A COMPARATIVE STUDY IN THE CHANGES OF LIPID PROFILE BETWEEN OOPHORECTOMIZED AND NON-OOPHORECTOMIZED WOMEN UNDERGOING HYSTERECTOMY

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ABSTRACT

BACKGROUND

We wanted to determine the association, if any, between types of hysterectomy w.r.t. preservation of ovaries and tubes and lipid profile. Women without tubes and ovaries are more susceptible to acute changes in lipid profile. Lipid profile is also significantly affected by bilateral salpingectomy in spite of preservation of ovaries. What is known already is that, risk of CVD increases after natural menopause but association with surgical premature menopause is still to be validated.

METHODS

A comparative study was undertaken to analyse the changes in lipid profile between oophorectomized and non-oophorectomized women undergoing hysterectomy. 45 participants enrolled in three different categories of total abdominal hysterectomy namely- control group-10, bilateral salpingectomy + TAH (16) and BSO+TAH (19) done for benign conditions. Preoperative and consecutive postoperative lipid profiles were obtained.

RESULTS

Total cholesterol changes are incremental in both TAH + BLS and TAH + BSO group. This may be also an acute response to surgery but requires a long-term follow up. Over three months postoperative-triglycerides, -LDL, -Total Cholesterol increased in TAH group by 12.2%, 6.15%, 3.16% to 35.44%, 41.53%, 17.26% respectively. HDL decreased from 16.7% three months postoperatively to 11.2% after six months of surgery. In TAH + BLS, total triglyceride, LDL, Total Cholesterol increased from 7.3%, 14.0%, 7.8% after three months postoperative to 27.9%, 24.03%, 11.4% following six months respectively. HDL decreased to 16.5 % from the preoperative level after 3 months and 10.8% after six months. Among the TAH + BSO group, total triglyceride, LDL, total cholesterol raised to 14.9%, 22.5%, 14.0% from the baseline after three months respectively and further increased to 22%, 32.3%, 21.9% after six months of surgery. HDL values showed a steady decline from 17.1 % to 20.1% after three months and six months of surgery respectively.

CONCLUSIONS

Women with lower ovarian reserve might be susceptible to development of cardiovascular risk factors, particularly dyslipidaemia even during the reproductive life span. A long-term follow up should be done for women who have undergone surgical menopause with sacrifice of both tubes and ovaries.

KEY WORDS

Surgical Menopause, Lipid Profile, Cardiovascular Risk Factors

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BACKGROUND

In view of lipid metabolism, adipose tissue and liver are the most important tissues for 17 beta estradiol, the main oestrogen source in a women's body. Lack of oestrogens in women after menopause may cause coronary heart disease.¹ It is considered that 25%-50% of positive effect of oestrogens which are given to postmenopausal is connected with their action on lipid metabolism.¹ In adipocytes, 17 beta estradiol can be stored as its esters with long chain fatty acids.¹

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It was proved that oestrogen receptors are present in adipocytes and hepatocytes, but their density is much lower than in gonads.

On the cellular level oestrogens regulate mRNA production for particular proteins among which are proteins involved in lipid metabolism.¹ In adipose tissue 17 beta estradiol has a direct effect on lipoprotein lipase (LPL) and hormone sensitive lipase. Indirect action of oestrogens on adipose tissue is connected with the stimulation of the releasing of other hormones which increase hormone sensitive lipase activity. To this group of hormones there belong catecholamines, growth hormone and glucagon.

In liver 17- beta estradiol regulates the rate of synthesis of structural apolipoproteins for VLDL & HDL. In conclusion, 17- estradiol by regulating lipid metabolism in adipocytes and hepatocytes modulates the concentration of lipid substances in plasma¹. The lack of 17-beta estradiol leads likely to various lipid metabolism disorders in women after menopause.

Premature menopause and bilateral oophorectomy in young women are associated with increased incidence of cardiovascular disease, myocardial infarction & overall mortality. Observational studies suggest an interval of 5-10yrs between loss of ovarian function & increased risk of cardiovascular disease. Compared with men, women generally have a lower potential for suffering cardiovascular events, but the risk of such morbidities increases after menopause. The Framingham cohort showed that the gender difference in risk of cardiovascular diseases (CVD) diminishes with each 10-year progression of age and that the age at menopause is inversely correlated with CVD risk.

In this study we have followed up with the lipid profile of three groups of hysterectomy patient including total abdominal hysterectomy (TAH), TAH+bilateral salpingectomy, TAH+bilateral salpingo-oophorectomy. There have been studies in the literature regarding the effect of bilateral salpingo-oophorectomy on lipid profile and consecutive associated cardiovascular risks, but to the best of our knowledge there has not been a study on the effect of bilateral salpingectomy on lipid profile.

