Original Article

Risk factors associated with secondary infertility in women of childbearing age: A matched case–control study

Madonna Ogechukwu Emmanuel, Joseph Ayodeji Olamijulo[1], Ekanem Effiong Ekanem

Departments of Community Health and Primary Care and [1]Obstetrics and Gynaecology, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria

ABSTRACT

Background: Childbearing and rearing are important events in every human life and are associated with the feeling of completeness, family integration, and happiness. However, approximately 1 in 10 couples worldwide experience difficulty in achieving conception.

Objective: This study aims to determine the risk factors associated with secondary infertility in women attending the obstetrics and gynecology clinics of a tertiary hospital in Lagos, Nigeria.

Methodology: This individually matched case–control study was carried out from July to October 2015. A total of 160 cases were recruited from the gynecology clinic and 160 matched controls were recruited from the antenatal clinic. Data were collected using a structured interviewer-administered questionnaire. The information collected included sociodemographic characteristics, social history, and obstetric and gynecological history. A conditional logistic regression analysis controlling for possible confounders, which included variables significant at the univariate level, was undertaken.

Results: Association with secondary infertility was found with a history of unsafe abortion (adjusted odds ratio [AOR] = 9.3607, confidence interval [CI] = 3.7664–23.2645), alcohol use (AOR = 16.8102, CI = 1.3972–202.2487), family history of secondary infertility (AOR = 4.7346, CI = 1.4892–15.0523), and history of sexually transmitted infections (AOR = 4.5428, CI = 1.7658–11.6866). Contrariwise, a history of regular menses and normal vaginal delivery, respectively, were found to be protective. No statistically significant relationship was observed between educational level or alcohol use of partners and secondary infertility in this study.

Conclusion: The extrinsic risk factors identified in this study should be taken into consideration when designing preventive and treatment programs toward reducing the burden of secondary infertility.

Key words: Gynaecological history; obstetric history; risk factors; secondary infertility; social history.

Introduction

A couple is usually considered infertile if they are unable to attain a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse without any form of contraceptive.[1] Infertility could be primary or secondary. Primary infertility refers to a condition in which the couple have never conceived while secondary infertility refers to a condition in which the couple who despite having achieved a pregnancy in the past (which may or may not have resulted to a child) are unable to do so again after a year or more of regular unprotected sexual intercourse.[2] The achievement of a normal pregnancy is seen as a test of the anatomical and functional integrity of the endocrine and the reproductive systems of both sexes.[3]

Access this article online	
Website: www.tjogonline.com	Quick Response Code
DOI: 10.4103/TJOG.TJOG_44_18	

Address for correspondence: Dr. Joseph Ayodeji Olamijulo, Department of Obstetrics and Gynaecology, College of Medicine, University of Lagos, Idi-Araba, Lagos, Nigeria.
E-mail: ayolamijulo@hotmail.com

How to cite this article: Emmanuel MO, Olamijulo JA, Ekanem EE. Risk factors associated with secondary infertility in women of childbearing age: A matched case–control study. Trop J Obstet Gynaecol 2018;35:249-55.

Infertility is a global health issue affecting approximately 8–15% of couples,[4-7] an estimation of 60–168 million people worldwide.[6] In general, one in ten couples experiences primary or secondary infertility and the majority of those who suffer this live or reside in the developing world. Worldwide rate of infertility varies dramatically corresponding to the incidence of preventable conditions leading to infertility.[8] It is estimated that approximately, one-third of the causes of infertility are due to male factors, one-third due to female factors, and the remaining to a combination of both male and female factors. In up to 20% of cases, the origin of the condition is labeled unexplained because it is never identified.[3,4] While primary infertility is common in developed countries, secondary infertility is more prevalent in developing countries.[2] In Sub-Saharan Africa, the prevalence of secondary infertility varies widely from 9% in Gambia, 11% in Ghana, 21.2% in Northwestern Ethiopia, and 20–45% in Nigeria.[7] In certain African regions, the prevalence of secondary infertility is more than 30%.[9] The high secondary infertility rate in Sub-Saharan Africa is thought to be associated with sexually transmitted infections (STIs) and medical interventions under unhygienic conditions, particularly during delivery and induced abortions.[9] It has been estimated that up to 65% of gynecological consultations are for infertility.[10] Infertility has been found to be a major public health problem in developing countries.[7,11]

