A CASE-CONTROL STUDY ON THE RELATIONSHIP BETWEEN
INDUCED ABORTION AND SECONDARY TUBAL
INFERTILITY IN VIETNAM

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Abstract: The incidence of induced abortion (IA) is high in Vietnam. The purpose of this study is to find out whether IA increases the risk of secondary tubal infertility. A case-control study was conducted at Tu Du Hospital in Vietnam between June and September 2001. Interviews were completed with 67 tubal infertility cases matched by age and residence to 67 controls. The median age of subjects was 34 years old. Proportion of subjects with history of IA was 50.8% and 44.8% for cases and controls, respectively. IA did not significantly increase the risk of secondary infertility. Age of first sexual intercourse was under 20 years old for 29.9% of cases and 9.1% of controls, and it significantly increased the risk of secondary infertility [odds ratio (OR) = 3.80]. This study was unable to identify IA as a risk factor of secondary tubal infertility. However, the increased OR for age at first sexual intercourse may imply that being sexually active at an earlier age increases the risk of getting both sexually transmitted diseases and unwanted pregnancies and in turn, increasing the risk of infertility. It is recommended to provide young women and men with the information about health risks related to sexual activity.

Key words: Abortion-induced, Sex-behavior, Genital-disease-female, Contraceptive-devices, Infertility
INTRODUCTION

About one fourth of pregnancies all over the world, approximately 50 million, are terminated every year, and half are performed under unsafe conditions by untrained providers\textsuperscript{13}. The incidence of induced abortion (IA) is especially high in developing countries and its complications thus are frequent in the regions. The safe IAs are those performed early in pregnancy by well-trained practitioners under hygienic conditions and are legally protected. When IAs are performed in safe conditions, the health risks of the procedure are very little. In developed countries, it is reported that the mortality rate of IA is less than one per 100,000 IAs, whereas the rate is as high as 283 in South and Southeast Asia\textsuperscript{9}. It is important to investigate the IA complications especially in developing countries to form strategies for the improvement of women's reproductive health.

Two-child policy has been implemented in Vietnam\textsuperscript{9}, and the country has recommended IA and an intrauterine device (IUD) as family planning methods allowing the maximum state control. With the vigorous family planning program, the Demographic Health Survey (DHS) in 1997 reported that 55.8\% of married women were using modern contraceptives, among which IUD was the most commonly used method\textsuperscript{9}. Contraceptive choice is limited and the proportion of those using modern methods other than IUD: oral contraceptives, condom, sterilization and injectables, was only 17\% in total. Another survey estimated that the proportion of women with unmet need for family planning was about 25\%\textsuperscript{9}. Consequently, Vietnam has become the country with extremely high IA rate; a Vietnamese woman has about 2.5 IAs during her reproductive years\textsuperscript{4}. IAs are commonly performed at primary level health services especially in rural areas, and many of IA providers are untrained. It is reported that one-third of women after IA have symptoms of complications, but only a half of them seek medical advice\textsuperscript{9}. Unsafe IA and its complications are not uncommon in Vietnam.

DHS reports that 3.5 per 100,000 women aged 15 to 49 years suffer from infertility in Vietnam\textsuperscript{9}. It is known that about 35\% of infertility cases are due to tubal and pelvic pathology\textsuperscript{6}. Although prospective studies in developed countries have reported that IA does not alter woman's subsequent fertility\textsuperscript{7,8}, IA could cause tubal damage leading to infertility, if not properly operated, as is often the case in developing world. Some case-control studies, including one from a developing country, found that IA could be a risk factor for secondary infertility\textsuperscript{8,10}, while some others did not\textsuperscript{11,12}. It was explained that the risk was too small to be detected or that the risk diminished when IA was performed under good medical condition. The health risk of IA may depend on the procedure, gestational age, and parity\textsuperscript{13,14}. In addition, there are other direct and indirect etiologies of tubal infertility: gonococcal, clamydial and other reproductive tract infections (RTIs), pelvic inflammatory disease (PID), pelvic tuberculosis, endometriosis, tubal ectopic preg-
nancy, abdominal or pelvic surgery, IUD use, number of sexual partners, early first sexual intercourse, and smoking\(^{16,11,12,15−17}\).

