discussed that in addition to ovarian and uterine factors, the smoking, obesity and occupation as well as life style [20-22] are other main determinants of female infertility in the societies. It should be noted that there is a dearth of information on factors associated with SI from Iran; therefore, study in this context is too important especially in developing countries.

Sistan and Baluchistan province is located in the southeast of Iran that have different atmosphere regarding cultural, social and economic status compared to another province in Iran. On the other hand, the child bring is important in this area and life style of the families is unacceptable and different from the other parts of Iran. Due to higher cost and time consuming, few of infertile women have access to effective infertility treatment, so recognition of menstrual-reproductive risk factor of SI could help in decreasing infertility in the future and promote the quality of couple's life in this region especially. Since most of SI is preventable, a better knowledge of modifiable risk factors may help to develop interventions targeted at those most at risk.

## MATERIALS AND METHODS

In this case-control study ,125 secondary infertile women as case group and 140 fertile women as control group were investigated in Zahedan, Southeast of Iran in 2015. SI was defined as having had regular unprotected intercourse for one year or more with at least one regular partner without conception in women who conceived at least once before. To be eligible for being case, women needed to be secondary infertile with up to 6 months of diagnosis between 21 and 45 years of age, residing in Zahedan, willing to contribute in the study, without history of infertility treatment, having had sexual intercourse at least once in the last 2 weeks, lack of infection after first childbirth, without ovary and endometrial disease, without history of radiotherapy and chemotherapy, without history of selective abortion and do not being vegetarian. Fertile controls were defined as currently pregnant or non-pregnant women who had at least one live birth. The eligibility criteria for controls were the same as for cases, except for fertility status and in case of pregnancy the gestational age should have been up to 3 months.

In this study the subjects were selected from the women referring to fertility clinics located in hospitals of Zahedan University of Medical Sciences and private office of the gynecologists in Zahedan city. The sampling method was quota sampling according to inclusion criteria. The share of the sample from clinics and offices was based on approximate number of daily referred patients. The controls selected from the same place as the cases. As soon as a case found in clinics or private offices, an eligible women referred to same place was considered as control of this case. If there were many eligible controls in the place, one or two (for 15 cases) control was selected randomly by simple random sampling using blindly hand-picking numbers from a bowl with regard to consent to participate in the study.

The study was approved by the Ethics Committee of Zahedan University of Medical Sciences. However, all participants justified regarding purposes of the study and participated in the study with informed consent.

The data were collected by two female trained and reliable staffs by interview using a structured questionnaire consist on reproductive history and socio-demographic variables including age, age of marriage, Job status, educational level, smoking (cigarette or hookah), smoking of husband, alcohol consumption, age at first pregnancy, first age at menarche, history of abortion, history of irregular menstruation, history of infertility in the family,

contraceptive pills consumption before first pregnancy, weight, height and Body Mass Index (BMI). The BMI was calculated as weight in kilograms divided by the square of height in meters. The measurement of weight and height were done by a trained staff and the instruments were calibrated regularly during the work.

**Statistical Analysis**

The Chi-square test and bivariate Odds Ratio (OR) were used to examine unadjusted association between menstrual-reproductive and socio-demographic variables with SI. The mean difference of quantitative variables between case and controls was evaluated by Independent sample T test. Moreover, a multiple logistic regression was used to determination of the predictors by controlling potential confounders. The Hosmer & Lemeshow method was used to model estimation and to evaluate the goodness-of-fit of the logistic regression model [23]. In this method the variable selection (including or excluding variables from the model) and modeling is based on Likelihood Ratio Test (LrTest). The statistic of LrTest is -2lnLR-(-2lnLF), in which the LR is the likelihood of the reduce model (the model with lower parameters) and LF is the likelihood of the full model (the model with higher parameters). The LrTest has Chi-square distribution with degrees of freedom of equal to different of two models parameters. The data were analyzed in Stata.12 software and the significance level was defined as $P<0.05$.

