TUBAL LIGATION AND GYNECOLOGICAL DISORDERS

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Dedicated to my Mother & Father

CERTIFICATE

This thesis is submitted by **Mrs. Ghazala Ashfaq** is accepted in its present form by the Department of Biological Sciences, Quaid-i-Azam University, Islamabad as satisfying the thesis requirements for the degree of Doctor of Philosophy in Biological Sciences.

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CONTENTS

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List of Tables

List of Figures

ABSTRACT

The present study was undertaken to examine gynecological consequences of tubal ligation in a cross section of Pakistani women from both urban and rural communities of Islamabad and Rawalpindi. The investigation was divided into three parts: (1) preligation history of a large sample (2893) of women interviewed face to face at Reproductive Heath Center, (2) postligation incidence of gynecological disorders (GDs) determined by interviews of women facilitated by Community Health Houses (CBS-1 and CBS-2), and (3) study of post ligation complications through data collected in a hospital setting (HBS-1) to assess incidence of GDs and their association with ligation, hysterectomy and any type of abdominal surgery (HBS-2).

The sociodemographic profile of women opting for ligation showed a generally low socioeconomic status of families. Almost $1/3^{rd}$ of the total sample (2893) was under 30 yrs of age and had no history of abortions, had a parity of < 6 and very low incidence of disease in both the urban and rural communities. The incidence of GDs was also extremely low, particularly in the urban women. The retrospective cohort study (CBS-1) of post ligation health and gynecological status of women has revealed a 2-fold greater incidence of GD in ligated cohort than in the control cohort (nonligated). Both cohorts had very close correspondence in mean age, duration of marriage, abortion rate, LCB (last child born age) and contraception. The majority of the women in this study were over 30 yrs of age, were married for over 10 years, had no experience of abortion, had LCB of >5 yrs and were non users of contraceptives, except a higher percentage (39.5 %) in the GD subgroup of control cohort. Also, a greater percentage of women had health problems in the GD subgroups of both the cohorts (ligated and nonligated) suggesting an association with health. The onset of GDs occurred about 2 years after ligation, suggesting possibility of a biological basis of change. Increased risk of GDs was evident for ligated cohort as compared to control cohort (RR. 2.46, 95 % CI $p < 0.001$).

The follow up study (CBS-2) of 111 women revealed a similar urban/rural ratio, low socioeconomic level, high contraception rate, LCB of >6 yrs (large gap since last child birth), no experience of abortions by majority of the women (80%). Most of the women were between 30- 35 yrs of age and had laparoscopic surgery. While a high percentage (87.3%) of the cohort had no preligation health problems, this percentage dropped by ~48%, 2.5 yrs after ligation (follow up 2 yrs postligation). About 1/3rd of the cohort suffered from GDs. On partitioning into GD and No GD subgroups, the subgroups did not differ in average age at ligation, number of conceptions and time since ligation. In both subgroups, laparoscopy dominated as method of ligation. Both the CBS-1 and CBS-2 studies showed that the ligated cohort had increased risk of GDs, especially menstrual disturbance as well as health complaints. Maximum menstrual disturbance was experienced by women of 35 yrs and younger age. This emerged as a consistent picture even after such confounders as age, parity, contraception, educational background and recall bias were accounted for.

The hospital-based (HBS-1) study also supported the above observations, revealing a strong association between ligation, GDs and health. The study also showed that tubal ligation is followed by a sequence of menstrual alterations. In both retrospective-cohort (CBS-1 & 2) and case-control analyses (HBS) in the present investigation, the majority of women underwent laparoscopy and nearly all had interval sterilization. In the HBS-1 study, GDs were recorded with considerable postligation delay in both the cases and the control women. This however, also coincided with approaching menopause (>40 yrs age, cases/control). Anemia in the majority of the cases group seemed related to GDs, of which menstrual dysfunction (increased duration and flow rate) was predominant followed by UVP. The majority of women with GDs (~80%) in this part of study were 35 yrs and younger age and ligation had a strong association with GDs (OR=2.29, 95% CI, $P<0.0001$) even after adjustment for such confounders as age, parity, conceptions, abortion, contraception, and other surgery. Menstrual dysfunction was evident in terms of both duration and flow with a positive association with ligation for women up to 35 yrs of age (OR= 5.25, CI 95%, $P<0.005$). The association between GDs and ligation appeared to be a

consequence of some physiological changes rather than representing an aging phenomenon. The low incidence of PID (pelvic inflammatory disease) affirms relatively safe surgical procedural handling of the subjects. This is also evident from the fact that none of the subjects reported postligation surgical complications.

The hospital-based study (HBS-1) also revealed that leiomyoma was a major uterine pathology followed by adenomyosis and endometrial hyperplasia in both the ligated and nonligated cases. This change tended to increase with age, providing evidence that age also has a role in this pathological state. Whether the observed marginal incidence of hyperplasia has implications of a cancerous state in the long term and also whether the overall uterine pathological state is an outcome of sterilization requires further studies. The study showed in addition that age and hysterectomy have a positive association in both the ligated and the nonligated women. The fact that the frequency of hysterectomy was greater in the ligated subjects especially with advancing age implies that there is need of care in advising women to opt for sterilization in view of the impeding risk of subsequent hysterectomy as management for GDs resulting from ligation.

Finally, the hospital-based study (HBS-2) that was aimed at analyses of sterilization hazards vis-à-vis any abdominal surgery, indicated that GDs indeed stem from ligation rather than any other type of abdominal surgical procedure. This observation also implies that ligation results in certain hormonal disturbances (ovarian) leading to sequalae that fall within the broad definition of post tubal ligation syndrome.

INTRODUCTION

Although in recent years, there has been much emphasis on family planning to stem the tide of rising world population, couples have practiced various techniques of controlling the size of the family from time immemorial. The Greeks called family planning "Atokion". In Aristotle's time, such techniques as annointing the uterus with oil of cedar and ointment of lead or frankincense in olive oil and, in the male, treatment of the phallus with juniper berries were commonly used as temporary means of birth control. The oldest written accounts of various vaginal-uterine pessaries and drinking condiments can be found in the 4000-year old ahun Papyrus and in Hippocratic textbooks. These primitive intrauterine methods were replaced in the last century by modern intrauterine devices (IUDs). Germans developed an intrauterine device made of silken thread and silver rings. In the 1950s, synthetic hormones came in the market as blockers of ovulation and the first contraceptive pill was approved by US Food and Drug Administration. While these means of female contraception together with use of condoms by the male counterpart represent temporary means of contraception, irreversible contraceptive approaches gained priority owing to both population pressure and clinical obligations of reproductive health of women. The compulsions of population control programs necessitated mass surgical sterilization, a method of permanent contraception. By 1990s, 6.5 million women were sterilized in India. Of the 137 million surgeries on women in the developing countries, 32.5 million were carried out in China alone (Church and Geller, 1990). In Pakistan, family planning program was started in mid 60s and was initially based on supply of clinical contraceptives, including intrauterine devices. These clinics were later converted into Sterilization Centers between 1970 and 1975. In 1982, Reproductive Health Services (RHS) Project was included in the National 5 year Development Plan. Its objective was to provide surgical contraceptive services. Between 1987 and 1993, 21,300 women were sterilized under RHS scheme. This was in addition to the over 18,000 surgical cases handled by an NGO, the Family Planning Association of Pakistan (Hakim and Zahir, 1994). Use of contraceptives by Pakistani women has since shown an increase from 9% in 1984 to 24% by 1997 (Hakim and Cleland, 1998), and 30 % by 2002 (PAP, 2002). One fourth of the current users have adopted female sterilization.

Surgical sterilization involves tubal ligation in the female and vasectomy in the male. The focus of the present study was on tubal ligation

with a view to understanding the immediate and long term impact of such surgery on gynecological health of women exposed to this treatment. Tubal ligation is the most widely used contraceptive method the world over. According to available statistics, 40% of the couples of 40 years of age prefer tubal ligation as the method of choice. The figure for women in USA between the ages 18-49 years stands at 20%. It has been reported that 29% of married women have undergone sterilization in Panama, 23% in Korea, 19% in Thailand, around 18% each in Brazil, El Salvador, Sri Lanka and Costa Rica (Church and Geller, 1990).

Tubal ligation is the method of choice for two reasons. On the one hand, it provides irreversible contraception to couples that do not want any children or have achieved the desired family size, especially when compulsions of population control programs are kept in focus. On the other hand, it ensures protection against high risk pregnancies, ensuring mother's health. The method involves blocking of transport of ovum from the ovary through the fallopian tube to the uterus. It is a two-step procedure in which the fallopian tube must be reached either by laparoscopy or by laparotomy and then the tube must be blocked for which a variety of techniques have been utilized. Tubal ligation can be carried out either immediately after delivery, i.e., as postpartum sterilization or about 40 days postpartum when it is called interval sterilization. (Lisken et al. 1985.)

While tubal ligation has the obvious advantage of promising permanent contraception, its total success in achieving the desired result has been suspected on the one hand and, on the other, has raised serious concerns regarding its post ligation impact on the reproductive health of women (Jelovsek, 2001). The present work was, therefore, planned to carry out a study to examine the impact of tubal ligation in a cross section of women belonging to the Islamabad-Rawalpindi area of Pakistan. Although research on reproductive health of women and contraception has received much attention in the developed countries (Contraception Report, 2001), only a few studies have been conducted on this subject in the Indo-Pakistan subcontinent as well as other parts of the developing world (Wasserheit *et al.*, 1989; Bhatia *et al.*, 1997).

Female sterilization involving tubal ligation has been the most widely practiced methods of contraception by women between the ages of 40-44 years in USA . Of the nearly 0.7 million tubal sterilizations, half have been done postpartum and half as interval sterilization (Westoff and Davis, 2000).

According to one survey of a group of over 10,000 women who had tubal ligation, the failure rate of sterilization appears to be much greater than the perceived standard failure rate (National Center for Health Statistics, 2001). The specific failure rates vary according to the various ligation methods, 3.7% with use of spring clip, 2.5% with bipolar coagulation and 0.8% with postpartum partial salpingectomy and unipolar coagulation each. Lowest failure rates in the group studied concern women older than 34 years. Besides lack of complete protection from further pregnancies, women also tend to complain of complications that are collectively known as "post tubal ligation syndrome" (Jelovsek, 2001). The aggregate symptoms that characterize this syndrome are pelvic pain, increased menstrual flow, cramps, altered hormonal profile, change in menstrual cycle and luteal phase defects of the reproductive cycle, general gynecological problems, change in sexual behavior and in mental health (Radwanska *et al.*, 1979; Cole *et al.*, 1984; Martinez-Schnell *et al.*, 1993; Sumiala. et al., 2000; Taner *et al.*, 1995; Pati and Cullins, 2000; Jelovsek, 2001). One of the consequences of tubal ligation in some cases is precipitation of menopause. Disruption of uteroovarian blood supply, as may happen in cases of cauterization, seems to be one of the most serious causes of post ligation abnormalities (Geber and Cadeno, 1996; Jelovsek, 2001). Menstrual problems following ligation are, more often than not, encountered by women in their 20's and less by those above 30 years of age. Regardless of whether such statistics reveal a real association with age or simply that contraception has greater urgency for younger women, they are the more frequent to undergo ligation and hence the resulting statistics concern this age group. Another consequence of ligation appears to be compulsion to undergo hysterectomy; (Cooper, 1983; Cohen, 1987; Fortney, 1988; Stergachis *et al.*, 1990; Kjer and Knudsen, 1990; Hillis *et al.*, 1990; Evans and Meyer, 1994; Rosenblatt *et al.*, 1996; Green *et al.*, 1996; Silver and Rochville, 1994; Zahir *et al.*, 1999.) because of menstrual difficulties and pelvic pain. Ectopic pregnancies have also been documented in sterilized women (National Center for Health Statistics, 1995). Among the advantages of tubal ligation is also its inverse relationship with ovarian cancer (Stergachis *et al.*, 1990; Green *et al.*, 1996; Silver and Rochville, 1994; Hankinson et al, 1993; Westoff and Davis, 2000). While relationship with other cancers of reproductive systems like breast, endometrium and cervix are under investigation for having any association or otherwise with tubal ligation. (Calle, et al., 2001; Brinton, et al., 2000; Lecy, et al., 2000 and Li, et al., 2000.)

In view of the above background, the present investigation was planned to determine the effects of tubal ligation and risk of disruption of gynecological health of women by conducting epidemiological study on a cross section of women residing in the Islamabad-Rawalpindi area of Pakistan. A major compulsion for conducting the present investigation was the unique socioeconomic background of women in Pakistan with low literacy rate, young age marriages, high parity, overall low contraception practice and prevalence of sterilization as the method of choice. It was hoped that the data so generated would help in defining determinants of post ligation risks and thence in helping policy makers and family planning programmers in developing guidelines for avoiding risk of tubal ligation, which may otherwise add to unnecessary post ligation management costs. In order to achieve these objectives, the study was based on (1) determination of sociodemographic profile of women enrolled for tubal ligation, (2) status of post ligation health condition (3) determine relative risk of gynecological disorders in sterilized women, and (4) determination of association of tubal ligation with gynecological disorders, menstrual characteristics, hysterectomy, uterine pathology and general abdominal surgery.