Infertility requires advanced and expensive medical techniques, which most Vietnamese patients cannot afford. An infertile couple with serious bilateral tubal damage has to spend at least 2,000 USD for one in-vitro fertilization, whose success rate is around 25−30% at Tu Du Obstetrical and Gynecological Hospital in Ho Chi Minh City [unpublished hospital report]. Therefore, finding the risk factors and reducing the number of infertility patients may lessen the burden on women, family, and society.

Approximately 5,000 secondary infertile patients received treatment at Tu Du Hospital in 1999 [unpublished hospital record]. About 50−60% of the patients had history of IA and 20% of them had tubal problems. Small studies at the hospital found that IA might be a risk factor for secondary infertility [Odds ratio (OR)=2.5, 95% CI: 1.6−3.9], and the risk increased to 4.2 (95% CI: 2.0−8.8) among patients living in provinces [unpublished hospital survey]. However, the previous studies included all types of secondary infertility and had several methodological limitations including observer and selection bias and limited consideration for confounding factors that are listed above. Efforts to minimize bias and confounding were made in this study to investigate the influence of IA over the secondary tubal infertility.

**METHODS**

*Study design and setting*

This was a hospital based matched case-control study conducted at Tu Du Hospital from June to September 2001.

*Study population*

We interviewed 134 women of reproductive age; 67 cases and 67 controls. Written consent was obtained from all subjects before the interviews. Cases were secondary tubal infertility women with first or higher-grade bilateral tubal damage confirmed by endoscopy, at least one previous conception (gestational age ≥20 weeks or ultrasound confirmed pregnancy), and husband’s normal semen analysis. Women with reproductive tract abnormalities, polycystic ovarian syndrome, central hypotalamic pituitary axis failure, abnormal ovulation, and hyper/hypothyroidism were excluded from the study. These criteria were applied in order to investigate factors associated specifically with secondary tubal infertility, not secondary infertility in general. Controls were women undergoing cesarean section with intact tubes (soft, no-adhesion, normal shape and normal size) confirmed during the operation. Women with reproductive tract abnormalities and history of infertility treatment were not included in the control group.

Cases and controls were matched by residence (rural or urban area) and age at the time of survey (within 2 years difference). Age was included as a matching
factor to equalize ability to reproduce between two groups. Residence was included because the previous studies at Tu Du Hospital suggested that IA in rural area might have stronger effect on subsequent fertility. Individual matching was used to maximize the efficiency of the analysis.

*Data collection*

Doctors at infertility and endoscopic operation departments selected the cases following the criteria described above and sent the patients to interviewers. The data of case’s age and residence was informed to doctors at the post-operation department to select matched controls from patients undergoing cesarean section. If more than one controls were identified for one case, the one listed on the top was chosen. Controls were sent to another group of interviewers.

Interviews were conducted by four trained medical students in patients’ rooms. The students were trained to interview and collect data. In order to minimize observer bias, study design and objectives were not explicitly explained to them. In addition, they were divided into 2 groups and each group was assigned to interview only infertility patients or patients after cesarean section. A structured questionnaire was used for the 15 to 20 minutes face to face interviews. The questionnaire included factors that were previously reported to relate with secondary infertility: socio-demographic factors (occupation, religion, education and family income), IA history (number of previous IAs and gestational age, time, type of service provider, place, and complications of the last IA), reproductive and medical history (usage of IUD and other contraceptive methods, history of gynecological diseases and RTI symptoms, age at first sexual intercourse, number of sex partners, and history of abdominal operation) and health behavior (smoking and drinking habit). Small reward was given to study subjects after the interview, with a contact information of the research group.

Prior to the main survey, a pilot study was carried out with 10 women who had cesarean section to confirm the feasibility of the survey, to check interviewers’ performance, and to revise the questionnaire. The response rate of the pilot study was 100%.