Secondary infertility, although not life-threatening, can have severe consequences for the couple affected, especially the women. In many African societies, infertile women are often isolated and stigmatized and may be made to leave the community.[2,5] Women perceive infertility as the most important sexual and reproductive health problem in Africa and efforts have been made to position infertility as an important issue within discussions on gender, sexual, and reproductive health.[8]

Factors associated with secondary infertility vary geographically as a result of sociocultural practices,[5] STIs and health sanitation practices on the part of the women and health practitioners. There is evidence that unsafe practices by health-care providers as well as by women during childbirth and postpartum period may lead to pelvic infection, tubal blockage, and infertility.[1] Bilateral tubal occlusion from infection is the most common cause of secondary infertility in women.[7]

The aim of this study is to determine the risk factors associated with secondary infertility in women of childbearing age as seen in a tertiary referral center in Lagos, Southwest Nigeria.

Methodology

This study was a matched case–control study to determine the risk factors associated with secondary infertility in women of childbearing age seen at the Lagos University Teaching Hospital, Lagos, Nigeria (LUTH). Patients who at the time of the study were diagnosed to have secondary infertility were recruited as cases and patients who were attending the antenatal clinic and had at least one living child were recruited as controls. The cases were selected by consecutive recruitment.

The LUTH is one of the three tertiary centers serving the Metropolitan city of Lagos, Nigeria, with an estimated population of 20 million people. Ethical approval was obtained from the Research and Ethics Committee of LUTH before commencement of the study. All consecutive patients with secondary infertility who gave written informed consent were recruited as cases from the gynecology clinic. For each case, a corresponding control of same age was recruited. Once a case was recruited, the corresponding control was approached at the antenatal clinic the following day by one of the researchers. The tool for data collection was a pretested structured questionnaire that was interviewer administered. The instrument solicited information on personal and reproductive history and history of exposure to possible factors that may be linked to secondary infertility.

For the purpose of the study, the following definitions were used: secondary infertility was defined as the failure to conceive after 1 year of regular intercourse without contraceptive in a woman who had conceived in the past irrespective of the outcome. Body mass index <18 was underweight and >25 was overweight. A syndromic approach was used to define STI. Women who reported history of lower abdominal pain, vaginal discharge, ulceration, and painful urination (or whose medical records indicated any of the above) were considered as having a history of STIs. Termination of pregnancy (abortion) was defined as a willful act to end a pregnancy.

Data analysis

Data analysis was done using SPSS Statistics for Windows Version 17.0, (SPSS Inc. Chicago, USA). Descriptive and inferential statistics were used in the presentation of results. Frequency tables were generated for all variables.

Data were rearranged in a manner that each case with its corresponding matched control were on the same row to facilitate the cross tabulation of concordant and discordant pairs. McNemar's Chi-square and matched odds ratio was subsequently computed from online GraphPad Software.[12]

The data were eventually reentered in a matched pair fashion and subjected to conditional logistic regression using Epi info 7 to estimate the adjusted odds ratio while controlling confounding variables.

Results

During the study period, 742 (50.07%) of the 1482 patients who attended the gynecology clinic had infertility. Table 1 shows the sociodemographic characteristics of the respondents. It shows the distribution according to the ethnicity, level of education, marital status, and religion of the cases and the controls. Ethnicity and religion were not significant risk factors for secondary infertility; whereas, secondary/tertiary education ($P = 0.041$) and being single ($P = 0.009$) were significant risk factors.

Table 2 shows the distribution of the respondents in relation to family history of secondary infertility and certain lifestyle practices. On family history of secondary infertility, cross tabulation of the 160 pairs between cases and controls showed 33 discordant pairs. Of these discordant pairs, there were 27 pairs where the controls had no family history of secondary infertility but the cases did and 6 pairs where the cases had no family history of secondary infertility but the controls did. This study showed a significant association between family history of secondary infertility and secondary infertility ($P = 0.0005$).