MATERIALS AND METHODS

GENERAL

Study population and investigative design :

The subjects for the study were recruited from the resident community or hospitals of Islamabad-Rawalpindi area. Women of reproductive age were randomly interviewed during field visits to communities or at Gynecological Wards of local hospitals. Information regarding the pertinent variables was obtained by adopting both retrospective cohort and case-control approach with the help of questionnaires specially designed for this purpose (see Appendix)

Various epidemiological designs, retrospective cohort and case control were adopted for gathering data to analyze possible association of tubal ligation with gynecological complications collectively called "post tubal ligation syndrome". Three different performas were designed to collect information to assess existence of this syndrome. The first of these focused on collection of demographic, reproductive and medical history of women aspiring for sterilization (period of study: 1993-1995). The collection of data for analysis was done by direct face-to-face interviews of women that were facilitated by a Reproductive Health Center (RHC). The second involved retrospective cohort study for analysis of relative risk for post ligation gynecological and health condition of the ligated cohort. Both control cohort and ligated cohort were recruited by visiting communities through Community Health Houses (CHH)(Period: 1998-2000). The third, based on case-control approach, aimed at hospital-based analysis of association, if any, between ligation and gynecological disorders during the period 1996-2000.

For purposes of the investigation, gynecological disorder (GD) was considered to be any complaint pertaining to menstrual impairment, postmenopausal bleeding (PMB), uterine pathology, vaginal discharge (infection) and utero-vaginal prolapse (UVP) for which a woman must consult a gynecologist.

The rationale of variables was based on the reported risk factors, conditions and status contributing to a particular gynecological disorder.

Ethical considerations:

Verbal consent of the subjects for participation in the study was obtained before conducting interviews. The subjects were assured of confidentiality of their identity. The data were, thus, entered by a code number allotted to individual subjects.

Analysis of data:

Analysis of data was done on group basis and not on individual basis. The data obtained were coded for type of study and the selected variables, followed by entry for analysis using SPSS Version 8. Computer Programme For the purpose of analysis, the multiple outcomes were reduced to a dichotomous outcome (i.e. yes/no) and analysed by 2x2 frequency tables. Odds Ratio (OR) and Relative Risk (RR) analyses were carried out using 2x2 tables and further analysed according to Mantel-Henszel x^2 summary (Kahn and Sempos, 1989) to asses association of ligation with GD and the effect of confounders. This method provides a weighted average of separate odds ratios and minimizes or eliminates the effect of confounders.

1. Preligation profile of women

This study was based on face-to-face interviews and was conducted at the Reproductive Health Centre (RHC), Islamabad, which provides tubal sterilization services to communities residing in the Federal Capital (urban population) and the peripheral rural areas. The women visiting the Centre belonged to different socio-economic backgrounds and localities. The information gathered included both independent and predictive variables guiding a woman to opt for permanent method of contraception. Only women opting for interval sterilization were included in the study. The baseline information (Proforma-I, Appendix 1) collected fell into four main groups:

a. ***Social characteristics***: Income, urban-rural background and years of schooling (educational status).

b. ***Demographic factors***: Age, number of pregnancies, parity and history of abortions.

c. ***Reproductive characteristics***: Menstrual history, marriage duration and history of contraceptive usage.

d. ***Health status:*** Pre-existing health and gynecological conditions.

According to NIPS, 1991 (National Institute for Population Studies), women opting for tubal ligation are usually in their 3rd to 4th decade of life. In view of a woman's reproductive age span of 15-48 years and to have representative data on women residing both in the urban and rural areas, 3000 women were to be interviewed. However, only 2893 women were interviewed during the period 1993-1995 with a response rate of about 96.4%. Addresses of 300 women were recorded for follow up (see below) as retrospective cohort study, two years after the date of ligation in order to find out long term effects (5 yr or more) of ligation on gynecological and medical health by focussing on (1) the status of menstrual cycle, (2) frequency of visits to gynecologists, and (3) post ligation health status.

2. Postligation health and gynecological condition

In order to determine relative risk of GD in ligated women as compared to women without this exposure a retrospective cohort study was conducted. To obtain information on gynecological status and post ligation health of women in different communities, field visits were made. The Prime Minister's Programme on Family Planning has been providing nationwide services to communities through trained lady health workers. The territory under the Federal Area of Islamabad comprises low income urban as well as rural areas in its vicinity. A supervisory team performs routine monitoring and holds family planning camps in coordination with the District Population Office, which provides services and follow up at the community level. The field visits were coordinated with this team after formal approval of the relevant authorities. Visits were made routinely to interview women at their homes. The communities are looked after by lady health workers located in Community Health Houses that maintain demographic and reproductive health records of the resident women. Since the resident women are familiar with the lady health workers, they do not hesitate to seek their assistance regarding day-to-day mother-child problems, general awareness of and motivation for health education, family planning and contraceptive supply. This community-based study (CBS) consisted of two groups of women. The first group (CBS-1) comprised ligated and control cohorts. The former comprised women who had undergone tubal ligation and the latter consists of women without this surgery. All information was collected on a proforma (Proforma-II, Appendix) designed for the purpose and was translated in Urdu (local language) to

achieve a uniform response. Baseline data pertaining to social characteristics, demographic factors, reproductive characteristics and health status were recorded along with post ligation health status and reproductive history, method of ligation (derived from records of the surgical centre and actual scar to differentiate between minilap and laparoscopy) and timing of ligation (postpartum or interval sterilization). The second group (CBS-2) consisted of women who had already been interviewed at the time of ligation at RHC (see 1 above) and whose status of health and menstrual history was already recorded with the aim of avoiding recall bias during follow up. Control cohort comprised women matched on age and parity with the follow up cohort.

CBS-1:

This community-based study was conducted by visiting women in their homes in communities surrounding the area of Islamabad and Rawalpindi. Women who had undergone tubal ligation at any stage of their life were interviewed. The aim of the visit was to assess prevalence of postligation complications, if any, and to circumvent hospital bias by asking questions in a hospital-free setting. The descriptive information covered age at ligation, parity, method of ligation, time since ligation, health status and possible gynecological disorders. The size of the sample was calculated by using WHO-devised computer program (Epi Info) designed on the basis of 11% rate of prevalence of tubal ligation (NIPS, 1991) and statistics of 2.6 million women of childbearing age. The calculated sample size turned out to be 500 (95% confidence level) but only 89% response rate could be achieved (N= 447).

The investigation was designed as a cohort study, with exposure to tubal ligation as a risk factor . These women were identified from the registers maintained by lady health workers at Community Health Houses under the Prime Minister's Programme (now named as Women's Health Project, Ministry of Health, Islamabad). Questions were asked regarding their health and gynecologic condition especially menstrual cycle, previous contraceptive use and time since gynecological problem . Visit to gynecologist or use of medication for gynecological problem was taken as indicator of presence of gynecological disorders . The criterion of selection as cohort for interview was "Pakistani women of over 30 years and ligated at least 6 months prior to the interview". The information collected on health and gynecological status was based on self-report. The control cohort consisted of women residing in

the same community, matched with the ligated cohort for age and parity and were without history of ligation. Both cohorts were asked the same questions.

CBS-2 (Follow up study):

The objective of the study was to find long-term effects of ligation on gynecological and health status of women at least 2 years after ligation of the 300 women previously identified as follow up cohort. The addresses of these women (both urban and rural) were recorded at the time of interview at RHC to develop their preligation profile. Of the 300 women initially registered for follow up, only 111 women (37%) could be traced. The response rate for the urban area was higher (about 50%) than the rate for the rural areas (26%). The distribution and number of the subjects according to urban-rural classification is shown in Tables 1 and 2.The reason of low response seems to be migration or other as yet incomprehensible reasons.

The control cohort having no history of exposure to the risk factor, was selected from the same communities and was matched to the follow up cohort for age, conceptions and age of the last child born. The number of women in this cohort was nearly three times that of the women in the follow up cohort (310:111).

Table 1. CBS-2. Distribution of follow up subjects from urban areas of Islamabad according to localities.

	Urban localities		
Follow up status	**100 qtrs**	**Rawal town**	**NIH colony**
Registered	46	25	17
Reporting	16	14	12

Table 2. CBS-2. Distribution of follow up subjects from rural areas of Islamabad according to localities.

	Rural Localities									
Follow up status	Kirpa	Chira	Alipur	Phulgran	Noorpur Shahan	Saidpur	Moora noor	Bani Gala	Malpur	Shadara
Registered	50	30	30	10	14	19	20	24	14	10
Reporting	6	5	9	7	2	3	17	12	9	4

3. Hospital-based analyses of postligation complication

Two separate studies were carried out in hospital setting. The objective was to determine association, if any, between ligation and gynecological health

Hospital Based Study-1 (HBS-1):

Case-Control approach was employed for this study. A sample of women visiting the hospital for remedy of gynecological disorders (as defined under general methodology) constituted the Cases group (irrespective of ligation history). Age matched controls (within 5 years of age) were women attending the Outpatient Department (OPD) of the same hospital for ailments other than gynecological or women who brought their child for paediatric consultation. According to Pakistan Demographic and Health Survey, (NIPS, 1991), women of 15-60 years of age comprise almost 50% of the women's population in Pakistan. On the basis of this percentage and to cover women in different phases of the reproductive life, a sample size of 688 was enrolled as Cases and a sample of 682 women as Controls during the period 1998-1999.

Federal Government Hospital (Polyclinic), Islamabad and Holy Family Hospital, Rawalpindi (which are also teaching hospitals) are the two main sources of medical facility with a substantial turnover of patients in their

gynecological departments. After prior permission, of respective head of gynea departments complete information pertaining to demographic, medical and gynecological history along with clinical diagnosis, laboratory investigations and management level for the visiting women were obtained from the patients in the hospital wards. (Proforma-III, Appendix). Menstrual cycle history based on past personal experience of the subjects as well as the most recent cycle (to overcome recall bias) was recorded.

The menstrual cycle was categorized as regular, irregular, menopause or lactation amenorrhoea. The cycle length was defined as short if its duration was < 20 days, average/normal if between 21-35 days, and long if it was > 35 days. Flow of menstrual blood was categorized as scanty, average or heavy according to individual perception. Uterine pathology was also recorded on the basis of ultra- sonographic and laboratory reports, if available. Data were gathered on management of gynecological disorders by hysterectomy as it indicates the length and severity of the complaint. The menstrual cycle changes and incidence of hysterectomy in Cases and Controls were analysed separately. The data were coded for different variables and entered in the SPSS Version 8, Computer Program.

Hospital-based Study-2 (HBS-2)

This was a retrospective cohort study undertaken to determine whether gynecological disorders have an association with ligation or stem from simply any abdominal surgery. The cohort comprised 204 ligated women selected from the study on hospital-based post ligation health condition (HBS-1) described in the previous section. The study utilized the baseline data already gathered. Age and parity matched control cohort (N=282) were women who had undergone abdominal surgery other than sterilization surgery. The post surgical time elapsed in both groups at the time of interview was at least 6 months. Questions related to health and reproductive life were asked, besides recording the date of surgery and date of presenting with any gynecological problem

RESULTS

1.Preligation profile of women.

Social characteristics:

The women interviewed during this survey were nearly uniformly distributed in rural and urban communities (1450 = 50.1% and 1443 = 49.9% respectively). The majority of the women turned out to be illiterate (80%, Table 3). Only an insignificant percentage of them were working women (4.2%), indicating general absence of physical strain that could otherwise influence their reproductive health/pregnancy. The educational and occupational background of the families (husband and wife) revealed a low socioeconomic level of the sampled population (Table 3).

Demographic factors:

Of the total sample of women ranging in age between 25 to 45 years, 31.5% were below 30 yrs and the rest above 30 yrs (Table 4). Most of the women had marriage duration of less than 15 yrs, parity of less than 6 and zero abortion rate in both the rural and urban communities (Table 3). The percentage of urban women with a parity of < 6 was 2-fold higher than that of women with parity of > 6. The frequency of single and multiple abortions was very low in both communities and the majority of women in the two communities experienced live birth. The last child born was over one year of age in the majority of women (Table 3).

Health and family planning status:

Table 3 also shows health and family planning history of the women interviewed. The percentage of women using contraceptives was nearly 50 % less as compared to women not on contraception. A greater percentage of urban women were on contraception than the rural women. As many as 94% women reported no significant medical history. This also indicates a history of trouble-free pregnancies and lack of postpartum complications. Only 4.2% had medical problems such as hypertension, diabetes and heart disease (not tabulated here), while 1.8% reported experience of abdominal surgery (Table 3) with hardly any difference between the rural and urban sample in this respect.

Reproductive characteristics:

The incidence of gynecological disorders (GD) (Table 3) was remarkably low (0.2%), showing high level of gynecological care and/or sound reproductive physiology. Interestingly, such disorders in the urban sample were nearly 1/20th of the rural sample. The majority of the women had regular cycle and about 29% of the total sample revealed lactational amenorrhea.

2. Postligation health and gynecological condition.

CBS-1

Demographic features

Partitioning of the ligated cohort (N=447) on the basis of incidence of GD or lack thereof yielded 165 (37.92%) women with GD and 282 (63.1%) without GD (Table 4).In contrast, the corresponding percentages for the control cohort (nonligated, N=507) yielded only 15% women with GD. There were no marked between and within group differences in average age of the women at the time of postligation interview. The time elapsed since ligation was greater for the GD subgroup than for the No GD subgroup of the ligated cohort. The average time since the ligated cohort was carrying GD turned out to be 2.7 years, indicating that its onset occurred well after the ligation procedure. Also, the rate of conception in both subgroups of the ligated cohort was greater (reflecting pregnancy burden) compared to these subgroups of the control cohort women. There were also no wide between group and within group differences in regard to LCB age and number of abortions (Table 4). The notable aspect of the comparison, thus, was a markedly greater incidence of GD in the ligated cohort compared to the control cohort (nonligated) and that the onset of GD in the ligated cohort occurred with considerable delay after ligation.