*Data management and analysis*

Data was entered into computer and analyzed using Stata version 6.0 (Stata Corporation, College Station, Texas, USA). Independent variables that were put into logistic regression analysis are listed in Tables 1 to 3. Discrete variables and categorical variables with more than one categories were tabulated with the dependent variable (cases=1, control=0) to find out the appropriate level for the categorization into dichotomies. OR of each independent variable and corresponding 95% confidence interval was then calculated using univariate conditional logistic regression analysis.
RESULTS

We analyzed the data of 67 secondary tubal infertility cases matched with 67 controls. The response rate of the present survey was 100%. Associations of demographic factors with the risk of secondary tubal infertility are shown in Table 1. The median age of cases and controls was 34, ranging from 25 to 43 years old. The number of women living in rural area was less than that in urban area for both groups. Women and husbands' occupation was not related to the risk of secondary tubal infertility. Proportion of subjects with higher education was 97.0% and 83.6% for cases and controls, respectively. Having higher education significantly increased the risk of secondary tubal infertility by 5.5 times (OR=5.50, 95% CI=1.22-

Table 1. Association of socio-demographic factors with secondary tubal infertility (univariate logistic regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case (N=67)</th>
<th>Control (N=67)</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agea</td>
<td>34 (25, 43)</td>
<td>34 (25, 43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residence (rural)b</td>
<td>30 (44.8)</td>
<td>30 (44.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupation (manual)</td>
<td>34 (50.8)</td>
<td>30 (44.8)</td>
<td>1.31</td>
<td>0.64-2.69</td>
</tr>
<tr>
<td>Education (secondary school or higher)</td>
<td>65 (97.0)</td>
<td>56 (83.6)</td>
<td>5.50</td>
<td>1.22-24.81*</td>
</tr>
<tr>
<td>Husband</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupation (manual)</td>
<td>52 (77.6)</td>
<td>45 (67.1)</td>
<td>1.64</td>
<td>0.77-3.64</td>
</tr>
<tr>
<td>Education (secondary school or higher)</td>
<td>63 (94.0)</td>
<td>57 (85.1)</td>
<td>3.00</td>
<td>0.81-11.08</td>
</tr>
<tr>
<td>Family income (not enough)c</td>
<td>0 (0.0)</td>
<td>5 (7.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a: Odds ratio was not shown because these were matching factors.
b: Odds ratio was not calculated because no case answered family income was not enough.
*p < 0.05

Table 2. Association of induced abortion with secondary tubal infertility (univariate logistic regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case (N=67)</th>
<th>Control (N=67)</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of induced abortion (yes)</td>
<td>34 (50.8)</td>
<td>30 (44.8)</td>
<td>1.27</td>
<td>0.64-2.49</td>
</tr>
<tr>
<td>Last induced abortiona</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age (less than 6 weeks)</td>
<td>20 (58.8)</td>
<td>18 (60.0)</td>
<td>0.67</td>
<td>0.11-3.99</td>
</tr>
<tr>
<td>Institution (hospital)</td>
<td>26 (76.5)</td>
<td>25 (83.3)</td>
<td>0.33</td>
<td>0.03-3.20</td>
</tr>
<tr>
<td>Provider (doctor)</td>
<td>20 (58.8)</td>
<td>22 (73.3)</td>
<td>1.00</td>
<td>0.20-4.95</td>
</tr>
<tr>
<td>Complication (yes)</td>
<td>6 (9.0)</td>
<td>2 (3.0)</td>
<td>3.00</td>
<td>0.60-14.86</td>
</tr>
</tbody>
</table>

a: Proportions are among those who experienced abortion
Table 3. Association of reproductive history, medical history and health behavior with secondary tubal infertility (univariate logistic regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case (N=67)</th>
<th>Control (N=67)</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUD use (yes)</td>
<td>14 (20.9)</td>
<td>25 (37.3)</td>
<td>0.38</td>
<td>0.16-0.93*</td>
</tr>
<tr>
<td>Gynecological diseases (yes)</td>
<td>40 (59.7)</td>
<td>29 (43.3)</td>
<td>1.78</td>
<td>0.93-3.44d</td>
</tr>
<tr>
<td>Age of first sexual intercourse (less than 20)</td>
<td>20 (29.9)</td>
<td>6 (9.1)</td>
<td>3.80</td>
<td>1.42-10.18*</td>
</tr>
<tr>
<td>Laparotomy (yes)</td>
<td>18 (26.9)</td>
<td>27 (40.9)</td>
<td>0.44</td>
<td>0.18-1.06</td>
</tr>
<tr>
<td>Active smoking (yes)</td>
<td>2 (3.0)</td>
<td>4 (6.0)</td>
<td>0.33</td>
<td>0.03-3.20</td>
</tr>
<tr>
<td>Passive smoking (yes)</td>
<td>45 (67.2)</td>
<td>46 (68.7)</td>
<td>0.94</td>
<td>0.48-1.86</td>
</tr>
<tr>
<td>Beverages</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coffee (yes)</td>
<td>3 (4.5)</td>
<td>5 (7.5)</td>
<td>0.60</td>
<td>0.14-2.51</td>
</tr>
<tr>
<td>Tea (yes)</td>
<td>9 (13.4)</td>
<td>9 (13.4)</td>
<td>1.00</td>
<td>0.40-2.52</td>
</tr>
</tbody>
</table>