On the smoking status of respondents, cross tabulation showed three discordant pairs; a pair where the control was a smoker, but the case was not and two other pairs where the cases were smokers but their controls were not. With a $P > 0.05$, this study shows no association between smoking status of respondents and secondary infertility. Out of the 160 pairs, on cross tabulation, there were 18 discordant smoking partners and 142 concordant pairs. This study showed no significant association with partner's smoking status and secondary infertility ($P = 0.2386$). However, the number of respondents or their partners that smoked was small. Cross tabulation of alcohol use between cases and controls showed 15 discordant pairs where alcohol use was different in matched cases and controls. Of these 15 pairs, there was a single pair where the control reported using alcohol, but the case did not and 14 pairs were the case reported using alcohol but the control did not. Analysis showed a significant association between female alcohol use and secondary infertility ($P = 0.0019$). Women who had secondary infertility were 14 times more likely to be alcohol users (odds ratio [OR] =14.000).With respect to alcohol use of partners of cases and controls, there were 52 discordant pairs (pairs where partners of cases and matched controls had different exposure to alcohol). There were also 15 pairs where the controls had partners who took alcohol and the cases did not and 37 pairs where the cases had partners who took alcohol and the controls did not. With a $P = 0.0036$, this study showed a statistically significant association between alcohol use of partners and secondary infertility.

The relevant obstetric and gynecological history of the patients is summarized in Table 3. There were 160 pairs in which cases and controls gave information on menstrual

Table 1: Sociodemographic characteristics

	Frequency (%)			Statistics	*P*
	Cases	Controls	Total		
Ethnicity					
Hausa	13 (8.1)	10 (6.3)	23 (7.2)	2.425	0.4891
Igbo	48 (30.0)	61 (38.1)	109 (34.1)		
Yoruba	80 (50.0)	70 (43.8)	150 (46.9)		
Others	19 (11.9)	19 (11.9)	38 (11.9)		
Total	160 (100.0)	160 (100.0)	320 (100.0)		
Religion					
Christianity	121 (75.6)	131 (81.9)	252 (78.8)	1.513	0.218
Islam	39 (24.4)	29 (18.1)	68 (21.3)		
Total	160 (100.0)	160 (100.0)	320 (100.0)		
Formal education					
None	1 (0.6)	0 (0.0)	1 (0.3)	9.956	0.041
Primary	10 (6.3)	8 (5.0)	18 (5.6)		
Secondary	44 (27.5)	66 (41.3)	110 (34.4)		
Tertiary	105 (65.6)	84 (52.5)	189 (59.1)		
Others	0 (0.0)	2 (1.3)	2 (0.6)		
Total	160 (100.0)	160 (100.0)	320 (100.0)		
Marital status					
Single	9 (5.6)	0 (0.0)	9 (2.8)	9.424	0.009
Married	145 (90.6)	155 (96.9)	299 (93.7)		
Divorced	6 (3.8)	5 (3.1)	11 (3.4)		
Total	160 (100.0)	160 (100.0)	320 (100.0)		

Table 2: Univariate analysis of the association between respondents' family history/lifestyle and secondary infertility

Variable	A	B	McNemarel χ^2	*P*	Crude OR	CI	
						Lower	Upper
Subject smoking	2	1	0.000	1.000	2.000	0.104	117.994
Partner smoking	12	6	1.389	0.2386	2.000	0.695	6.495
Subject takes alcohol	14	1	9.600	0.0019	14.000	2.130	591.969
Partner takes alcohol	37	15	8.481	0.0036	2.467	1.321	4.838
Family history of secondary infertility	27	6	12.121	0.0005	4.500	1.820	13.329

A, Pairs where cases were exposed but controls were not; B, Pairs where controls were exposed but cases were not; CI, Confidence interval; OR, Odds ratio

cycle. Of these, there were 30 discordant pairs. In 5 of the 30 discordant pairs, the cases had regular menstrual cycles but controls did not and in 25 pairs, the controls had regular menstrual cycles but the cases did not. There was a significant relationship between menstrual cycle and secondary infertility with a $P = 0.0005$. With an OR = 0.200, a regular menstrual cycle is protective against secondary infertility. With regard to a history of STIs, 25.6% of cases and 10.6% of controls had a history of STIs. This shows a statistically significant relationship between history of STIs and secondary infertility ($P = 0.0002$).