Table 3. Preligation (baseline) profile of women interviewed at Reproductive Health Center (RHC).

Characteristics	Rural (1450)	Urban (1443)	Total 2893	Percentage
Socioeconomic:				
Literate	11.1	27.3	575	20
Working	3.3	6	121	4.2
Demographic:				
Age				
<30	29.72	33.3	911	31.5
>30	70.27	66.7	1982	68.5
Marriage duration				
<15	89.1	75.9	2574	88.97
>15	10.9	11.2	319	11.02
Reproductive:				
Pregnancy				
Parity				
<6	67.7	70.68	2016	69.68
>6	31.3	29.3	877	30.31
Abortions (No)				
0	82.06	78.1	2317	80.1
1	15.22	18.7	489	16.9
>1	2.82	3.2	77	3
Last Pregnancy outcome				
Live birth	93.9	90.71	2671	92.3
Stillbirth/Abort.	6.1	9.28	221	7.6
Last childbirth				
<1year	38.6	37.3	1097	37
>1year	61.2	63.3	1793	62
Health & Famiy Planning:				
Health				
No disease	94	94	2719	94
Disease	4.4	4.3	154	6
Surgery abd.	1.8	1.7	51	1.8
Contraception				
Yes	29.6	39.1	993	34.4
No	70.4	60.9	1900	65.7
Gyne disorder				
Yes	0.3	0.13	6	0.2
No	99.7	99.86	2887	99.8
Menstrual cycle				
Regular	69.9	71.5	2046	70.7
Irregular	0	0.1	2	0.1
Lact. Ammenor.	30.1	28.3	845	29.2

Health characteristics

Table 5 shows age distribution, marriage duration and health status of the women of both the cohorts, each partitioned into GD and No GD subgroups. Regardless of GD status, the majority of the women in the two groups (ligated cohort and control cohort) were over 30 yrs of age (premenopausal range) and married for over 10 yrs. In the control cohort , a greater percentage of women in both subgroups (GD, No GD) had a parity of < 5 (>70%) compared to the ligated cohort (lesser pregnancy burden). In both subgroups of the ligated cohort, parity of < 5 or > 5 was in a ratio of nearly 50:50. There were no marked between group or within group differences in respect to abortion rate. The majority of women in both subgroups of the two cohorts did not experience abortion (67-75%). In both the cohorts, a markedly high percentage of women were not using contraceptives. However, a noticeably higher percentage of control cohort with GD were on contraceptives. Both cohorts had previously experienced surgery other than ligation surgery. In the ligated cohort, the percentage of women exposed to such surgery was much lower in both subgroups (GD, No GD) compared to the control cohort subgroups. In the control chorot, a higher percentage of women with GD experienced such surgery as opposed to the No GD subgroup (51 vs 33%). Such a trend was evident in the ligated cohort too (21.8 vs 15.9%). The majority of women (over 78%) in the two subgroups of the ligated cohort had no surgical history of this kind. The majority of women in the No GD subgroup of the ligated cohort and in both subgroups of the control cohort were free of health problems (Table 5).However, the GD women in both the ligated and control cohort had substantially greater incidence of health problems (40% and 17.2% respectively) than the No GD subgroup. It should also be noted that the collective percentage of women with health problems was greater in the ligated than in the control cohorts. A much greater percentage of the ligated cohort, regardless of GD history, experienced interval sterilization, laparoscopic surgery, were above 30 yrs of age and had undergone ligation surgery for longer than a year (Table 6).

The ligated cohort was found to be at 2-fold greater risk for developing GD as compared to the control cohort. (RR = 2.46, CI 95%, P < 0.0001, Table 7). Also, when this analysis was performed, combining it with MH x^2 Summary, to control for confounders (age, contraception, parity, abortions, health), the relative risk for GD in ligated cohort held (Table 8).

Table 4. CBS-1. Baseline statistics of total sample of women (N=954). Data (mean ± SD) based on information collected at the Community Health House (hospital-free environment) as part of the study on postligation health and gynecological status. Ligated Cohort (ligated) and Control Cohort (nonligated) are dichotomized as GD and No GD subgroups.

Parameters	Ligated Cohort (447)		Control Cohort (507)	
	GD (165, 37%)	No GD (282, 63%)	GD (76, 15%)	No GD (431, 85%)
Age (yr)	38.6±6.0	39.0±6.4	40.1±7.6	37.7±9.8
Time Since Married (yr)	18.5±6.2	19.2± 6.8	19.2±9.0	7.2±9.6
Time Since Ligation (yr)	4.1±4.5	2.5±4.2	-	-
Time Since GD (yr)	2.7±2.7	-	3.7±4.4	-
Conception (No.)	6.4±1.9	6.0±1.9	4.8±2.4	4.8±2.4
LCB (yr)	7.3±4.2	9.1±23.9	9.2±6.8	7.2±6.6
Abortion (No.)	0.4±0.9	0.3±0.7	0.4±0.8	0.5±0.9

Table 5. CBS-1. Baseline statistics of total sample of women (N=954). Data based on information collected at the Community Health House as part of the study on post ligation health and gynecological status. For other details see Table 4.

Parameters	Ligated cohort (447)				Control cohort (507)			
	GD (165)		No GD (282)		GD (76)		No GD (431)	
	No	%	No	%	No	%	No	%
*Age at Interview								
<30 y	18	10.90	34	12.0	14	18.4	122	28.3
>30 y	147	89.9	348	87.9	62	81.5	309	71.7
Time Since Married								
<10 y	16	9.6	25	8.9	16	21.1	120	27.4
>10 y	149	90.3	257	91.1	60	78.9	311	72.6
Parity								
<5	83	50.4	143	51.8	54	71.1	329	76.3
>5	82	49.6	139	49.2	22	28.9	102	23.7
Abortions								
Nil	123	74.5	213	75.5	56	73.6	291	67.5
Yes	42	25.5	69	24.5	20	26.4	140	32.5
LCB:								
<1yr	7	4.3	14	4.9	8	10.5	81	18.7
>1 yr	158	95.7	268	95.1	68	89.5	350	81.3
Contraceptive Use:								
No	135	81.8	233	82.6	46	60.5	347	80.5
Yes	30	18.2	49	17.4	30	39.5	84	19.6
Surgery History:								
Yes	36	21.8	45	15.9	39	51.4	143	33.2
No	129	78.2	237	84.1	37	48.6	288	66.8
*Health Problem:								
Yes	66	40.0	79	28.1	13	17.2	37	8.6
No	99	60.0	203	71.9	63	82.8	394	91.4

*post ligation

Table 6. CBS-1. Baseline particulars of the Ligated cohort only on the basis of gynecological status arranged as a dichotomous variable.

Parameter	GD (165)		No GD (282)	
	No	%	No	%
Sterilization Method				
Minilap	61	36.9	111	39.3
Laparoscopy	104	63.0	171	60.3
Timing of Ligation:				
Postpartum	31	18.7	48	16.3
Int. Steril.	134	81.2	236	83.6
Age at Ligation:				
< 30	59	29.9	97	34.3
> 30	106	64.2	185	65.6
Time Since Ligation				
<1y	16	9.69	37	13.1
>1y	149	90.3	245	86.8

Table7. CBS-1. Relative Risk (RR) analysis using binary table to show the risk for ligated cohort to develop gynecological disorders (GD).

Surgical status	Gynecological status			
	GD	NO GD	Total No	RR (95%CI)
Ligated	165	282	447	
Non-Ligated	76	431	507	2.46* (1.94 - 3.13)

*P =<0.0001

Table 8. CBS–1. Relative Risk of gynecoloical diorder (GD) in ligated and nonligated cohort and Mantel-Henszel X^2 analysis of probable confounders.

Surgery	GD	No GD	RR (95%CI)	GD	No GD	RR (95%CI)	MH X^2 Summ
			Age Class				
	<30yr			>30yr			
Ligated	18	34	3.36** (1.81 – 6.26)	147	248	2.23** (1.72 – 2.89)	2.3 (1.85 – 2.99)
Non ligated	14	122		62	309		
			Contraception				
	Yes			No			
Ligated	30	49	1.82* (1.19 – 2.79)	135	233	3.13** (2.32 – 4.24)	2.71 (2.12 – 3.47)
Non ligated	30	114		46	347		
			Parity				
	<5			>5			
Ligated	83	43	4.60** (3.49 – 6.06)	82	39	3.97** (2.64 – 5.97)	4.33 (3.42 – 5.46)
Non ligated	55	329		21	102		
			Abortions				
	Yes			No			
Ligated	42	69	3.03** (1.88 – 4.86)	123	213	2.27** (1.72 – 3.00)	2.44 (1.92 – 3.10)
Non ligated	20	140		56	291		
			Health Problems				
	Yes			No			
Ligated	66	79	1.75* (1.06-2.89)	99	203	2.38** (1.80 – 3.15)	2.20 (1.73 – 2.81)
Non ligated	13	37		63	394		

*P=<0.05 **P=<0.001

CBS-2 (follow up group)

Baseline data

Only 111 of the 300 women originally registered for follow up and ranging in age between 26-41 yrs reported for interview Table (9). The majority of the respondents were from urban communities. Most of them belonged to the lower socioeconomic stratum as inferred from literacy level (most being illiterate) and occupational status of the families (Table 9). Only 20% of the women had one or more abortion. Most women who had ligation belonged in the age range of 30-35 yrs (52.5%) and the percentage of women with ligation time of less than 5 yrs was slightly greater than the percentage of those who had it for over 5 yrs (Table 9).

Table 9. CBS-2. Baseline characteristics of women reporting for follow up (N=111). Age: 26- 41 yrs.

Parameter	No.	Percentage
Residential Status:		
Urban	58	52.2
Rural	53	47.7
Occupation:		
Non Working	104	93.6
Working	007	06.3
Education:		
Illiterate	93	83.7
Primary	11	09.9
Middle	01	00.9
High School	06	05.4
Abortions		
0	89	80.0
≥ 1	22	20.0
Age at Ligation		
<30 yr	35	31.5
30-35 yr	58	52.5
>35 yr	18	16.2
Time Since Ligation		
<5 yr	59	53.1
>5 yr	52	46.8

The majority of follow up women had undergone interval sterilization by laparoscopic procedure in nearly all cases (95.44%, Table 10). Over 87% respondents had no prior health problems at the time of ligation but after ligation the percentage of healthy women decreased to about 49%. Body ache, weakness and weight gain were the outstanding new complaints. Gynecological disorders were reported by 38.73% women (Table 10), thus registering a marked increase over their baseline status (0.2% preligation, Table 3).

Table 10. CBS-2. Postligation study in relation to health and gynecological disorders. Effect of ligation on health and gynecology of the ligated follow up women (age: 32.93 ± 3.51, range 26-41 yr). See Table 4 for baseline data.

Parameter	No.	Percentage
Method of Ligation:		
Minilap	5	4.5
Laparoscopy	106	95.49
Health before Ligation:		
No problem	97	87.3
Hernia	6	5.4
Diabetes	1	0.9
Hypertension	2	1.8
Jaundice	1	0.9
Abdominal	4	3.6
Body Ache	0	0
Weakness	0	0
Thyroid	0	0
Health Postligation:		
No problem	54	48.64
Hernia	0	0
Diabetes	3	2.7
Hypertension	3	2.7
Jaundice	1	0.9
Thyroid	5	4.5
Abdominal	0	0
Body Ache	20	16.01
Weakness	16	14.41
Weight Gain	9	8.10
Gynecological Disorders:		
No	68	61.26
Yes	43	38.73

Table 11. CBS-2. Baseline data of ligated follow up women after partitioning on the basis of gynecological condition (GD, No GD groups).

Parameter	GD (43)	No GD (68)
	Mean ± SD (Range)	Mean ± SD (Range)
Age at Ligation: (Yr)	33.17 ± 3.18 (26 – 41)	32.55 ± 3.98 (26 – 40)
Conception: (No)	6.17± 1.79 (3 – 11)	5.86 ± 01.4 (04 –10)
Time Since Ligation: (Yr)	4.79 ± 1.27 (2 – 7)	4.88 ± 1.15 (2.9 – 5.4)

When the follow up group was partitioned retrospectively into GD and No GD groups, only negligible differences were detectable in respect to conceptions prior to ligation as well as age at ligation and time since ligation (Table 11). Of the 111 women, the percentage of GD women younger than 30 yrs and between 30-35 yrs were nearly equal (~39 and ~42%), with women over 35 yrs of age constituting a very low percentage (Table 12).

The GD group reported slightly higher percentage of urban than rural women (58% vs 42%)(Table 13). As stated earlier and also shown in Table 13, the women with or without GD belonged to low socioeconomic status (see literacy level and occupation of families). The percentage of non-working women was higher in both groups compared to the working women (Table 13), indicating a less strenuous life style. The majority of the women in both groups underwent laparoscopic surgery (Table 13). No marked differences between GD and No GD classes were noticeable in respect to the above parameter. The percentage of women with GD free of postligation health problems was far less compared to the percentage of women without GD (Table 14). The health problems in women with GD included especially body ache, weakness and weight gain (Table 14). Of the various gynecological disorders, 72% of the GD women had menstrual complications (Table 14).

Table12. CBS-2. Distribution of follow up women into GD and No GD categories according to age.

Age Class	GD		No GD	
	Total No	Percentage	Total No	Percentage
<30yr	17	39.5	18	26.5
30 – 35	18	41.8	40	58.8
>35yr	08	18.6	10	14.7

Table 13. CBS-2. Baseline characteristics of the ligated follow up group classified retrospectively according to postligation status of gynecological disorders. See Table 4 for baseline data of the total sample.