* p < 0.05  
# p < 0.1

IA did not significantly increase the risk of secondary tubal infertility (OR=1.27, 95% CI=0.64-2.49), but the proportion of subjects with history of IA was higher for cases; 50.8% and 44.8% for cases and controls, respectively (Table 2). More than half of women had the last IA performed at hospital and by doctors. Proportions of women who had the last IA at hospital, performed by a doctor, and without any complication were less among the case group, but these were not identified as the statistically significant factors associated with the secondary tubal infertility.

IUD use had a significant protective effect on secondary tubal infertility (OR=0.38, 95% CI=0.16-0.93) (Table 3). Past history of gynecological diseases increased the risk with borderline significance. Proportion of subjects with age of first sexual intercourse under 20 years old was 29.9% for cases and 9.1% for controls, and the factor increased the risk of secondary tubal infertility 3.8 times (OR=3.8, 95% CI=1.42-10.18). History of laparotomy, smoking and drinking beverages were not significant factors.

DISCUSSION

In our study, experience of IA was not found as a risk factor of secondary tubal infertility although the proportion of women with IA history was higher in the case group. There are four possible explanations. First, the effect of IA on secondary tubal infertility itself may be too small to be detected with our limited number of subjects. Second, the difference in the feeling toward reporting IA history might have masked the risk of IA. Infertility patients may hide their past IA history because of their feeling of guilt that the IA might have caused her current medical
problem. On the contrary, pregnant woman in the control group may be more open about telling their pregnancy history during the interview. Third, our study population was distinctly different from the general population in Vietnam. Most women were with sufficient family income and high education level, and they obtained IAs at hospitals performed by doctors. When IA is performed properly, the rate of complication including infertility is very little as reported from developed countries\textsuperscript{7,8}.

Fourth, the time lag between the survey and the occurrence of infertility might have masked the association of IA and infertility. For example, when an infertility case is 34 years old, age of matched control will be in the range of 32 to 36 in our study. If infertility has occurred at the age of 24, the control will have about 10 more years under the risk of getting unwanted pregnancy compared with her matched case. Perhaps because of this time lag, the proportion of women with multiple IAs was higher in the control group than in the case group (Table 4). The median age of our cases was high with a long history of infertility, thus, the effect of this time lag was not negligible. Supporting our speculation of the bias from the time lag, the median age of last IA was 24 years old for the cases and 30 for the controls ($p<0.001$, Wilcoxon–Mann–Whitney rank sum test). By matching cases and controls using the age that the case was diagnosed as infertile, this time lag would decrease. However, it is difficult to detect the occurrence of infertility exactly, and prospective study design is recommended in future investigations.

Even with the above explanation, one may wonder why the previous studies at the same hospital identified IA as a risk factor of secondary infertility as mentioned in the introduction. First of all, they used parity as one of matching criteria to eliminate the difference in the ability to reproduce between two groups. With this matching criteria, non-infertile women with high ability to reproduce and with many previous IAs would not be included in the control group, and thus, odds ratio could increase. Secondly, the previous study selected subjects from 18 to 35 years old women. This might have shortened the length of the time lag explained above. In our study, half of cases were older than 35 years old and they had been infertile for years. Thirdly, they investigated secondary infertility patients in general and did not specify their study population to the secondary \textit{tubal} infertility patients. IAs may cause infertility through a pathway other than tubal damage, which may be the.

<table>
<thead>
<tr>
<th>Number of induced abortions</th>
<th>$N$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case ($N=67$)</td>
</tr>
<tr>
<td>Non</td>
<td>33 (49.3)</td>
</tr>
<tr>
<td>Single</td>
<td>32 (47.8)</td>
</tr>
<tr>
<td>Multiple</td>
<td>2 (2.9)</td>
</tr>
</tbody>
</table>
reason why the previous studies found significant association. Fourthly, there was a potential observer bias in the previous studies, in which interviewers were the principle investigators who were not blinded from the study purposes. It is possible that interviewers unintentionally tried to obtain more information about IA from the cases than from the controls.