## RESULTS

The purpose of the study was explained to all participants (125 cases and 140 controls) in the local language and all data were collected from the subjects, so that there was no missing data. Of 240 women, 68(28.3%) selected from private offices of gynecologists and the others selected from hospitals' gynecology clinics. A total of pregnancies reported 138 and 317 in secondary infertile and fertile women, respectively. The mean age of the cases was the same as controls. However, the mean age of marriage, age at first pregnancy and age at first menarche in secondary infertile women was more than in fertile women (Table 1), but only the difference of age at first menarche (P=0.0001) were statistically significant in bivariate analysis so that the women with secondary infertile relationships were more likely to have had higher age of menarche (adjusted OR = 1.21, CI =1.07-6.1). Although the mean difference of the age at first conception between cases and controls was not statistically significant in bivariate analysis, but the multiple logistic regression model showed that the secondary infertile women were more likely to have had the first conception in older age (adjusted OR = 1.71, CI=1.12-5.3). On the other hand, although in bivariate model the chance of having more number of pregnancies among secondary infertile women was more than fertile ones (unadjusted OR =5.4, CI=2.4-12.3), but this variable did not remained in the final multiple model. Regarding other reproductive history factors, the menstrual cycle was important factor in increasing the chance of SI, so that both bivariate analysis (unadjusted OR=5.7, CI=2.2-10.4) and multiple logistic regression model (adjusted OR=3.91, CI= 1.5-6.7) showed that the women with irregular menstruation have more chance to have got SI. As another result, although the contraceptive pills consumption before first pregnancy for at least 6 months increase the likelihood of SI in bivariate analysis (unadjusted OR=2.96, CI=1.3-11.3), but by the multiple logistic regression analysis, this variable was not considered as independent predictive factor for this outcome. The variables including number of previous pregnancies and history of infertility in the 1st degree family were not related to SI at present study.

Regarding socio-demographic variables, the educational level and job status distribution was similar in both cases and controls groups (Table 1). As another potential independent variable, the BMI was related to SI and higher BMI (adjusted OR=1.19, CI=1.003-8.1) increases the likelihood of SI of the women in this study.

There was no interaction between the independent variables in increasing the odds of SI and the Hosmer & Lemeshow test showed a goodness-of-fit for the model adjustment ($p = 0.44$).

**Table 1: Univariate and multiple exact logistic regression analysis of the some socio- demographic characteristics and reproductive history factors associated with the SI in women (variables with P<0.2 in the bivariate analysis entered in multiple regression models using Hosmer-Lemsho Method for model building)**

| Independent variables | | Cases N=125, n(%) | Controls N=140, n(%) | bivariate OR ( 95% CI) | Multivariate and Adjusted OR[6] (95% CI) |
|---|---|---|---|---|---|
| Total number of pregnancies[1] | | 138 | 317 | - | |
| Age, Mean(Sd) | | 26.3(5.1) | 25.2(6.4) | P=0.12 | NS[4] |
| Husband's age Mean(Sd) | | 26.9(7.4) | 24.4(6.6) | P=0.18 | NS[4] |
| Age at marriage, Mean(Sd) | | 21.2(7.5) | 19.8(6.8) | P=0.11 | - |
| Age at first conception, Mean(Sd) | | 22.9(7.7) | 21.2(6.5) | P=0.052 | 1.71 (1.12-5.3) [3,5] |
| Age at first menarche, Mean(Sd) | | 13.4(4.9) | 11.1(3.7) | P=0.0001 | 1.21 (1.07-6.1) [3] |
| BMI, Mean(Sd) | | 26.5(8.1) | 24.2(6.9) | P=0.006 | 1.19 (1.003-8.1) [3] |
| Education | Up to primary | 87(69.6) | 90(64.3) | 1.27(0.8-5.7) | NS[4] |
| | More than primary | 38(30.4) | 50(35.7) | | |
| Job | Housewife | 94(75.2) | 99(70.7) | 1.25(0.4-18.3) | NS[4] |
| | Practitioner | 31(24.8) | 41(29.3) | | |
| Number of Pregnancies | 1 | 99(79.2) | 58(41.5) | 5.4(2.4-12.3) [5] | NS[4] |
| | ≥2 | 26(20.8) | 82(58.5) | | |
| Contraceptive pills consumption before first pregnancy[2] | Yes | 46(36.8) | 23(16.4) | 2.96(1.3-11.3) [5] | NS[4] |
| | No | 79(63.2) | 117(83.6) | | |
| History of infertility in the 1st degree family | Yes | 9 (7.2) | 8 (5.7) | 1.28(0.6-9.7) | NS[4] |
| | No | 116(92.8) | 132 (94.3) | | |
| Menstrual cycle | Irregular | 61(48.8) | 20(14.3) | 5.7(2.2-10.4)[5] | 3.91 (1.5-6.7) [3] |
| | Regular | 64(51.2) | 120(85.7) | | |