Parameter	GD		No GD	
	Total No	Percentage	Total No	Percentage
Residential Status:				
Urban	25	58.2	33	48.5
Rural	18	41.8	35	51.5
Occupation (husband):				
Unskilled	24	55.8	22	32.3
Skilled	14	32.6	31	45.5
Govt. Servant/Office Work	05	11.6	15	22.2
Occupation (wife):				
Non working	40	93.1	64	95.6
Working	03	06.9	04	04.4
Education (husband):				
Illiterate	24	55.8	15	23.0
Primary	09	20.9	12	17.5
Middle	04	09.4	14	20.5
High School	06	13.9	27	39.0
Education (wife):				
Illiterate	39	90.7	54	79.5
Primary	03	06.9	08	11.7
High School	01	02.4	06	08.8
Ligation history:				
Minilap	01	02.4	04	05.8
Laparoscopy	42	97.6	64	94.2

Table 14. CBS-2. Health and reproductive status reported by the ligated follow up group, beginning with 2 years after ligation (see Table 11 for baseline data).

Parameters	GD		No GD	
	No	Percentage	No	Percentage
Health Problem				
None	16	34.88	40	57.35
Weight Gain	05	11.62	04	05.88
Diabetes	01	02.32	03	04.41
Body Ache	11	25.57	02	02.94
Weakness	07	16.27	10	14.70
Thyroid	03	06.97	09	13.23
Gynecological Disorders:				
Menstrual Disorder	31	72.10		
Others	12	27.90	-	-

Relative Risk analysis

Descriptive data of ligated cohort and the control (non ligated) cohort are shown in Table 15.Comparison of relative risk of GD for both the cohorts was 1.97 (Table 16, 95 % confidence limit, p <001). This association between ligation and GD persisted even after adjustment for confounders. (Table 17).

Table 15. CBS-2. Community based retrospective cohort study. Baseline statistics (mean ± SD) of ligated cohort and control partitioned by gynecological status

Parameters	Ligated (111)		Control (310)	
	GD (43)	No GD (68)	GD (61)	No GD (249)
Age (yr)	37.41± 4.28	38.15± 3.48	37.32±5.31	35.95±5.96
Time since Married (yr)	13.95±4.24	15.42±3.60	16.54±6.26	15.24±7.28
Conception (No.)	5.86±1.41	6.18±1.80	4.92±2.36	4.42±2.04
LCB (yr)	6.39±2.58	6.2±2.17	6.66±5.49	5.90±4.85

Table 16. CBS-2. Relative Risk of gynecological disorder for the ligated cohort and the control.

	GD	No GD	RR (95%CI)
Ligated Cohort (111)	43	68	
			1.97*
Control Cohort (310)	61	249	(1.42 – 2.72)

*P= < .0001

3. Hospital-based analyses of postligation complication

HBS-1

Demographic characteristics

This hospital-based case-control study attempted to resolve possible association between sterilization and gynecological disorders. It involved a total of 1366 women. Of these, 684 constituted cases comprising women reporting to the hospital for GD complications and 682 controls visiting the hospital for other complaints and included only women free of GD. Baseline statistics of the two groups are shown in Table 18.

It was found that women in both groups (cases and control) had undergone ligation. It turned out that slightly less than three times as many cases (219) as the controls (88) were ligated (Table 18). The ligated and non-ligated subgroups of the cases as well as the ligated subgroup of the controls had women of statistically comparable average age, marriage duration, and conception. The nonligated subgroup of the control was relatively younger. A history of somewhat lower marriage duration, conception rate and lower last childbirth age was reported by the non-ligated controls compared to all other subgroups. The onset of GD in both subgroups of the cases was recent relative to time since ligation (a gap of ~ 6yrs). This taken together with the perimenopausal average age of the cases constitutes a noteworthy feature of the results.

Tables 19 shows family planning, health and gynecological history of the cases (GD) and the controls (No GD) after partitioning the cases and the control groups into ligated and nonligated subgroups. The ratio of ligated : nonligated subjects in cases group was approximately 1 : 2, whereas this ratio for control subjects was about 1 : 7.

Table 17. CBS-2.Relative Risk of ligated cohort and control (non ligated) , to have gynecological disorder (GD) when adjusted for probable confounders.

Surgery	GD	NO GD	OR	GD	NO GD	OR	MH X^2 Summ
			Age Class				
	<35yr			>35yr			
Ligated	16	14	3.22**	27	54	1.39*	1.87
Non Ligated	30	151	(2.02 – 5.142.95)	31	98	(0.90 –2.24)	(1.36-2.57)
			Health History				
	No			Yes			
Ligated	16	39	1.65**	27	29	1.85	1.70*
Non Ligated	48	224	(1.01 – 2.68)	13	25	(0.85-3.99)	(1.13 – 2.57)
			Contraception				
	No			Yes			
Ligated	28	43	2.59**	15	25	1.25	1.91
Non Ligated	33	184	(1.69 – 3.97)	28	65	(0.75-2.07)	(1.38 – 2.63)
			Parity				
	<5			>5			
Ligated	21	30	2.35**	22	38	1.32	1.80
Non Ligated	43	202	(1.53 – 3.59)	18	47	(0.79 – 2.22)	(1.29 – 2.49)
			Abortion				
	Nil			Yes			
Ligated	36	53	1.96**	7	16	1.85	1.9426**
Non Ligated	45	173	(1.36 – 2.82)	15	76	(0.85 – 3.99)	(1.40 – 2.09)

*P=>0.05 **P=<0.001

Table 18. HBS-1. Hospital-based study for analysis of post ligation complications. Baseline statistics (mean ± SD) of cases (GD group) and controls (No GD) partitioned by ligation status

Parameters	Cases (684)		Control (682)	
	Ligated (219)	Non Ligated (465)	Ligated (88)	Non Ligated (652)
Age (yr)	41.9±6.9	40.8±8.7	40.94±7.7	37.9±9.9
Time since Married (yr)	21.9±6.7	20.95±8.6	22.4±7.9	17.38±9.7
Conception (No.)	6.38±2.2	5.32±2.5	6.30±2.1	4.77±2.2
LCB (yr)	10.14±4.7	9.6±6.3	9.5±5.7	7.40±6.7
Abortion (No)	0.58+1.15	0.72+1.0	0.48 ± 0.8	0.54±0.84
Time Since Ligation (yr)	8.6+4.5	-	8.1+6.0	-
Time Since GD (yr)	2.7±2.7	2.1±2.56	-	-

Table 19. HBS-1. Hospital-based study for analysis of post ligation complications. Baseline family planning and health statistics of cases(GD group) and controls (No GD group) on the basis of ligation status

Parameter	Cases (684)		Control (682)	
	LIGATED(219) %(No)	NONLIGATED(465) %(No)	LIGATED(88) %(No)	NONLIGATED(594) %(No)
Contraception				
Yes	2.7(6)	5.3(26)	6.8(8)	21.5(128)
No	97.3(213)	94.4(439)	93.2(82)	78.5(466)
Abortions				
Yes	29.2(64)	43.7(203)	31.2(33)	32.8(195)
No	70.8(155)	56.3(262)	68.9(73)	67.2(399)
Non lig. Surgery				
Yes	16.4(36)	18.3(85)	24.8(28)	29.3(174)
No	83.6(183)	81.7(380)	73.6(78)	70.7(420)
Health Problems				
Yes	13.7(30)	11.4(53)	10.3(9)	7.28(43)
No	86.3(189)	88.0(412)	89.7(79)	92.8(551
Hemoglobin (g/dl)				
> 12	41.1(90)	44.3(208)	-	-
< 12	58.4(128)	55.2(259)	-	-
Bld. Sugar (mg/lit)				
>200	25.1 (55)	43.9(206)	-	-
<200	74.91(164)	73.1(34)	-	-

Table 20. HBS-1. Hospital based study for analysis postligation complications. Nature and frequency of gynecological disorders of cases (GD) and relationship with ligation status

Gynecological Disorder	Cases (688)			
	Ligated		Non Ligated	
	No	%	No	%
None	-	-	-	-
Menstrual	178	81.3	375	80.6
PMB	3	1.4	19	4.1
PID	4	1.8	6	1.1
UVP	34	15.5	61	12.9
Sec Infertility	-	-	5	1.0

The relationship of gynecological status at ligation with age (cases/controls combined) is shown in Table 21. A noticeably greater percentage of < 30 yr women belonged in the GD group than in the No GD group (34.71% vs 28.41%). On the other hand, a slightly greater percentage (39.8%) of women between 30-35 years were in the No GD group. The overall proportion of women of 35 yrs or under in the GD group was greater than that of the older women (perimenopausal).

In order to determine the association of ligation with GD in the cases, odds ratio (OR) was calculated by placing the cases and the controls in a binary table (Table 22). Ligation and GD showed a positive association as revealed by an OR of > 1.0 (2.39 and 4.23,CI 95%, P < 0.0001). When the effect of confounders such as age, parity, abortions, preexisting gynecological status, health condition, ligation time, ligation procedure, postligation time and age of last childbirth were adjusted in binary variables, the association held (sterilization : GD, >1.0 OR regardless of confounders). The association held even when Mantel-Henszel summary quation was applied. When parity was controlled, a decrease in OR was evident but it non the less, maintained the association. The analyses indicates cause and effect relationship between sterilization and GD (Table 23).

Table 21. HBS-1. Hospital-based study of analysis of postligation complications. Association of gynecological disorders in ligated (N=307) women with age at ligation (cases and control combined).

Age Class	Ligated Women (Cases/Control)			
	GD (219)		No GD (88)	
	Total No	%age	Total No	%age
<30 yr	76	34.7	25	28.4
30 – 35 yr	75	34.2	35	39.8
36 – 40 yr	46	21.0	18	20.5
>40 yr	22	10.0	10	11.4

Table 22. HBS-1. Hospital-based Case- control analysis of postligation complications showing Odds Ratio (OR) for association between ligation and gynecological disorders.

	GD	NO GD	OR (95%CI)
Ligated (307)	219	88	3.18*
Non ligated (1059)	465	594	(2.39 – 4.23)

*P= < .0001

Table 23. HBS-1.Hospital- based study for analysis of postligation complications showing Odds Ratio (OR) for association between ligation and gynecological disorders and effect of confounding factors

Surgery	GD	NO GD	OR	GD	NO GD	OR	MH X^2 Summ
			Age Class				
	>35yr			<35yr			
Ligated	175	66	2.11**	44	22	5.7**	2.63**
Non Ligated	340	271	(1.51 – 2.95)	125	323	(1.91 –3.00)	(2.02 – 3.63)
			Health History				
	No			Yes			
Ligated	30	9	2.70*	189	79	3.20**	3.14**
Non Ligated	53	43	(1.08 – 6.90)	412	551	(2.37-4.33)	(2.36 – 4.19)
			Conception				
	<5			>5			
Ligated	108	55	2.7**	88	34	2.87**	2.77**
Non Ligated	209	219	(1.83 – 3.98)	320	355	(1.84 – 4.49)	(2.68 – 3.70)
			Parity				
	<5			>5			
Ligated	122	41	3.28**	120	42	2.2**	2.75**
Non Ligated	391	431	(2.21 – 4.88)	169	130	(1.42 – 3.40)	(2.06 – 3.68)
			LCB				
	<5yr			>5yr			
Ligated	47	27	1.89*	195	56	2.43**	2.26**
Non Ligated	181	196	(1.09 – 3.26)	379	265	(1.72 – 3.46)	(1.69 – 3.02)

Contd.

Abortion							
	Yes			**No**			
Ligated	76	21	1.35*	166	62	3.15**	2.55**
Non Ligated	166	62	(0.74 – 2.47)	323	380	(2.24 – 4.43)	(1.94 – 3.49)
Contraception							
	Yes			**No**			
Ligated	8	6	2.6*	234	77	2.7**	2.69**
Non Ligated	60	117	(0.77 – 8.98)	500	444	(2 – 3.66)	(2.02 – 3.59)
Other Surgery							
	Yes			**No**			
Ligated	43	21	2.47*	199	62	3.01**	2.88**
Non Ligated	132	159	(1.35 – 4.54)	428	402	(2.17 – 4.19)	(2.16 – 3.83)

*P=>0.05
**P=<0.001

Table 24 shows the menstrual history of the cases (GD) and the controls (No GD). Over 97% of both the cases and the controls reported regular cycle in the past. The extremely low level of irregularity was similar in the two groups. The most recent cycle was irregular in a significantly higher percentage (over 87%) of cases than in the controls (about 1.3%). Even when menopausal stage was included as a normal/regular process, then the percentage of cases with regular cycle increased to at most 13% as opposed to 92% for the controls. Thus considerable disturbance of the menstrual cycle became evident in the cases group. The duration of the cycle was also disturbed in the majority of the cases (Table 24). Short cycle was reported by a much higher percentage of the cases (53%) compared to the controls (2.6%). Both groups suffered from long cycle but the percentage of such women was very low (1.5-4%). Menstrual flow too was drastically disturbed in the cases with 63% showing heavy flow as opposed to 68% of the controls with normal flow. The shortness of the cycle in the cases group is thus understandable in view of the heavy flow reported by the women (Table 24).

Table 24. HBS-1. Hospital based study for analysis of post ligation complications showing status and duration of menstrual cycle as well as level of menstrual flow in case and control groups.