Total Abdominal Hysterectomy and Bilateral Salpingectomy v/s Bilateral Salpingo-Oophorectomy

Among women of reproductive age, hysterectomy is (in developed countries) the second most frequently performed surgical intervention, superseded only by Caesarean section. Women with only removal of uterus had 3 times greater risk of CVD, but if ovaries are also removed the risk rises 7 times.²

In India, the incidence of hysterectomy is about 4-6% of adult Indian women out of which 90% are performed for benign indications.³ Another study from Gujarat pointed out that 7-8% of rural women and 5% of urban women had already undergone hysterectomy at an average age of 37 year.⁴

Risk-reducing and elective salpingo-oophorectomies are the removal of the ovaries for the potential benefit of preventing long-term morbidity and mortality. The term risk-reducing salpingo-oophorectomy implies that the ovaries are normal at the time of removal. Removal of the ovaries during hysterectomy is, indeed, a matter of debate.⁵ According to large case-control studies, oophorectomy and the resulting surgical menopause increase the long-term risk for cardiovascular, psychosexual and cognitive dysfunctions.⁶ Moreover, a prospective study showed that oophorectomy along with hysterectomy lowers the risk for ovarian cancer, whereas the incidence of fatal and non-fatal coronary heart diseases increased. As only one in 1500 women aged 50 years and one in 400-600 women aged 60-70 years develop ovarian cancer in the course of one year (National Cancer Institute, 2004),⁷ ovarian cancer remains a relatively rare disease, responsible for 16 000 fatalities per year in the USA. Heart disease, in contrast, is a major killer causing 490 000 deaths among American women annually.⁸ Thus, an overall significant negative association of the effect of oophorectomy with mortality (All causes) was found. Moreover, none of the groups (Or age groups) displayed a positive correlation between oophorectomy and increased survival.⁹ In contrast, a recent study failed to detect a significant increase in cardiovascular events after bilateral oophorectomy performed at the time of hysterectomy.¹⁰

However, while both the studies investigated large sample sizes, follow-up times were considerably different, i.e. patients in the National Health Service study in the UK were followed for 24 years,⁹ whereas data from the Women's Health Initiative study were evaluated for just 8 years after oophorectomy—which obviously limits the information content regarding the long-term effects on women's health.¹⁰ Accordingly, a prophylactic bilateral oophorectomy may do more harm than good. The removal of the ovaries at the time of hysterectomy should thus be approached with great caution, especially in premenopausal women. This is reflected by a guideline from the American College of Obstetricians and Gynaecologists (ACOG), which recommends conservation of the ovaries, at least for premenopausal women with no known genetic risk for ovarian cancer (ACOG, Practice bulletin No. 89; 2008).

After hysterectomy, the Fallopian tubes can no longer fulfil their previous physiological function. The blind-ended remnants of the Fallopian tubes may instead give rise to multiple complications, the most frequent (35.5%) being hydrosalpinx (Morse, 2002,¹¹ Repasy et al., 2009,¹²) which requires revision surgery in 7.8% of patients (Morse et al., 2006).¹³ Further possible problems originating from retained Fallopian tube remnants are summarized in Fig. 1 (Basu and Ward, 2007; Singla, 2007; Ghezzi et al., 2009; Timor-Tritsch et al.,¹⁴ Rezvani and Shaaban,¹⁵ 2011).

Thus, bilateral salpingectomy concomitant with hysterectomy is widely recommended to avoid subsequent tubal pathology.¹²

METHODS

This study has been conducted at Medical College Hospital Kolkata over a period of 6 months. Inclusion Criteria: Patients of reproductive age group attending gynaecology OPD for benign causes with cervical and endometrial biopsy report to rule out malignancy and previous no history of chemotherapy were included.

Study Design

Comparative study.

Sample Size

10, 16, 19 each in TAH, TAH+ BLS, TAH+ BSO respectively.

Inclusion Criteria

Age less than 45 yrs. selected for conservation of ovaries (Out of which 10 patients randomly selected for only hysterectomy and 16 patients selected for salpingectomy in addition to hysterectomy).

Exclusion Criteria

Patients with adnexal masses, proven gynaecological malignancies, deranged lipid profile preoperatively, previously known heart disease.

Sampling Technique

Random.

IEC Clearance

Approved and informed consent received.

Figure 1. Human Reproduction, Vol. 26, No. 11 pp. 2918–2924, 2011¹²

RESULTS

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
Age	TAH	10	42.7000	.9487	40.0000	43.0000	43.0000	<0.0001
	TAH BLS	16	42.5625	2.9205	35.0000	46.0000	43.0000	
	TAH BSO	19	47.4211	3.6563	42.0000	54.0000	48.0000	