*[1]excluding last pregnancy for fertile women, [2]consumption of contraceptive pills for at least 6 months before first pregnancy, [3]Significant at level P<0.05, [4]No Significant, [5]due to collinearity between age at first pregnancy and age of marriage, only the age at first pregnancy inserted to multiple model, [6] each variable adjusted for the other variables based on Hosmer-Lemeshow method to model building.*

## DISCUSSION

This study revealed that generally the women with SI are more likely to have menstrual-reproductive problems and different socio-demographic characteristics and reproductive history factors contribute unequally in increasing the chance of SI in southeast of Iran. However, some menstrual-reproductive factors such as menstrual cycle, history of infertility in the 1st degree family, number of pregnancies, age at first conception and age at menarche were assessed in this study to assessing and/or approving those confounding role for each other in a statistical model. The results were partly in line with the previous studies [19,20] that have approved the relation of obstetric history factors with SI.

This study showed that higher age at menarche and postponement in first conception after marriage could be increase the chance of SI in women. The previous study in Iran [24] has shown that the higher age at marriage of women could be a predictor for SI but our study did not approve this relation. On the other hand, in Iran usually the couples who marry late, delay the conception and this situation could explain the effect of first productivity in higher age on SI. Regarding age at menarche it should be noted that the previous studies have approved the effect of age at menarche and infertility [25, 26]. As the result of previous study the fecundity declines with age [27], thus this may account for the higher fecundity among women with an earlier age at menarche. However, this result is not parallel with some studies [28,29], which concluded that age at menarche was not associated with fecundity. The difference might be due to the variety on study population and study design, so that conducted the study in a specific subgroup and excluded women with irregular menstrual cycles and might have selection bias. The menstrual cycle was another factor that was related to likelihood of infertility and the women with irregular menstruation have more chance to have got SI. This result is concordance with previous studies around the word [30,31].

It seems that aging men has impact on SI due to male sexual function. On the other hand, the sperm quality or quantity can be changed due to changes in health or beginning certain new medications [32]. Since all participants have had pregnancy during 2 last year and also the husband's age mean was not different between cases and controls, therefore, infertility in men could not be possessed as important factor in this study.

Although, the cigarette smoking can also impact egg quality and increase complications during a pregnancy [35,36)] but the women and their husbands' smoking were not related to SI in this study. The determination of history,

duration and quality status of cigarette smoking is not simple and inappropriate measurement of this exposure could explain this result.

Although the previous studies have noted that tobacco smoking significantly increase the risk of SI [37, 38], but neither women tobacco use not her husband's smoking or tobacco use were not related to SI in this study.

In this study we used female trained staffs to perform the interview to reduce the difficulties of obtaining data. Since most of the independent variables were objective and the controls were the women who had attended in private offices or clinics for other obstetrics' complain, therefore, the controls are from the population base of the cases and possibility of recall bias is very low. On the other hand we firstly identified the potential confounding factors and then controlled those methodologically using valuable statistical models. Hence, it seems that the results of this study could be valid and reliable. However, conducting of this study encountered some limitations; since women experiencing SI reported many pregnancies than fertile women in, the contributions of pregnancy-related and obstetric events to cases were probably underestimated. It should be noted that due to the case-control design of this study, temporal relationships between life style and reproductive history related factors and infertility cannot be ascertained. Finally lack of infertility treatment center was an administrative limit in this study regarding data collection. Although the advice and cooperation of midwives and gynecologists rectified the problem, but the managing and conducting similar study in places that have infertility treatment center could help to better detection of the related factors.