Parameter	Cases		Control	
	No	%	No	%
Menstrual Status:				
Past:				
Regular	668	97.7	672	98.4
Irregular	16	2.3	10	1.5
Amenorrhea	-	-	-	-
Menopause	-	-	-	-
Recent:				
Regular	58	8.50	516	75.7
Irregular	595	87.0	9	1.3
Amenorrhea	-	-	45	6.7
Menopause	31	4.50	111	16.3
Menstrual Duration:				
No menses	31	5.0	156	22.9
Short	365	53.2	18	2.6
Average	251	36.7	498	73.0
Long	35	5.0	10	1.5
Menstrual Flow:				
No menses	31	4.2	156	22.9
Scanty	44	6.4	34	5.1
Average	177	25.9	467	68.3
Heavy	432	63.2	26	3.8

In order to determine whether there is any effect of advancing age on association between ligation and menstrual cycle, OR was calculated on the basis of age classes (Table 25). Since the OR remained significantly high as age increased to level 2 (i.e. 35 years), ligation had a positive association with the irregular menstrual cycle. Significant association did not hold for age classes above 35 years (OR = 1.07 95% CI. 0.64-1.80, p > 0.05).

Table 25. HBS-1. Hospital-based study for analysis of post ligation complications. Odds ratio (OR) showing association of menstrual status with ligation status according to age class of Cases and Control groups combined.

Age class	Ligation Status	Menstrual Status		Total	OR (95%CI)
		Irregular	Regular		
< 30 yr	Yes	13	12	25	3.53** (1.41-8.84)
	No	55	177	232	
30 – 35 yr	Yes	27	14	41	5.25**(2.45-11.40)
	No	58	158	216	
36 – 40 yr	Yes	54	37	91	1.07*(0.64-1.80)
	No	140	104	243	
> 40 yr	Yes	99	51	150	2.58**(1.70-3.91)
	No	158	210	368	

*P >0.05
**P<0.001

For resolving the status of uterine pathology in relation to ligation practice, the ultrasonography data available for the cases were analyzed (Table 26) for different age classes of ligated (N=198) and non-ligated (N=422) women. The proportion of women with and without the pathology was almost 50:50 in the ligated subgroup. It was slightly greater in the nonligated group. The abnormality generally increased with increasing age of women in both groups.

Table 26. HBS-1. Hospital-based study for analysis of post ligation complications. Status of uterus on the basis of ultrasonography (USG) in ligated and nonligated groups (cases) and relationship with age

Ligation Status	Uterine Status	Total		Age Class (yrs)			
				20 – 30	31 – 35	36 – 40	>40
Ligated (198)	Normal	No	99	11.0	9.0	26.0	53.0
		%	50.0	11.1	9.0	26.2	53.5
	Enlarged	No	16	-	3.0	4.0	9.0
		%	8.0	-	18.7	25.0	56.2
	Fibroid	No	83	2.0	16.0	25.0	40.0
		%	42.0	2.4	19.2	30.1	48.1
Non ligated (422)	Normal	No	169	20.0	21.0	56.0	72.0
		%	40.1	11.8	12.4	33.1	42.6
	Enlarged	No	42.0	6.0	7.0	15.0	14.0
		%	9.9	14.2	16.6	35.7	33.3
	Fibroid	No	211	25.0	29.0	63.0	94.0
		%	50.0	11.8	13.7	29.8	44.5

Histological Studies

Histological assessment of changes in the uterus of ligated N= 88) and nonligated (N= 145) cases (GD proup)was carried out and is reflected in (Table 27). Normal histology was characterized by proliferative and secretory endometrium (Fig. 1a,b), whereas abnormal pathology was evident in the form of adenomyosis, endometrial hyperplasia (Fig. 2c,d) and leiomyoma. The most dominant of these was adenomyosis in both the ligated and nonligated cases. When leiomyoma and adenomyosis were considered together, a greater percentage of ligated cases turned out to show abnormal uterine status. Hyperplasia was evident in both cases subgroups but again a greater percentage of the ligated cases exhibited such a change whereas a higher percentage of malignancy was recorded in the nonligated women (Fig. 3a,b).

The frequency of hysterectomy as a management recourse increased with age in both groups (Table 28). The differences between ligated and nonligated women at various age levels were negligible. A marginally greater percentage (32%) of nonligated women of age 36-40 yrs needed hysterectomy, while this situation reversed at age >40 yrs (59:55%, ligated: non ligated).

The main gynecological problem in both groups of hysterectomized cases (Table 29) was menstrual disorder (>75% cases) followed by UV

prolapse (over 17% cases). Calculation of OR revealed a positive association between ligation and hysterectomy (OR = 1.77, CL 95%, P< 0.001, (Table 30).

Table 27. HBS-1.Hospital based study for analysis of post-ligation complications. Uterine histopathological findings in ligated and nonligated groups.

Histopathology	Ligated		Nonligated	
	No	%	No	%
Proliferation Phase	5	5.68	18	12.41
Secretory Phase	10	11.36	19	13.10
Hyperplasia	10	11.36	10	6.89
Malignancy	2	2.27	12	8.27
Adenomyosis	23	26.13	29	20
Leiomoyma	17	19.31	30	20.68
Adenomyosis&Leimyoma	11	10.22	7	4.82
Cervical Pathology	11	12.5	15	10.34

HBS-2

Table 31 shows characteristics of women who had sterilization surgery (ligated cohort) and those who had experienced only non-sterilization abdominal surgery (control cohort). About twice as many non-sterilized control cohort as the ligated cohort were under 30 years of age. Although the percentage of the ligated cohort with GD was slightly less than that of the No GD ligated cohort, the incidence of GD in the ligated cohort was 2- fold greater (42% vs 20% respectively) compared to the control cohort (abdominal surgery). In the latter cohort, over 79% women had no GD. Menstrual irregularity was low in both cohorts but was 2-fold greater in the ligated than in the control cohort. The data on GD and menstrual irregularity thus show a positive association of sterilization surgery with postligation gynecological disorders.

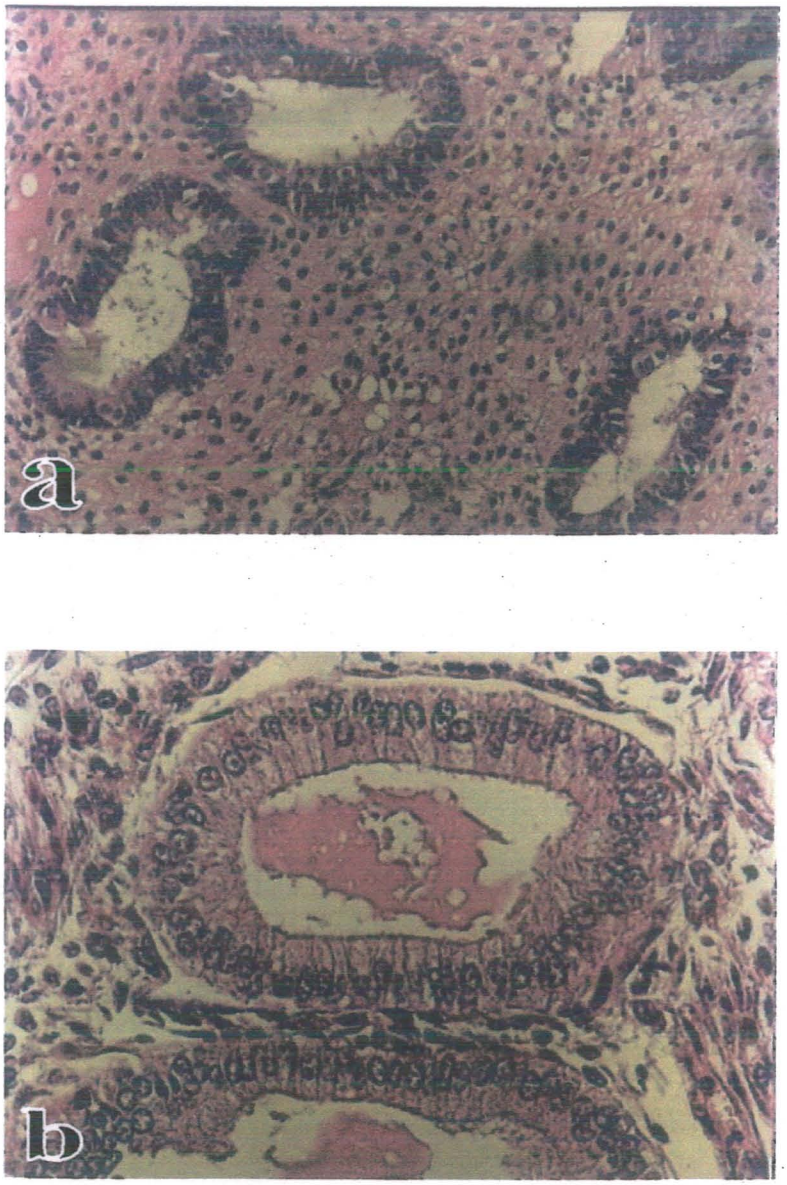
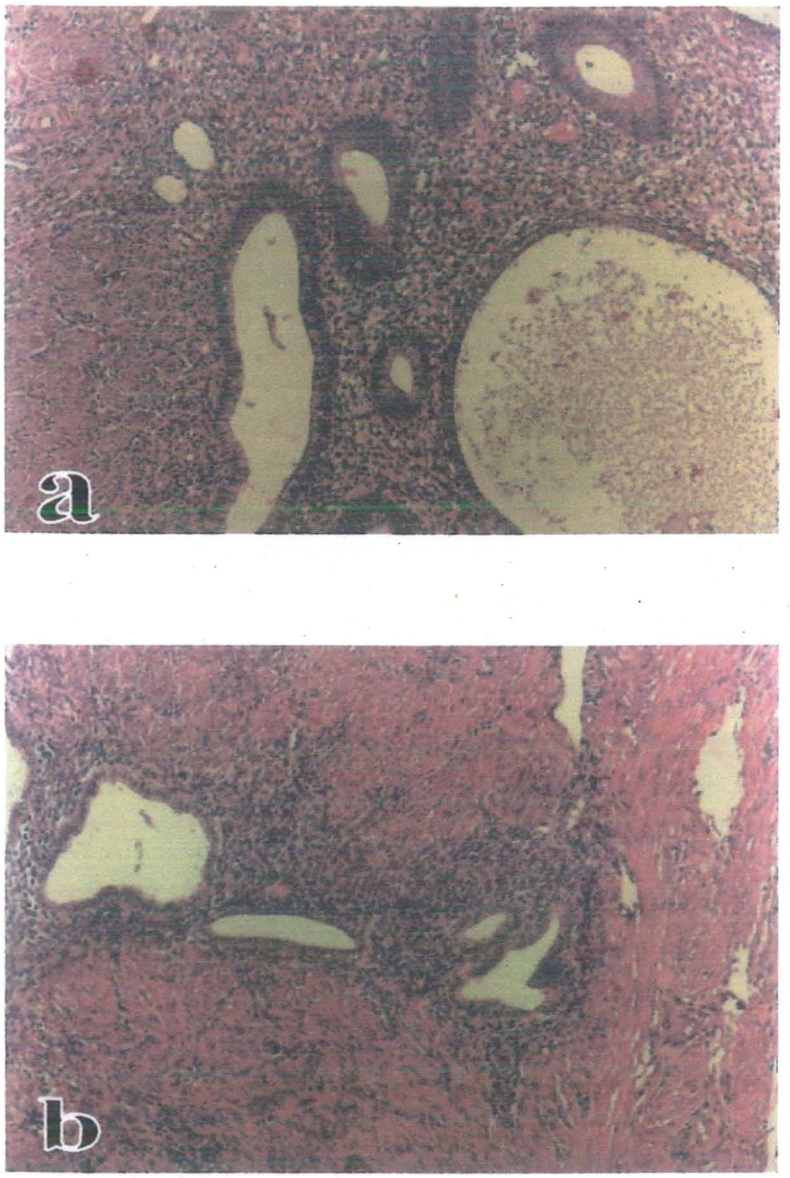
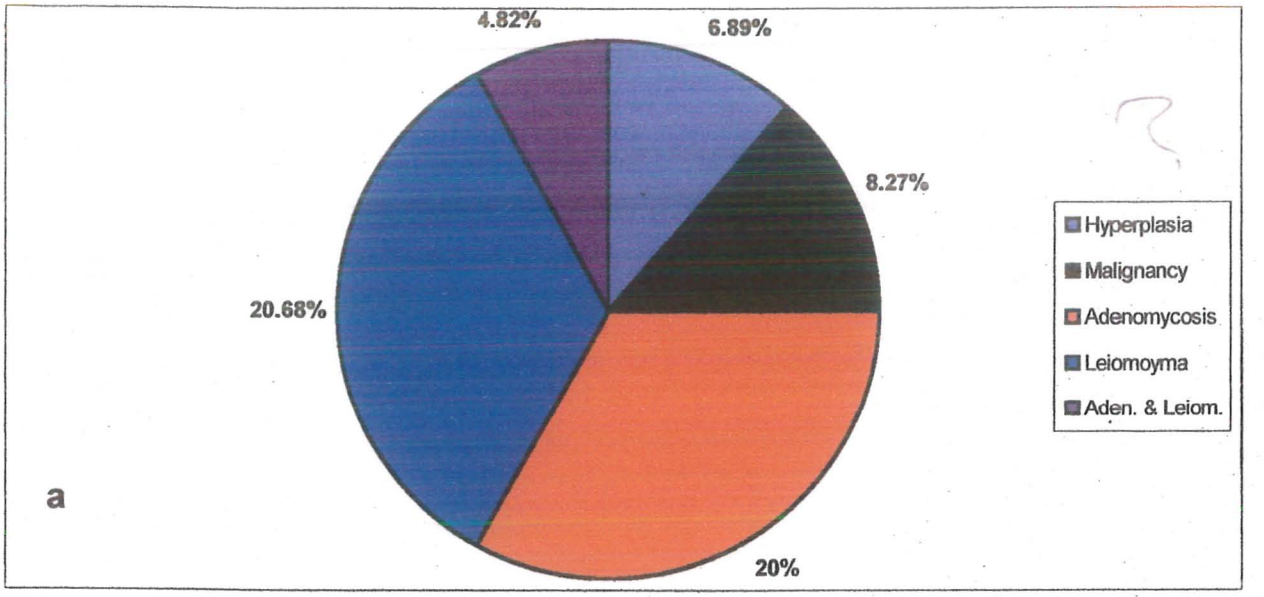


Fig. 1a-b. Uterine endometrium (a) endometrial glands in mid proliferative phase. H & E.. x 528, (b) late secretory phase. H & E. x 1320



'ig. 2a-b Uterine endometrium (a) endometrial hyperplasia is evident in the troma and glands are dilated. H & E x 132 (b) Note adenomyosis, indicated y the invasion of myometrium by endometrial tissue. H & E. x 53.