There was no history of ectopic pregnancy among the controls. There were 21 pairs of the 160 pairs where cases had history of ectopic pregnancies but controls did not. There was a statistically significant relationship between history of ectopic pregnancy and secondary infertility ($P = 0.0001$). There were 69 pairs where cases had positive history of induced abortions, but the controls did not. There were also 7 pairs where controls had positive history of induced abortions but the cases did not. At $P = 0.0001$, this showed a statistically significant relationship between history of induced abortion and secondary infertility. There were 67 discordant pairs on cross tabulation of history of miscarriage; 58 pairs where cases had a history of miscarriage but the controls did not and 9 pairs where controls had miscarriages, but the cases did not. Thus, there was a statistically significant relationship between history of miscarriage and secondary infertility ($P = 0.0001$).

Table 3 also depicts the mode of delivery experienced by the respondents during their last child birth. There were 102 pairs where controls had spontaneous deliveries but the cases did not. There were also 4 pairs where cases had spontaneous deliveries but the controls did not. There were 22 discordant pairs on cross tabulation of last delivery by assisted vaginal delivery. Of these 22 discordant pairs, there were 9 pairs where cases had assisted vaginal delivery but the controls did not and 13 pairs where the controls had assisted deliveries but the cases did not. There were 24 pairs where cases had cesarean sections but the controls did not and 3 pairs where the controls had cesarean sections but the cases did not. Cases were 8 times more likely to have had cesarean section than controls. Conversely, statistical analysis showed that spontaneous vaginal delivery was protective (OR = 0.039, $P = 0.0001$) against secondary infertility.

The factors found to be significant on univariate analysis were further subjected to multivariate analysis. Table 4 shows that educational level, a woman's alcohol use, family history of secondary infertility, history of STIs, history of abortion, and irregular menstrual cycles were associated with secondary infertility.

Discussion

This study found that infertility remains a significant gynecological problem accounting for 50.07% of all patients attending the gynecology clinic of a tertiary center in Lagos, Nigeria. Various factors associated with secondary infertility have been identified by previous authors.[13-17] This study found that family history of infertility, use of alcohol, previous history of induced abortion, previous delivery by cesarean

Table 3: Relationship between obstetric and gynecological history and secondary infertility

Variable	A*	B*	McNemar's χ^2	P**	Crude OR	CI	
						Lower	Upper
Regular menstrual cycle	5	25	12.033	0.0005	0.200	0.060	0.532
History of STI	40	12	14.019	0.0002	3.333	1.714	6.000
History of spontaneous miscarriage	58	9	30.667	0.0001	5.273	2.74	11.141
History of induced abortion	69	7	48.961	0.0001	9.857	4.537	25.428
History of spontaneous vaginal delivery	4	102	88.764	0.0001	0.039	0.010	0.104
History of operative vaginal delivery	9	13	0.409	0.5224	0.692	0.261	1.751
Cesarean delivery	24	3	14.815	0.0001	8.000	2.430	41.504

CI, Confidence interval; OR, Odds ratio; STI, Sexually transmitted infection; P**, Statistical significance at $p<0.05$

Table 4: Risk factors for secondary infertility: Multivariate analysis (conditional logistic regression of predictors)

Variable	Regression coefficienct (SE)	Adjusted OR (95% CI)	*Z* statistic (*P*)
Family history	1.5549 (0.5901)	4.7346 (1.4892-15.0523)	2.6348 (0.0084)
Patient uses alcohol	2.8220 (1.2692)	16.8102 (1.3972-202.2487)	2.2235 (0.0262)
Partner uses alcohol	0.1155 (0.4444)	1.1224 (0.4697-2.6817)	0.2598 (0.7950)
Regular menses	2.1837 (0.7602)	0.1126 (0.0254-0.4997)	2.8727 (0.0041)
History of STI	1.5135 (0.4821)	4.5428 (1.7658-11.6866)	3.1394 (0.0017)
History of induced abortion	2.2365 (0.4645)	9.3607 (3.7661-23.2645)	4.8149 (0.001)

SE, Standard error; CI, Confidence interval; OR, Odds ratio; STI, Sexually transmitted infection

section, and history of STI were risk factors for secondary infertility. Conversely, regular menstrual cycles and normal vaginal delivery appeared protective. There was no significant relationship between smoking and infertility in this study. This was in contrast to findings in other studies where specific body systems affected by the hazardous effects of cigarette smoking were identified.[18-21] A possible explanation for this could be that the prevalence of smoking was generally very low in this study.