## CONCLUSION

It has found that menstrual-reproductive factors are associated with SI after adjusting for socio-demographic factors. The women planning to become pregnant should consider this issue and promoting life style in any aspect may help them to become pregnant. However, management of the infertility problem should include the suitable way of preventing SI considering underlying causes such as revealed factors in this study. On the other hand, the psychological and financial supports should be regarded to manage this problem. Since infertility is increasing public health issues in Iranian women, and menstrual-reproductive factors are related to secondary infertility, so more attention should be paid to safe practices during menstruation, delivery, and the postpartum period for women in general. However, recommend health education and awareness messages in this regard is too important.

**Acknowledgement**
This study was conducted under the supervision of Deputy of research affiliated to Zahedan University of Medical Sciences. Hereby, the researchers appreciate all women who helped and warmly collaborated with us in conducting this research.

## REFERENCES

[1]Lunenfeld B, Van Steirteghem A: *Hum Reprod Update* **2004**, 10:317-326.
[2] Dyer SJ. *J Psychosom Obstet Gynaecol* **2007**, 28:69-77.
[3] Orji EO, Kuti O, Fasubaa OB: *Int J Gynaecol Obstet* **2002**, 79(1):61-62.
[4]Van Balen F, Bos HM: *Ob Gyn* **2009**, 1:106-121.
[5]Dyer SJ, Abrahams N, Mokoena NE, van der Spuy ZM: *Hum Reprod* **2004**, 19:960-967.
[6] Volgsten H, Skoog Svanberg A, Ekselius L, Lundkvist O, Sundstrom Poromaa I. *Fertil Steril*. **2010**; 93(4): 1088-96.
[7] Volgsten H, Ekselius L, Poromaa IS, Svanberg AS. *Acta Obstet Gynecol Scand*. **2010**; 89(1): 27-34.
[8] Drosdzol A, Skrzypulec V. *J Sex Med*. **2009**; 6(12): 3335-46.
[9] Drosdzol A, Skrzypulec V. *J Psychosom Obstet Gynaecol*. **2009**; 30(1): 11-20.
[10] Shea O. Rutstein and Iqbal H. Shahinfecundity, infertility and childlessness indeveloping countries DHS comparativereports No. 9, Calverton, Maryland, USA:ORC Marco and the World Health Organization, **2004**. P: 56.
[11] Direkvand Moghadam A, Delpisheh A,Khosravi A. *Biosci Biotechnol Res Asia*. **2013**; 10(2): 559-67.
[12] Kumar D. *Rural Remote Health*. **2007**; 7(2): 456.
[13] Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. *PLoS Med*. **2012**; 9(12): e1001356.
[14] Unuane D, Tournaye H, Velkeniers B, Poppe K. *Best Pract Res Clin Endocrinol Metab*. **2011**; 25(6): 861-73.
[15] Chandra A, Martinez GM, Mosher WD, Abma JC, Jones J. *Vital Health Stat* 23. **2005**; 23:1-160.
[16] Mohammad K, Ardalan A. *J Reprod Infertil*. **2009** Oct-Dec; 10(3): 213–21.