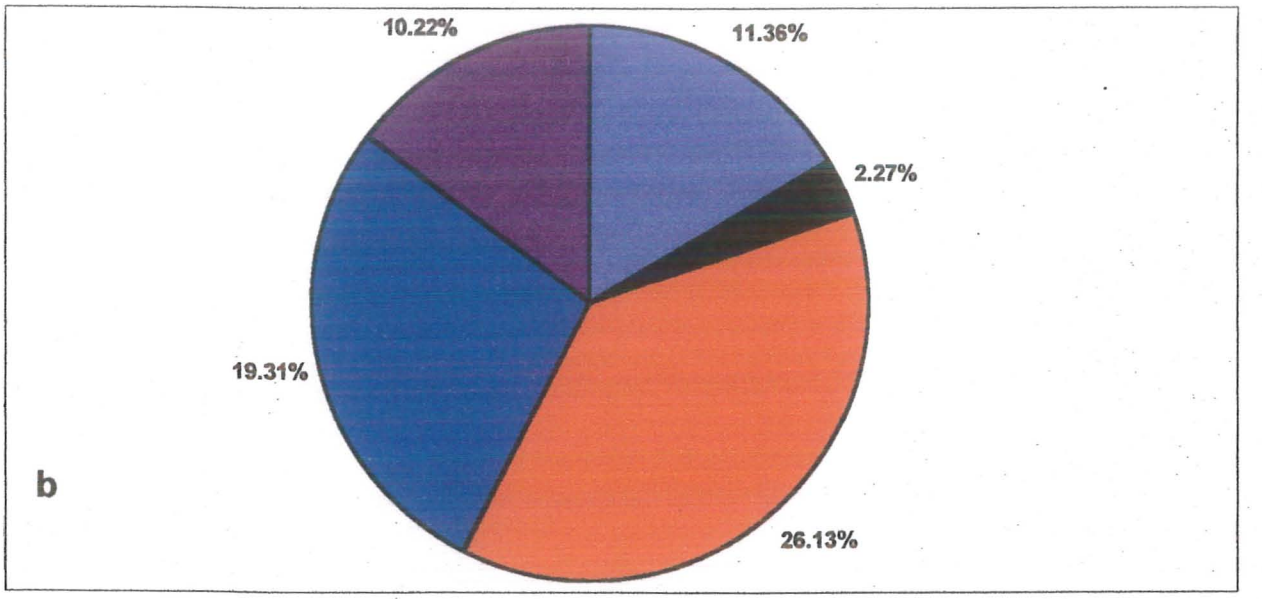


Fig. 3 a, b. Hospital based study for analysis of postligation syndrome. a. Uterine histopathological findings in nonligated group. b. Uterine histopathological findings in ligated group.

Table 28. HBS-1. Hospital based study for analysis of postligation complications. Frequency of hysterectomy in the ligated and nonligated cases (GD group) and association with age.

	Age Class (yrs)				
Group	20-30	31-35	36-40	>40	Total
Ligated	3	14	35	74	126
(%)	(2.3)	(11.1)	(27.7)	(58.7)	(100)
Non ligated	6	22	69	119	216
(%)	(2.7)	(10.1)	(31.9)	(55.0)	(100)

Table 29. HBS-1. Hospital-based study for analysis of postligation complications. Frequency of GD and type of disorder in hysterectomized women.

Group	Menstrual	PMB	UVP	PID	Total
Ligated	100	2	22	2	126
(%)	(79.0)	(2.0)	(17.4)	(2.0)	(100)
Non ligated	163	11	38	1	216
(%)	(75.4)	(5.09)	(17.5)	(2.16)	(100)
Total	263	13	60	3	342
(%)	(76.0)	(3.8)	(17.5)	(1.26)	(100)

Table 30. HBS-1. Hospital-based study for analysis of postligation complications. Odds ratio (OR) showing association between ligation and rate of hysterectomy in the cases group. Referent = ligated; H = hysterectomy, NH = no hysterectomy.

Group	Cases		OR
	H	NH	(95% CI)
Ligated	126	116	
			1.77*
Non ligated	213	347	(1.29 -2.43)

*P=<.001

Table 31. HBS-2. Hospital based study for analysis of postligation complications. Gynecological characteristic of women (N=204) exposed to sterilization and abdominal surgery (N=281).

Parameter	Cases (Sterlization Surgery)		Control (Abdominal Surgery)	
	No	%	No	%
Age				
<30yr	25	12.3	71	25.3
>30 yr	176	87.7	210	74.7
Gynecological Disorder				
Yes	85	41.7	57	20.3
No	119	58.3	224	79.7
Menstrual Status				
Regular	157	77	223	79.2
Irregular	27	13.2	22	7.8
Amenorrhoea	20	8.8	36	12.8

Further analyses were carried out to delineate differences in characteristics of women on the basis of their GD status regardless of the type of surgery (sterilization or abdominal). Tables 32 lists the baseline demographic and reproductive characteristics in dichotomous variables of GD and No GD. The GD women were slightly more parous and had older LCB than the No GD women . Both groups (GD/No GD) were dominated by a greater percentage of women over 35 yrs of age (average age). The percentage of ligated women was greater than that of the nonligated women in the GD group. The ratio of minilap : laparascopy was nearly similar in the GD and No GD groups but the percentage of women experiencing minilap and laparoscopy as well as postpartum and interval sterilization was greater in the GD group than in the No GD group (Table 33). Most women in both groups underwent interval sterilization and the proportion of women experiencing postpartum and interval sterilization was substantially greater in the GD group. Most of the women in the two groups were over 30 yrs of age, with only a third of the women in both groups were < 30 yrs. Both groups were characterized by majority of women with low parity (<5) and LCB of >I yr. In both groups, the majority of the women were married for over 10 yrs, were not on contraception and had not experienced abortions. However, the GD group showed more women on contraception than the No GD group, while more abortions were experienced by the No GD group. The

fact that the GD group had more ligated women shows an association of ligation with GD but the use of contraceptives in this group is also noteworthy. The percentage of women ligated for over a year was high in both the GD and No GD groups. Menstrual irregularity was experienced by a noticeably high percentage of the GD women (83%), where ligation frequency was also high.

Table 32. HBS-2. Hospital based study for analysis of postligation complications. Baseline characteristics of total women (sterilized and abdominal surgery) according to gynecological status.

Parameter	GD Mean ± S.D. (Range)	No GD Mean ± S.D. (Range)
Age at interview (yr)	39.68±6.63 (24-58)	37.54±7.92 (24-65)
Parity (No)	5.15±1.98 (1-11)	4.16±1.98 (1-10)
LCB (yr)	8.78±5.31 (0.30 - 25)	7.04 ±6.04 (0.10 - 30)

Table 34 shows a risk ratio of sterilization surgery to non sterilization surgery (2.05 RR, CL 95%, P<0.0001). Various confounders had no effect on this risk ratio (high RR persisted in every case, even when Mantel-Hanszel summary was calculated), (Table 35).

Incidence of GD in the ligated and control cohorts different time postligation was also analysed in relation to time after surgery (Fig. 4). Its incidence was considerably greater in the ligated cohort than in the control cohort as time after surgery progressed. The difference at 2-3 yrs and 5+ yrs was statistically significant ($p<0.05$)

Table 33. HBS-2. Hospital-based study for analysis of postligation complications. Baseline particulars of the combined study population (sterilization/abdominal surgery groups) on the basis of gynecological status arranged as dichotomous variables.

Parameter	GD		No GD	
	No	%	No	%
Ligation Status:				
Ligated	85	59.9	119	34.7
Non Ligated (Abd. Surg. Gp.)	57	40.1	224	65.3
Sterilization Method:				
Minilap	39	45.9	54	45.4
Laparoscopy	46	54.1	65	56.6
Time of ligation:				
Postpartum	21	24.8	30	25.2
Int. sterilization.	64	75.2	89	74.8
Age at ligation:				
< 30	32	37.6	46	38.65
> 30	53	62.35	73	61.34
Married Since:				
< 10 y	19	13.4	58	16.9
> 10 y	123	86.6	285	83.1
Parity				
< 5	112	78.9	284	82.8
> 5	30	21.1	59	17.2
Abortions:				
Nil	108	76.1	215	62.7
Yes	34	23.9	128	37.3
LCB:				
< 1yr	5	3.5	47	13.7
> 1 yr	137	96.5	296	86.3
Contraceptive use:				
No	108	76.1	290	84.5
Yes	34	23.9	53	15.5
Time since ligated:				
< 1y	2	2.35	4	3.36
> 1y	83	97.84	115	96.63
Menstrual cycle:				
Regular	40	28.16	303	88.3
Irregular	89	82.67	3	0.87
Lactation Ammenorrhea	6	4.2	13	3.79
Menopause	7	4.92	24	6.99

Table 34. HBS-2. Hospital-based study of postligation complications. Risk of GD in ligated women (ligated cohort) relative to women experiencing abdominal surgery (control cohort).

Surgical Status	GD (142)	No GD (343)	RR (95%CI)
Ligated cohort	85	119	2.05* (1.55 – 2.73)
Control cohort	57	224	

*P = <0.0001

Table 35. HBS-2.Hospital based retrospective cohort study. Relative Risk (RR) of association between tubal ligation and postligation syndrome adjusted for probable confounders .

Surgery	GD	NO GD	RR	GD	NO GD	RR	MH X^2 Summ
Age Class							
	<30			**>30**			
Sterilization	11	14	3.47** (1.63 – 7.38)	74	105	1.81** (1.34 –2.45)	1.97** (1.49 –2.60)
Non Sterilization	9	62		48	162		
Contraception							
	Yes			**No**			
Sterilization	11	16	1.05 (0.60 –1.80)	74	103	2.72** (1.91 –3.87)	2.18** (1.62 –2.93)
Non Sterilization	23	36		34	187		
Parity							
	<5			**>5**			
Sterilization	60	91	1.87 (1.37 – 2.56)	25	28	3.40** (1.43 – 8.04)	2.07** (1.54 – 2.78)
Non Sterilization	52	193		5	31		
LCB							
	<1yr			**>1yr**			
Sterilization	4	9	3.74 (1.27-11.0)	81	110	1.66** (1.24-2.22)	1.74 (1.31-2.30)
Non Sterilization	7	78		50	146		
Abortion							
	Yes			**No**			
Sterilization	17	31	2.38* (1.33 – 4.25)	68	88	1.82** (1.32 – 2.52)	1.93** (1.46 – 2.57)
Non Sterilization	17	97		40	127		

*P=>0.05 **P=<0.001

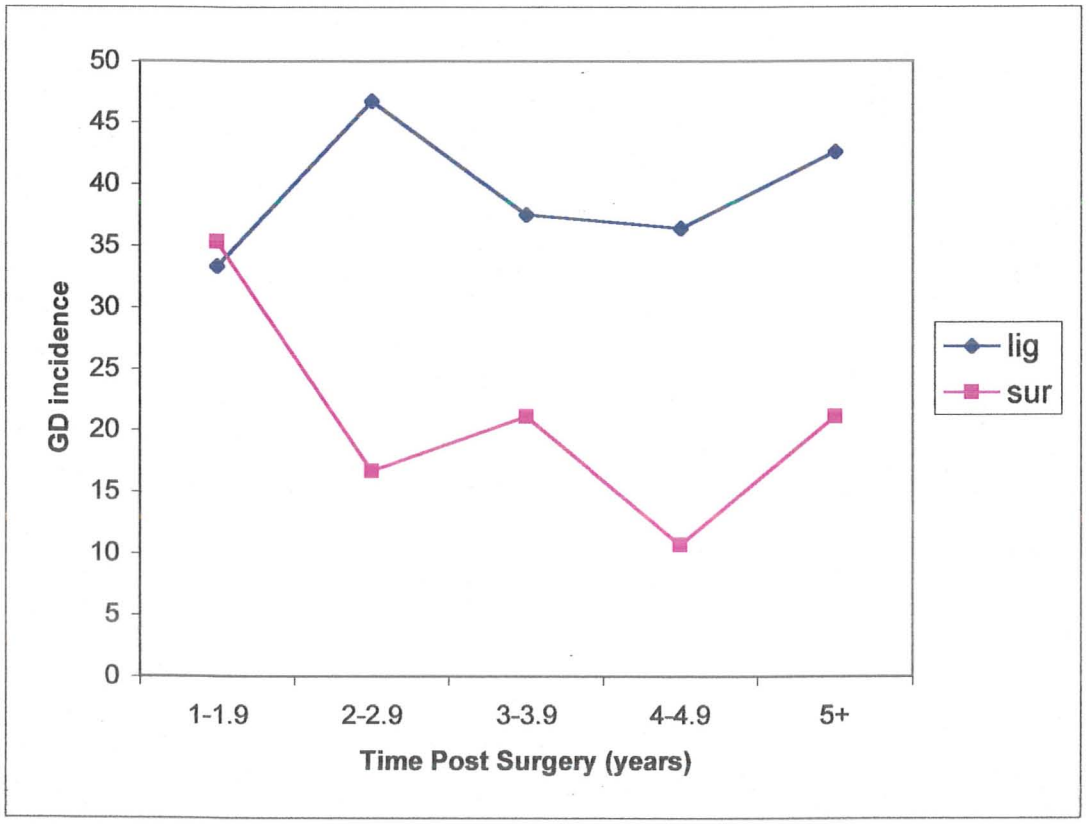


Fig. 4 Incidence of gynecological disorders in ligated (lig.)and abdominal surgery (abd.surg.) groups in relation to time after surgery.