Many studies have demonstrated the link between alcohol intake and infertility, though it remains unclear as to what amount is related to an increased risk.[19] This study observed a significant difference in alcohol intake between the two groups. From this study, women whose partners used alcohol were more than twice as likely to have secondary infertility (OR = 2.467, $P = 0.0036$) and women who used alcohol were 14 times more likely to have secondary infertility (OR = 14.00, $P = 0.0019$). This finding supports previous research in this area which has linked alcohol and secondary infertility.[19-22] Risk of infertility, having a miscarriage, and decrease in number of oocytes have all been associated with female alcohol intake.[19] Evidence of the association might have been stronger if there had been an objective way of quantifying usage.

One interesting finding in this study was the association between family history of secondary infertility and secondary infertility. The role of genetics in infertility has always been of interest, though much information about its role in secondary infertility is not known. A study described the role of inherited thromobophilia in secondary infertility.[23] This finding on family history is in consonance with another study carried out in Alexandria where infertility was associated with family history of infertility among mothers and sisters.[24] In this study, respondents with a family history of secondary infertility were 4.5 times more likely to have secondary infertility. (OR = 4.500, $P = 0.0005$). Aside from genetics, family history may also reflect similarity in lifestyles and harmful practices among family members that may impact negatively on reproductive function.

There was a statistically significant relationship between positive history of STIs and secondary infertility ($P = 0.0005$, OR = 3.333). This showed that women with a history of STI were more than three times likely to have secondary infertility. A link has been established between STIs and secondary infertility.[25] This study however did not establish the diagnosis of STI among the study participants using conventional clinical or laboratory standard but employed the syndromic approach.

This study found a significant association between menstrual history and secondary infertility. A regular menstrual cycle was protective against secondary infertility (OR = 0.200, $P = 0.0005$). This corroborates another hospital-based case–control study which showed a high association between menstrual disorders or irregular menstrual cycle and secondary infertility.[25] This is not surprising because irregular menstrual cycle is associated with anovulation. A history of ectopic pregnancy was significant in the univariate analysis but not significant in the multivariate analysis. A study done in Iran also found no significant difference between cases and controls on history of ectopic pregnancy.[26] Similarly, a study carried out in the Southwest of Nigeria found no significant relationship between ectopic pregnancy and secondary infertility.[27] However, ectopic pregnancy has been associated with smoking,[22] septic abortion,[8,28-32] genital tuberculosis, *Chlamydia trachomatis* infection, and secondary infertility in other research works.[8,26,28-32] This study found a statistically significant relationship between induced abortion and secondary infertility. The problem of unsafe abortion has been a subject of numerous publications.[10,27] In Nigeria, unsafe abortion accounts for 4% of maternal death and is associated with serious morbidities in those who survive.[27] Findings in this study corroborate reports by other researchers.[26,27,33] There was a statistically significant difference between the two groups on history of miscarriage ($P = 0.0007$). Recurrent pregnancy loss has also been associated with chromosomal and endocrine factors, blood coagulation function, uterine deformity, autoimmune diseases, infections, preterm delivery, and perinatal deaths.[18,34] Past obstetric history can also be a risk factor for secondary infertility. Some studies have shown that women delivered by cesarean section were less likely to have a subsequent pregnancy compared with those who had instrumental or assisted vaginal delivery and spontaneous vaginal delivery.[35,36] This study found that previous cesarean section was a risk factor for secondary infertility. This is important giving the worldwide trend of astronomical increase in cesarean section rate. The decision for cesarean intervention should not be taken lightly and should be clinically justified.

Study limitations

This is a hospital-based study and the findings may not be representative of what happens in the general population. The population studied was relatively small and a larger population is desirable to increase the power and applicability of the study. Certain social practices such as smoking are relatively uncommon in our environment, especially among women. Furthermore, the diagnosis of STI was not made using the conventional microbiological criteria but on the syndromic approach.