[17] Mohammad Mehdi Akhondi, Koorosh Kamali, Fahimeh Ranjbar, Mahdi Shirzad, Shiva Shafeghati, Zohreh Behjati Ardakani, et al. **2010**. *Iran J Public Health*. **2013** Dec; 42(12): 1398–1404.
[18]Hosseini J, Emadodin M, Mokhtarpoor H, Sorani M. *Iranian Journal of Obstetric, Gynecology and Infertility*. **2012**; 15(29):1-7.
[19] Dhont N, Luchters S, Muvunyi C, Vyankandondera J, De Naeyer L, Temmerman M, et al. *BMC Women's Health.* **2011**, 11:32.
[20] Delpisheh A, Brabin L, Brabin BJ. *Womens Health* (Lond Engl). **2006**; 2(3):389-403.
[21] Gudmundsdottir SL, Flanders WD,Augestad LB. *Hum Reprod*. **2009**; 24(12): 3196-204.
[22]Hadigheh Kazemijaliseh1, Fahimeh Ramezani Tehrani, Samira Behboudi-Gandevani, Farhad Hosseinpanah, Davood Khalili & Fereidoun Azizi. *Global Journal of Health Science*; Vol. 7, No. 6; **2015**
[23] Hosmer DW, Lemeshow S. Applied logistic regression. 2nd Ed. New York: John Wiley & Sons; **2001**.
[24]Yadollah Ahmadi Asr Badr, Kazem Madaen, Sakineh Haj Ebrahimi, Amir Hassan Ehsan Nejad, Hossein Koushavar. *Urology Journal*. Vol. 3, No. 2, 87-91 Spring **2006**.
[25] Chen J, Zhong C, Liang H, Yang Y, Zhang O, Gao E, Chen A, Yuan W, Wang J, Sun F, Miao M. *Eur J Obstet Gynecol Reprod Biol.* **2015** Nov;194:68-72. doi: 10.1016/j.ejogrb.**2015**.08.016. Epub **2015** Aug 21.
[26]Guldbrandsen K, Håkonsen LB, Ernst A, Toft G, Lyngsø J, Olsen J, Ramlau-Hansen CH2. *Hum Reprod.* **2014** Sep;29(9):2058-64. doi: 10.1093/humrep/deu153. Epub 2014 Jul 24.
[27] O'Connor KA, Holman DJ, Wood JW. *Maturitas* **1998**;30:127–136.
[28] Axmon A, Rylander L, Albin M, Hagmar L. *Hum Reprod* **2006**;21(5):1279–84.
[29] Wise LA, Mikkelsen EM, Rothman KJ, et al. *Am J Epidemiol* **2011**; 174(6):701–9.
[30] Small, Chanley M. Manatunga, Amita K. Klein, Mitchel‡; Feigelson, Heather S. Dominguez, Celia E. McChesney, Ruth; Marcus, Michele. *Epidemiology*. **2006**;17(1):52-60.
[31]Henrik A. Kolstad, Jens Peter Bonde, Niels H. Hjøllund, Tina K. Jensen, Tine B. Henriksen, Erik Ernst, Aleksander Giwercman et al. Menstrual cycle pattern and fertility: a prospective follow-up study of pregnancy and early embryonal loss in 295 couples who were planning their first pregnancy. Presented in part at the International Symposium on Environment, Lifestyle and Fertility, Aarhus, Denmark, December 1–7, **1997**.
[32] Atif Abdulhamid Katib, Khalid Al–Hawsawi, Wael Motair, Abdallah Makhloof Bawa. *Cent European J Urol* **2014**; 67: 184-188
[33] Practice Committee of the American Society for Reproductive Medicine. Obesity and reproduction: a committee opinion. *Fertil Steril.* **2015** Nov;104(5):1116-26. doi: 10.1016/j. fertnstert.**2015**.08.018. Epub 2015 Oct 1.
[34] Best D, Bhattacharya S. H*orm Mol Biol Clin Investig.* **2015** Aug 18. pii: /j/hmbci.ahead-of-print/hmbci-2015-0023/hmbci-**2015**-0023.xml. doi: 10.1515/hmbci-**2015**-0023. [Epub ahead of print]
[35] Revonta M, Raitanen J, Sihvo S, et al. *Sex Reprod Health* **2010**; 1: 91-8.
[36]Kelly-Weeder S, Cox CL. *Women Health* **2006**; 44: 1-23.
[37] Anastasia Tzonou, Chung-cheng Hsieh, Dimitrios Trichopoulos, Dionisios Aravandinos, Anna Kalandidi, Dionisios Margaris, Marlene Goldman, Nektaria Toupadaki. *Journal of Epidemiology and Community Health* **1993**; 47: 36-39.
[38] Arbabisarjou, Azizollah, Imani Mahmoud, *Intensive Care Med* ,**2013**, 39 (suppl 1): S1-S200. Doi:10.1007/s00134-013-2950-8.