One important finding in the present study was that being sexually active before the age of 20 increased the risk of secondary tubal infertility. One study in Nairobi obtained the same result\(^{10}\). Sexually active young women expose themselves to certain reproductive health risks. Women with early age at first sexual intercourse experience pre-marital sexual relation with their future husbands or boy friends. With lack of contraceptive knowledge, it is not rare for them to become pregnant. These pregnancies are often considered as unwanted under family pressure objecting her to marry or considering her education and career, and many of them end in IA\(^ {18}\). Young women are also biologically and socially vulnerable to RTIs\(^ {19}\). Their likelihood of contracting the infection is higher because of the immaturity of their cervix, and the disease tends to be left untreated because of their less access to reproductive health services compared with older women. Both IA and RTIs could lead to primary or secondary infertility.

Other significant factors related to the secondary tubal infertility were women’s education and history of IUD usage. Most of infertile patients must have moderate to good economic status to be able to afford the infertility treatment. Economic status and level of education often goes hand in hand, and this may explain the higher proportion of women with high education in the case group. In our study, there were only five women with not enough income and all were in the lower education group. We selected controls from a group of women who were able to afford cesarean section at the central hospital, in order to minimize the imbalance of socio-economic status between the two groups. However, the relationship between education and infertility still remained. The infertility treatment often requires couples to go through the same costly procedure several times, and the total treatment cost becomes far more expensive than the cost of one or two cesarean sections. More financially wealthy and higher educated populations are likely to be included in the cases because of the difference in cost between infertility treatment and cesarean section. Moreover, it is reported in Vietnam that the proportion of women with IA history is higher among higher educated women: 3.9% for no education, 4.1% for some primary education, 5.7% for primary level completed, 8.6% for lower secondary level completed, and 9.3% for higher secondary level completed groups\(^ {19}\). The proportion of IA experienced women was also higher for those with secondary school or higher education in our study: 23.1% for lower and 50.4% for higher education groups. Thus, it is possible that the education had a significant effect over infertility through the IA history.

IUD usage appeared to be a protective factor of secondary tubal infertility, probably because of the high reproductive ability among controls and their tendency
to use effective contraceptive methods. On the contrary, cases rarely use the contraceptive devices because they are trying to conceive. The significance of IUD use was obtained because of the retrospective nature of the study, which is another reason to recommend prospective study design to determine the effects of IA on fertility.

History of gynecological diseases had a borderline significance to increase the risk of secondary infertility. Although all cases had bilateral tubal damage, indicating the past inflammation around the tubes, the history of gynecological infection did not increase the risk. This may be due to a limitation in obtaining the medical history through a personal interview. Women are likely to have asymptomatic RTIs\(^{20}\) and they may fail to report their infections during the interview. In addition, the tests to detect RTIs including gonococcal and clammydial infections are not commonly used in Vietnam. Pregnant women and infertile patients are not screened for these infections and we were unable to compare the test results in the present study. It is needed to promote RTI detection in order to prevent PID and other complications.

Although not significant, our results showed higher proportion of women with IA history among the secondary tubal infertility patients compared with controls. It was noteworthy that IA performed at hospital, by doctors and without complications were less common among the cases, indicating the effects of unsafe IAs. The recent maternal mortality in Vietnam was reported to be about 160 per 100,000 live births and IA was one of the major factors related to the maternal mortality\(^{21}\). A situation analysis of reproductive health services in Vietnam revealed that less than one-third of IA clients had a blood test or had blood pressure and pulse taken before the procedure\(^{22}\). In about 8% of IA cases, cannula was reused without disinfecting, and in only one-sixth of cases, providers disinfected their hands. More efforts are required to provide safer IA and effective contraceptives, especially at the primary level of medical service. At the same time, further prospective study with a larger sample size is needed to investigate the effect of IA performed in various settings over fertility and women’s health in general. With the trend of more young single Vietnamese women becoming sexually active at an early age, Vietnamese government and health care workers should establish more effective educational programs to provide knowledge about safe sex, RTIs, and contraception to minimize the risk of infertility among young couples.

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REFERENCES