Conclusion

Infertility remains a significant burden for the gynecologist and a common morbidity index for women in Nigeria. Family history, lifestyle practices including alcohol use can impact on fertility. Furthermore, obstetrical and gynecological history such as STI, ectopic pregnancy, induced abortion, and delivery by cesarean section were found to be risk factors for secondary infertility. Conversely, regular menstrual cycle and spontaneous vaginal delivery were protective against secondary infertility. It is apparent from these findings that some factors associated with secondary infertility are modifiable and that a good knowledge of risk factors associated with secondary infertility will be beneficial in the prevention and management of this condition.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Sami N, Ali TS, Wasim S, Saleem S. Risk factors for secondary infertility among women in Karachi, Pakistan. PLoS One 2012;7:e35828.
2. Dhont N, Luchters S, Muvunyi C, Vyankandondera J, De Naeyer L, Temmerman M, *et al.* The risk factor profile of women with secondary infertility: An unmatched case-control study in Kigali, Rwanda. BMC Womens Health 2011;11:32.
3. Agboola A. Textbook of Obstetrics and Gynecology for Medical Students. 2nd ed. Ibadan: Heinemann Educational Books; 2006. p. 128.
4. Emily M. A global perspective on infertility; an unrecognized public health issue. International Health No. 18. University Center for International Studies, Chapel Hill, North Carolina, USA. 2004.
5. Roupa Z, Polikandrioti M, Sotiropoulou P, Faros E, Koulouri A, Wozniak G, *et al*. Causes of infertility in women of reproductive age. Health Sci J 2009;3:80-7. Available from: http://www.hsj.gr/. [Last accessed on 2018 Mar 21].
6. Boivin J, Bunting L, Collins JA, Nygren KG. International estimates of infertility prevalence and treatment-seeking: Potential need and demand for infertility medical care. Hum Reprod 2007;22:1506-12.
7. Adewunmi AA, Etti EA, Tayo AO, Rabiu KA, Akindele RA, Ottun TA, *et al*. Factors associated with acceptability of child adoption as a management option for infertility among women in a developing country. Int J Womens Health 2012;4:365-72.
8. Okonofua FE. Female and Male Infertility in Nigeria. Department of Public Health Sciences, Division of International Health. Sweden: Karolina Institute Stockholm; 2005.
9. Lobo R, Martin K. Infertility and Women. Hormone Health Network; January, 2012. Available from: https://www.hormone.org/~/media/Hormone/Files/Questions%20and%20Answers/Women/FS_MWH_Infertility_Women_EN%20612.pdf. [Last accessed on 2018 Mar 21].
10. Eyo UE, Upuji FI, Ukpong EI. Termination of pregnancy (TOP) related infertility in women in Akwa Ibom state. Acad Res Int 2012;3:120-4. Available from: http://www.journals.savap.org.pk. [Last accessed on 2015 June 12].
11. Mascarenhas MN, Cheung H, Mathers CD, Stevens GA. Measuring infertility in populations: Constructing a standard definition for use with demographic and reproductive health surveys. Popul Health Metr 2012;10:17.
12. GraphPad Software. McNemar' Test to Analyze a Matched Case Control Study. Available from: http://www.graphpad.com/quickcalcs/mcNemar1. [Last accessed on 2015 Apr 15].
13. Shamila S, Sasikala S. Primary report on the risk factors affecting female infertility in South Indian districts of Tamil Nadu and Kerala. Indian J Community Med 2011;36:59-61.
14. Sudha G, Reddy KS, Reddy KK. Association between body mass index and infertility. Asia Pac J Soc Sci 2009;1:73-81.
15. Sadia S, Waqar F, Akhtar T, Sultana S. Characteristics of infertile patients with ovulatory dysfunction and their relation to body mass index. J Ayub Med Coll Abbottabad 2009;21:12-6.
16. Basso O, Baird DD. Infertility and preterm delivery, birthweight, and caesarean section: A study within the Danish National Birth Cohort. Hum Reprod 2003;18:2478-84.