DISCUSSION

Contraception in general and sterilization in particular have far reaching significance for family planning and population control. This has been and continues to be of paramount importance for developing countries. Since the major focus in family planning programs has traditionally been on female contraception, serious concern relates to women's reproductive health and the kind of service available to them for alleviating their problems, both in individual terms and social context. While temporary contraceptive methods in the female have been prevalent for quite some time, female sterilization as an irreversible means of contraception has gained popularity over the last few decades, especially in the industrialized countries. Very often and fortunately, a decision pertaining to sterilization as the ultimate recourse is increasingly based on mutual consent of couples. In the United States of America, almost 72% of combined male and female sterilizations consisted of female tubal sterilization during the period 1998-2000 (Piccinino and Mosher, 1998, Pati and Cullins, 2000). Globally, over 190 million couples opted for sterilization by the year 2000 (Pati and Cullins, 2000), most of which have been interval sterilizations.

Whereas tubal sterilization has provided a permanent means of controlling unwanted pregnancies, it has not been free of both immediate and long-term reproductive health complications for women opting for the procedure. Concomitant with this realization, provision of universally available health services to ensure clinical care and proper standards for sterilization has been urgently felt. This implies not only safety from gynecological morbidities but also complete physical, mental and social well being of women pertaining to reproductive system, its functions and processes (UN, 1994). It was in this context that the present investigation was undertaken to examine gynecological consequences of tubal ligation in a cross section of Pakistani women. The overall study population for baseline data and selection of follow up cases comprised a mix of urban and rural women (nearly 50:50 ratio) belonging to the Islamabad-Rawalpindi area, where better consultative facilities than elsewhere exist and hence a relatively better level of awareness of family planning and women's health is anticipated. The socio-demographic profile of women opting for ligation and interviewed at the RHC prior to sterilization revealed a generally low socio-economic status of the families as judged from their literacy level and occupational background. Nearly 1/3 of the sample was under 30 years of age and had no history of abortions. The latter fact is not surprising because,

on the one hand, the Pakistani society is generally free of premarital sex and married couples are desirous of children and, on the other, it reflects on unhampered pregnancies/delivery (unless extraneous circumstances dictate otherwise) that would otherwise constitute a compulsion for abortions. The women had average parity of less than 6 and very low incidence of disease in both the urban and rural communities. It is particularly noteworthy that the women showed low incidence of gynecological disorders that were also far less in the urban, as one may expect, than in the rural women. It is possible that such low incidence of reproductive system-associated diseases as well as GD is related to daily observance of personal hygiene as part of religious practice. This observation has also been made in another study on a South Indian community where the Muslim component of the community sample showed total absence of reproductive system-related diseases compared to other religious groups (Bhatia *et al.*, 1997). As a matter of general practice and to obviate any risk of regret, the Reproductive Health Centres (RHC) in Pakistan do not enrol women for sterilization who do not have at least one male child of at least 10 years of age. In communities of Pakistan with low educational and economic level (usually in rural set-up), it is also common to marry girls at a very young age (15.6 $\pm$ 4.4 years, Hakim & Cleland, 1998). It is owing to this eligibility requirement at RHCs that the population average age of women seeking sterilization (preligation study) turned out to be around 30 years (a gap of over 10 years on the average since marriage).

The CBS-1 postligation retrospective cohort study (ligated vs nonligated control cohort) dichotomized into GD and No GD subgroups revealed (1) two fold greater risk of GD in the ligated cohort than in the control cohort (nonligated), and (2) fairly close correspondence regarding mean age, duration of marriage, abortion rate, LCB and contraception. The majority of women in this sub sample were over 30 yrs of age, were married for over 10 yrs, had no experience of abortion, had LCB of > 1 yr (cessation of further pregnancies) and yet were non users of contraceptives. Some notable differences pertained to noticeably higher percentage of women with experience of surgery other than ligation (perhaps pregnancy-related). Furthermore, a substantially greater percentage of women had health problems in the GD subgroup of both the ligated and control cohorts as compared to the No GD subgroup of these cohorts, suggesting an association of GD with health problems. However of those women that had GD, health problems were far greater in the ligated cohort compared to the control cohort indicating increased risk of GD in the former cohort. Also, onset of

GD occurred about 2 yrs after ligation suggesting possibility of a biological basis of such change. Risk ratio analysis also revealed over 2-fold greater risk (RR 2.46, 95% CI, P< 0.0001) of GD in the ligated cohort than in the control cohort.

The CBS-2 postligation follow up sub sample of 111 women revealed comparable baseline urban/rural ratio, low socioeconomic level, high conception rate, LCB of > 6 yrs (considerable gap since last live childbirth), no abortion experience by majority of the women and majority of the ligated women being 30-35 yrs of age. Most of the women underwent laparoscopic surgery. A very high percentage of the women (87%) had no preligation health problems. However, this percentage dropped to 49% two and more years after ligation. Over a third of the sample showed GD. When examined after partitioning into GD and No GD subgroups, the two subgroups did not differ in regard to average age at ligation, number of prior conceptions and time since ligation. In both subgroups, laparoscopy dominated the surgical treatment and although the socioeconomic status was generally low in both groups, the educational and occupational background of the No GD control cohort was slightly better, this perhaps being one reason for their better gynecological management. Again, a higher percentage of the GD subgroup of the ligated cohort, were of 35 yrs of age and younger, had postligation health complications comprising body ache, weakness and weight gain and showed menstrual disturbance. Weakness was also quite pronounced in the No GD subgroup of the control cohort, but it appeared to be associated with greater incidence of thyroid malfunction than to ligation.

Prospective studies in the past on effect of tubal ligation on reproductive health and gynecological status, two or more years after surgery, have yielded conflicting results. Studies, where women have been observed for 4-6 years after surgery, have yielded only equivocal evidence of menstrual disturbance following ligation (DeStefano *et al.*, 1985; Pickersgill *et al.*, 1999; Rulin *et al.*, 1993; Vessey *et al.* 1983). Self report and hospital-based data gave generally similar evidence regarding GD and ligation. Often, self-reports underestimate the gravity of the problem as has been observed by Bhatia *et al.* (1997) in a study in South Indian women. Depending on the site of puncture for sterilization, herniation has been recorded in several studies (Boike *et al.*, 1995; Kadar *et al.*, 1993; Mc Murrick and Polglase, 1993; Montz *et al.*, 1994; Plaus, 1993), highlighting a surgical procedural complication as is also evident in a small percentage of sterilized women in the present study (data not reproduced here).

Sterilization has been shown to reduce the risk of pelvic inflammatory disease (PID) by preventing spread of infection from the lower genital tract to the peritoneal cavity (Droegemueller *et al.*, 1987; Green *et al.*, 1991; Haji, 1978; Poma, 1980; Vessey *et al.*, 1983). Some reports, however, have given contrary results in this regard indicating that the protection is not absolute (Green *et al.*, 1991; Phillips and d'Ablaing, 1986; Reedy *et al.*, 1994; Weeks and Entman, 1991). Sterilization is known to provide several other advantages in terms of health of ligated women. One of these is reduced risk of ovarian cancer. This has been found to be true in spite of a maximum period of 15 years of observation following sterilization. This advantage seems to result from protection of the ovaries against oncogenic viruses (Wahlberg, 1994) and environmental carcinogens that may be inadvertently introduced into the vagina or the perineum (Green *et al.*, 1997; Irwin *et al.*, 1991; Ryder and Vaughan, 1999; Silver and Rockville, 1994; Whittemore *et al.*, 1988; Cramer, et al., 1995). Another advantage of ligation is lack of any detrimental effect on sexual relationship and coital desire and even improvement in sexual performance of sterilized women (Cooper *et al.*, 1985; Kjer, 1990; Phililiber and Philliber, 1985; Shain *et al.*, 1991) because of reduced anxiety for unwanted pregnancy (Shain *et al.*, 1991).

The retrospective cohort community-based studies comprising the Health House and the follow up sub samples collectively revealed that ligation is a risk for gynecological disorders, especially menstrual disturbance, as well as health complications. The onset of GD occurred in the ligated women with a delay. Women under 35 yrs experienced maximum menstrual disturbance. This emerged as a consistent picture even after such confounders as age, parity, contraception, educational level and recall bias were accounted for. The results of the hospital-based study (HBS-1) presented here also support this observation revealing a strong association between ligation, GD and health. Studies during the last two decades or so have yielded considerably discordant information on gynecological morbidity and its relationship with sterilization (Vessey *et al.*, 1983; Huggins and Sondheimer, 1984; De Stafano *et al.*, 1985; Rulin *et al.*, 1993; Pickersgill, 1999). Several investigators have presented evidence that tubal ligation results in what has been described as post-tubal ligation syndrome. Yet the existence of this syndrome has been widely debated by others. A major reason for the debate has been lack of consensus on its precise definition. According to one view, it is a complex of largely psychosomatic symptoms dominated by menstrual disorders (Gentile *et al.*, 1998; Visvanathan and Wyshak, 2000). Another view states that it is characterized

by increased menstrual flow or cramps, increased premenstrual syndrome and gynecological problems in general with the additional implication that sterilization speeds up menopause (Jelovsek, 2001). Peterson *et al.* (2000) have argued that the debate on existence of post tubal ligation syndrome persists not only because the syndrome has been ill defined but also because many women show menstrual abnormalities after sterilization. They further state that the two are coincidental simply because both sterilization and menstrual disorders are quite common. Earlier reviews (Black and Sclare, 1968; Haynes and Wolfe, 1970; Muldoon, 1972; Schwyhart and Kutner, 1973) on the subject dealt with gynecological status and emotional consequences of tubal ligation when neither the technology was very advanced nor ligation was a preferred recourse. It has been reported that one of the most common postligation gynecological symptoms is dysfunctional uterine bleeding (Muldoon, 1972; Lu and Chun, 1967; Rubinstein *et al.*, 1976). This has been observed in the present investigation as well. That tubal ligation is followed by a sequence of menstrual alterations has also been demonstrated in more recent studies (Harhgrove and Abraham, 1981; Donnez *et al.*, 1981; Shain *et al.*, 1989; Thranov *et al.*, 1992; Hakverdi *et al.*, 1994). Other investigators (Cole *et al.*, 1984; Rivera *et al.*, 1989; Rulin *et al.*, 1993) have not been able to confirm this observation. Evidently, the conflict seems to stem from lack of appropriate controls for confounders in the study designs of some of the studies. Thus, it has been noted that the evidence of positive association of ligation with GD presented by some of the investigators (Williams *et al.*, 1951; Muldoon 1972; Madrigal *et al.*, 1975; Neil *et al.*, 1975; Huez *et al.*, 1983) suffers from lack of adjustments for contraceptive usage, pre-existing gynecological diseases, age, education, parity, gravidity and even the additional constraint of recall bias vis-à-vis menstrual history. Also, where perimenopausal women dominate the study population, the chances of disturbed menstrual cycle increase simply because of approaching menopause. In retrospective analysis of postligation syndrome, recall of menstrual parameters several years later introduces a bias that confounds proper evaluation of the data. In a large number of studies, where the subjects have been on oral contraceptives prior to ligation, the women tend to develop postligation menstrual disorders as a result of cessation of contraception (Peterson *et al.*, 2000). This observation has been substantiated by negative evidence of association with menstrual disturbance following exclusion of such subjects from the analysis (Stock, 1978). In their study, Vessey *et al.* (1983) could hardly find any evidence of long term sequalae of tubal ligation. On the other hand, Martinez-Schnell *et al.* (1993) examined postligation menstrual complications in a multicenter prospective

study of 5000 women and concluded that there is an increase in odds of risk of at least one of the several menstrual dysfunctions in the 5th year of follow up compared to the early postligation period. Increase in risk of menstrual dysfunction in yearly follow up has also been reported by Goldhaber et al. (1993).