17. Kubo H. Epidemiology of infertility and recurrent pregnancy loss in a society with fewer children. J Japan Med Assoc 2008;137:17-22. Available from: http://www.med.or.jp/english/023-028.pdf. [Last accessed on 2013 Mar 31].
18. Sharma R, Biedenharn KR, Fedor JM, Agarwal A. Lifestyle factors and reproductive health: Taking control of your fertility. Reprod Biol Endocrinol 2013;11:66.
19. Gaur DS, Talekar MS, Pathak VP. Alcohol intake and cigarette smoking: Impact of two major lifestyle factors on male fertility. Indian J Pathol Microbiol 2010;53:35-40.
20. Macaluso M, Wright-Schnapp TJ, Chandra A, Johnson R, Satterwhite CL, Pulver A, *et al.* A public health focus on infertility prevention, detection, and management. Fertil Steril 2010;93:16.e1-10.
21. Soares S. Cigarette smoking and fertility. Reprod Biol Insights 2009;2:39-46. Available from: http://www.la-press.com. [Last accessed on 2013 Jul 14].
22. Ivanov P, Gecheva S, Tsvyatkovska T, Georgieva G, Komsa-Penkova R, Konova E, *et al.* Inherited thrombophilic factors in women with secondary infertility. Akush Ginekol (Sofiia) 2012;51:3-7.
23. Samiha M, Hassan AH, Nehed M, Fayek E, Gehan S. Risk factors for primary and secondary female infertility in Alexandria: A hospital based case control study. J Med Res Inst 2008;27:255-61. Available from: http://www.mri.alexu.edu.eg/gnuboard4/bbs/board.php?bo_table=journal&wr_id=101&year=2006&no=4. [Last accessed on 2013 May 24].
24. Dhont N. Clinical, epidemiological and socio-cultural aspects of -infertility in resource-poor settings. Evidence from Rwanda. Facts Views Vis Obgyn 2011;3:77-88.
25. Gravett CA, Gravett MG, Martin ET, Bernson JD, Khan S, Boyle DS, *et al.* Serious and life-threatening pregnancy-related infections: Opportunities to reduce the global burden. PLoS Med 2012;9:e1001324.
26. Orji EO. Comparative study of the impact of past pregnancy outcome on future fertility. Singapore Med J 2008;49:1021-4.
27. Kramer HM, Rhemrev JP. Secondary infertility caused by the retention of fetal bones after an abortion: A case report. J Med Case Rep 2008;2:208.
28. Salma J, Sohail M, Sarwat F, Afzeal A. Maternal morbidity and mortality; association with unsafe abortion. Prof Med J 2012;19:797-803. Available from: http://www.theprofessional.com. [Last accessed on 2013 Apr 20].
29. Grimes DA, Benson J, Singh S, Romero M, Ganatra B, Okonofua FE, *et al.* Unsafe abortion: The preventable pandemic. Lancet 2006;368:1908-19.
30. Singh S, Moore AM, Bankole A, Mirembe F, Wulf D, Prada E. Unintended Pregnancy and Induced Abortion in Uganda: Causes and Consequences. New York: Guttmacher Institute; 2006. Available from: http://www.gutmacher.org. [Last accessed on 2013 Apr 20].
31. Wahab EO, Ajadi AO. Causes and consequences of induced abortion among university Undergraduates in Nigeria. International Population Conference 2009: International Union for the Scientific Study of Population. Marrakech Morocco; 20th September – 2nd October, 2009.

Available from: http://www.iussp2009.princeton.edu/paper/90906. [Last accessed on 2013 Apr 20].

32. Neisani SE, Amini L. Relationship between adverse pregnancy outcomes and secondary infertility. J Reprod Infertil 2010;11:153. Available from: http://www.Jri/en.showarticle.aspx?id=419. [Last accessed on 2013 Jun 01].
33. Bhattarchaya S, Bhattarchaya S. Effect of miscarriages on future pregnancies. Womens Health 2009;5:5-8. Available from: http://www.futuremedicine.com. [Last accessed on 2013 Apr 15].
34. Mumtaz H, Meerjady SF, Shirin S. Factors associated with secondary infertility. Ibrahim Med Coll J 2011;5:17-21. Available from: http://www.banglajol.info/index.php/IMCJ/article/view/9856. [Last accessed on 2013 Jun 17].
35. Bhattacharya S, Porter M, Amalraj E, Templeton A, Hamilton M, Lee AJ, *et al.* The epidemiology of infertility in the North East of Scotland. Hum Reprod 2009;24:3096-107.
36. Mollison J, Porter M, Campbell D, Bhattacharya S. Primary mode of delivery and subsequent pregnancy. BJOG 2005;112:1061-5.