In both, the retrospective cohort and case control analyses in the present investigation, the majority of the women were exposed to laparoscopic surgery and nearly all underwent interval sterilization. Newton and Gillman (1980) have claimed that sterilization, in particular laparoscopic, is entirely free of hazards as judged from a 5-year follow up work covering over 2000 women. Taner *et al.* (1995) have also obtained only non significant dysmenorrhea and cyclic pelvic pain following ligation by several different sterilization methods. In a case-control study, Peterson *et al.* (1999) studied over 9000 women and observed that the sterilized women are at no greater risk of menstrual disturbance than the non sterilized women--an observation that has been further strengthened in a more recent study by these workers (Peterson *et al.*, 2000). Earlier, Rulin *et al.* (1993) provided evidence of a strong association between ligation and perimenopausal symptoms, which in turn are indicative of increase in susceptibility to diseases of aging including psychological disorders (see also Snowden, 1989; Richards *et al.*, 1999; Visvanathan and Wyshak, 2000). In the present hospital-based case-control study (HBS-1), gynecological disorders were recorded with a considerable postligation delay in the cases, whereas the control women were entirely free of GD(by definition). However, in this particular study the symptoms also coincided with approaching menopause as the average age of the women happened to be around 40 yrs in both the ligated and nonligated subgroups. The health status of women in this study appeared to be unrelated to ligation status (majority of cases and controls being healthy). Anaemia (<12g/dl Hemoglobin, Table 19) in the majority of the cases group seemed to be a consequence of gynecological disorders, of which menstrual dysfunction was the most predominant (Table 20) followed by UVP. The majority of the women (~80%) with GD were under 35 yrs of age and ligation had a strong association with GD (OR = 2.92, $P<0.0001$). This association between sterilization and GD held even when confounders such as age, parity, conception, abortion, contraception, education and other surgery were accounted for. The method of selecting confounders in the present study was rather crude as only two levels of individual confounders were selected for purposes of statistical analysis. Whether selection of additional

subcategories of these confounders would yield different OR values can only be judged following further study.

Prior to ligation, the majority of the cases women had regular menstrual cycle, it became irregular in most of the sample both in terms of duration and flow. A positive association of ligation with menstrual dysfunction was evident for all age groups, but this association was significant only for women with average age of 35 yrs and younger group only (OR 5.25,CL 95% $P<0.05$). It is well known that menstrual abnormalities prior to ligation and/or withdrawal of contraceptives at the time of ligation serve as the most obvious confounders of association between GDs and sterilization (Pati and Cullins, 2000). However, their confounding effect is negated by the preligation menstrual cycle data as well as by the appropriate adjustments in odds ratio analysis. Thus, it appears that the positive association between GDs and ligation is a consequence of some physiological alterations following ligation rather than its being an outcome of merely aging phenomenon. The incidence of both PMB and PID was extremely low in the ligated subgroups of the GD cases. The former was apparently low because of the low number of women in the menopausal age class. According to Levgur and Duvivier (2000), PID risk is often associated with the surgical procedure itself rather than being a consequence of ligation and its biological accompaniments. Low incidence of this GD complication in the present study also affirms that surgical procedural handling of the subjects was well controlled. In fact, none of the subjects reported postligation surgical complications and their hospital records also did not reveal such complications

Among the common benign pathologies of the uterus, leiomyoma has been considered as one of the major compulsions for hysterectomy in the United States of America (Chen *et al.*, 2001). Fibroid growth is well known to be associated with estrogen and progesterone dominance (Butram and Reiter, 1981; Andersen, 1998). Early onset of menarche (Parazzini *et al.*, 1988; Marshall *et al.*, 1997) and high level of education (Parazzini *et al.*, 1988; Samadi *et al.*, 1996) are related to the odds of increased risk. Parity and oral contraceptives have been shown to have a protective effect against fibroids (Ross *et al.*, 1986; Parazzini *et al.*, 1988; Samadi *et al.*, 1996; Marshall *et al.*, 1998). In a recent study on premenopausal women in USA, Chen *et al.* (2001) demonstrated that the risk of uterine fibroids increases in ligated women during the 4^{th} decade of their life, menstrual cycle length of ≥ 30 days, bleeding of > 6 days and even due to genetic predisposition.

Contraceptive use and abortions have no association with fibroids. The greatest risk factor, however, is increasing age. In the present hospital-based study on Pakistani women, leiomyoma constituted a major uterine pathology followed by adenomysis, endometrial hyperplasia and some malignancy cases in both the ligated and nonligated women. Although the two groups differed insignificantly in this regard, 50% of the ligated women did show this pathological state, which tended to increase with advancing age, thus providing evidence of a strong effect of age. Hyperplasia of the endometrium is a state that may presage endometrial cancer and is a hormone-related gynecological alteration. Its association with tubal ligation has so far remained elusive. In fact, a non significant protective effect of sterilization on endometrial cancer has been provided by Kelsey (1982). Analysis of this aspect in a large multicenter population also revealed a non significant protective effect of sterilization against endometrial cancer (Castellsagne *et al.*, 1996). Lacey *et al.* (2000) have demonstrated lack of an association between sterilization and this type of uterine pathology. In the context of the present work, further analysis is essential to ascertain whether or not the marginal incidence of hyperplasia is a risk for cancer and whether the overall incidence of uterine pathology is indeed an outcome of sterilization or is merely an aging phenomenon.

The present hospital-based case-control study (HBS-1) also revealed a positive association between gynecological disorders and hysterectomy in both the ligated and nonligated women. However, the frequency of hysterectomy was greater in the ligated women compared to the nonligated women. Risk of hysterectomy has been a topic of some interest since long and it has also been shown in some of the past investigations that sterilized women are more likely to undergo this GD management (Goldhaber, 1993) which adds a financial burden. In Goldhaber's study, the relative risk (RR) of hysterectomy is significantly greater than 1.0 for all age groups. According to Chi and Feldblum (1982), the risk is greater for women older than 35 yrs as opposed to younger women. In contrast, other workers have shown a 2-fold greater risk of hysterectomy for women under 25 yrs (Rivera, 1989; Meyer, 1994). The work of Rulin (1993) on long term effects of ligation has shown increased rate of hysterectomy in ligated women. In a population-based comparison involving follow up of 9 years, Cohen (1987) showed an OR of 1.6 for association between sterilization and hysterectomy. The rate of such surgery was higher for ages between 25-29 yrs after adjustments for

previous gynecological history, marital status, number of physician visits and hospitalisation. Templeton and Cole (1982) carried out a study of data on Scottish women and concluded that the sterilized women stand at greater risk of GD and its subsequent management by hysterectomy. This was later substantiated by Cooper (1983) showing that the risk of hysterectomy for menorrhagia doubles after ligation but his work has not provided any information regarding preligation menstrual status of the subjects. Hillis *et al.* (1997) have demonstrated that the risk of hysterectomy is higher in women who had gynecological morbidity prior to ligation compared to women without such history. These workers were, however, unable to resolve whether the sterilized women had greater probability of undergoing such surgery more frequently than did their nonligated counterparts. Keeping in view the majority of evidence of greater risk of hysterectomy in women < 30 yrs of age, Hillis *et al.* (1997) have argued that any differences in risk of hysterectomy between ligated and nonligated women reflect non-biological effect of ligation. Hysterectomies have been frequently performed in cases suffering from leiomyoma, adenomysis and endometrial carcinoma and even endometrial hyperplasia, the last of these in rare instances may progress to a carcinogenic state (Desforges, 1993). Another common compulsion for hysterectomy is dysfunctional uterine bleeding (Cooper, 1983) and pelvic relaxation (Stergachis, 1990). The latter is an outcome of high parity and the former is related to prior contraceptive usage and its subsequent withdrawal. Stergachis (1990) also showed that women at 20-29 yrs and unmarried women >30 yrs of age are more likely to have subsequent hysterectomy where tubal ligation has no correlation with risk of hysterectomy within ~ 4 yrs of follow up. The indication from this study is that cessation of contraception at sterilization in young women and incidence of fibroids and other pre-existing gynecological disorders are a likely compulsion for hysterectomy rather than it being an outcome of postligation complications. A comprehensive review of this subject by Pati and Cullins (2000) shows that no known biological mechanism can be invoked in support of cause and effect relationship between ligation and hysterectomy. The data generated in the present investigation, indicate that the need of hysterectomy increases with advancing age and stress that care is necessary in advising couples to opt for sterilization with focus on the impending risk of subsequent hysterectomy as management for GDs resulting from ligation.

A comparison of gynecological status of the ligated women and those with history of only other type of abdominal surgery (HBS-2) revealed that

the former group stood at greater risk of GD than the nonligated controls. This suggests that it is ligation surgery that puts women at higher risk of gynecological disorders, possibly involving certain hormonal alterations or modification of uterine growth factors. Adjusted analysis for confounders was particularly called for by the comparatively lower mean age and parity. Young women are usually prone to caesarean abdominal surgery owing to an active reproductive life. Also, caesarean deliveries generally limit childbirth and hence lead to low parity. Furthermore, risk of gynecological disorders increases both due to shorter gaps between pregnancies and tendency to use contraceptives.

In conclusion although both laparoscopy and interval sterilization have been generally deemed to be safe methods (Jamieson *et al.*, 2000), with least post surgical complications, the data developed presently provide strong evidence of sequalae that fall within the broad definition of a post tubal ligation syndrome. The ensuing GDs consequent to ligation as reported in the present work do not appear to be a consequence of surgical procedure but outcome of biological alterations in, perhaps, ovarian hormonal physiology ensuing from vascular modifications and subsequent ovarian dysfunction. Thus, from the standpoint of local family planning programmes and policies aimed at safeguarding the reproductive health of women and to curtail unwanted pregnancies, recourse to female sterilization requires critical decision making.

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APPENDIX

Proforma - I

HEALTH AND GYNEA HISTORY OF TUBAL LIGATION CASES

Name of the Client _____

Husband's Name _____

Age of the Client (years) _____

Age of Husband (years) _____

Occupation of Husband _____

Occupation of Wife _____

Education of Wife: *1 Illiterate, 2 Primary, 3 Middle, 4 High school or above*

Education of Husband: *1 Illiterate, 2 Primary, 3 Middle, 4 High school or above*

Duration of Marriage *(years)* _____

Total Number of Children Born: _____

Number of Children Alive: *Boys* _____ *Girls* _____

Age of the last living Child: *Years* _____ *Months* _____

Total Number of: *Still birth:* _____ *Spontaneous* _____

Induced _____ *Abortions* _____

Outcome of the Last Pregnancy: *1 = Live, 2 = Still Birth, 3 = Abortion*

Previous use of Contraceptives:

0=None

1 = Oral Pill

2 = IUD

3 = Foam/jelly/Diaphragm

4 = Rhythm/Withdrawal

5 = Condom

6 = Injectable

7 = Combination of above methods

Menstrual History:

Date of LMP _____ *1 = Regular 2 = Irregular*

Flow: 1 = Scanty 2 = Normal 3 = Heavy

Past Health History:

1 = Diabetes

2 = Hypertension

3 = Peritonitis

4 = Hernia

5 = Lung Infection

6 = Jaundice

7 = Heart Disease

8 = History of Drug Allergy

9 = Any Abdominal Operation

0 = None

Ligation procedure :

Minilap = 1

Laproscopy = 2

Laprotomy = 3

Proforma - II

POST LIGATION HEALTH AND GYNEA CONDITION

Name: _____

Address: _____

Husband Name: _____

When married: _____

History of Pregnancy:

No of Children _____

Age of Last Child _____

Deliveries: *Home / Hospital*

No of Abortion: _____

Nature of abortion _____ *spontaneous / induced*

Time since last abortion: _____

History of Surgery:

*LSCS / Appendix / Hernia / Others*_____

Time of surgery _____

Any health problem post surgery _____

History of Contraception:

*Pills/Injections/IUDs/ligation/others*_____

How long/duration of use? _____

When was tubal ligation performed? _____

Time of ligation postpartum _____

*Name of hospital/city*_____

*Any health problem since ligated?*_____

(Weight gain, vaginal discharge, urinary problem, menstrual)

Have you seen a doctor for the same? _____

Menstrual History:

Do you have regular menses _____

Do you have pain with menses _____

Do you need medication for that _____

How is your menstrual flow: _____ *Heavy / Average / Scanty*

Since how long are you having this problem? _____

Have you seen a doctor for the same? _____

Management / medication received _____

Any hospital record available _____

Record of reports if available *Hb., Urine RE, Blood Chem., Others*

Proforma - III

Hospital based Study for Post Ligation Syndrome

ID No. _____

Age _____

Body Mass Index _____

Menstrual History.

Menarche age (yrs) _____

Cycle length (Days) _____ *(1=<21, 2=21 – 35, 3=>35)*

Regularity: Regular / Irregular

Flow: Heavy / Moderate / Scanty

Medical History.

Hypertension *Y/N*

Diabetes *Y/N*

Thyroid *Y/N*

Drug use History:

Pregnancy History:

Conceptions _____

Live births _____

Last birth _____

Abortions _____

Last abortion _____

Contraception.

Oral Pill / Injectable / IUD / Combination / Others

Duration (Months) _____

Surgery History

Procedure _____

Time since Procedure _____

Ligation.Minilap / laparotomy / laparoscopy

Time of ligation . post partum/interval .

Age at ligation _____

Presenting complaint (PC):

PC since _____

PC _____

Menstrual irregularity. *(Menorrahgia / Metrorrahgia / Polymenorrhea)*

Pain Lower Abdomen. *Vaginal Discharge / Mass Abdomen / Urine Frequency / Urine Retention*

USG: *Uterus size (small/medium/large.), Fibroid*

Ovaries: normal/abnormal.

Laboratory investigation.

Heamoglobin (g/dl): < 12 , =12 , >12

Blood sugar (mg/l): <150, >150.

Papsmears. *Normal / Abnormal*

Histopathology _____

Management: *Drugs, DNC, Myomectomy, Hysterectomy, Laprotomy*