Table 1. Distribution of Mean Age in Groups

Pre-Operative (mg/dl)					Post-Op 3 m (mg/dl)				Post-Op 6 m (mg/dl)			
	TG	HDL	LDL	TC	TG	HDL	LDL	TC	TG	HDL	LDL	TC
TAH	101.40 ±21.49	53.10 ±8.13	78.00± 26.73	145.40 ±20.4	113.80 ±17.05	44.20 ±11.01	82.80± 26.41	150.00 ±19.89	137.37 ±14.21	47.10 ±14.25	110.40 ±12.39	170.50 ±12.24
TAH +BLS	119.13 ±25.18	46.31 ±6.12	93.88± 18.02	160.31 ±16.94	127.98 ±25.02	41.31 ±6.26	107.00 ±20.27	171.63 ±19.16	152.31 ±27.63	38.63 ±6.26	116.44 ±21.25	178.53 ±19.69
TAH + BSO	165.74 ±12.74	41.84 ±6.12	121.58 ±23.06	190.42 ±25.14	190.47 ±25.14	34.68 ±25.00	148.89 ±22.55	217.05 ±22.72	202.16 ±13.43	33.42 ±8.21	160.95 ±22.23	232.21 ±21.11

Table 2. Summary of Changes in Lipid Profile Over 6 Months

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
Pre-Op TG	TAH	10	101.4000	21.4900	89.0000	152.0000	91.0000	<0.0001
	TAH BLS	16	119.1250	25.1843	89.0000	172.0000	114.0000	
	TAH BSO	19	165.7368	12.7360	141.0000	182.0000	165.0000	

Table 3. Distribution of Mean Pre-Op TG in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
Total Tg 3 m	TAH	10	113.8000	17.0542	95.0000	134.0000	118.0000	<0.0001
	TAH BLS	16	127.8750	25.0197	96.0000	179.0000	124.0000	
	TAH BSO	19	190.4737	15.2584	156.0000	226.0000	186.0000	

Table 4. Distribution of Mean Total Triglyceride (TG) 3 m in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
TG 6 Mon.	TAH	10	137.3750	14.2120	121.0000	158.0000	135.5000	<0.0001
	TAH BLS	16	152.3125	27.6350	104.0000	210.0000	155.0000	
	TAH BSO	19	202.1579	13.4340	184.0000	238.0000	198.0000	

Table 5. Distribution of Mean TG 6 Mon. in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
HDL Pre-Op	TAH	10	53.1000	8.1302	34.0000	64.0000	55.0000	0.0011
	TAH BLS	16	46.3125	6.1179	38.0000	59.0000	46.0000	
	TAH BSO	19	41.8421	7.5811	30.0000	51.0000	42.0000	

Table 6. Distribution of Mean HDL Pre-Op in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
HDL 3 m	TAH	10	44.2000	11.0131	34.0000	56.0000	41.0000	0.0067
	TAH BLS	16	41.3125	6.2580	30.0000	55.0000	41.5000	
	TAH BSO	19	34.6842	7.2958	25.0000	46.0000	35.0000	

Table 7. Distribution of Mean HDL 3 m in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
HDL 6 m	TAH	10	47.1000	14.2552	30.0000	62.0000	49.5000	0.0022
	TAH BLS	16	38.6250	6.2597	28.0000	50.0000	39.0000	
	TAH BSO	19	33.4211	8.2146	24.0000	48.0000	30.0000	

Table 8. Distribution of Mean HDL 6 Mon. in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
Pre-Op LDL	TAH	10	78.0000	26.7291	50.0000	103.0000	84.0000	<0.0001
	TAH BLS	16	93.8750	18.0217	62.0000	126.0000	97.5000	
	TAH BSO	19	121.5789	23.0562	79.0000	172.0000	115.0000	

Table 9. Distribution of Mean Pre-Op LDL in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
LDL 3 m	TAH	10	82.8000	26.4146	54.0000	107.0000	92.0000	<0.0001
	TAH BLS	16	107.0000	20.2748	76.0000	143.0000	107.5000	
	TAH BSO	19	148.8947	22.5509	117.0000	190.0000	144.0000	

Table 10. Distribution of Mean LDL 3M in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
LDL 6 m	TAH	10	110.4000	12.3935	87.0000	129.0000	111.0000	<0.0001
	TAH BLS	16	116.4375	21.2539	86.0000	152.0000	111.5000	
	TAH BSO	19	160.9474	22.2398	137.0000	199.0000	153.0000	

Table 11. Distribution of Mean LDL 6M in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
TC Pre-Op	TAH	10	145.4000	20.4081	123.0000	164.0000	153.0000	<0.0001
	TAH BLS	16	160.3125	16.9380	134.0000	187.0000	165.0000	
	TAH BSO	19	190.4211	25.1359	138.0000	241.0000	194.0000	

Table 12. Distribution of Mean TC Pre-Op in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
TC 3 m	TAH	10	150.0000	19.8886	128.0000	168.0000	158.0000	<0.0001
	TAH BLS	16	171.6250	19.1551	145.0000	210.0000	173.5000	
	TAH BSO	19	217.0526	22.7241	182.0000	260.0000	210.0000	

Table 13. Distribution of Mean TC 3 Mon. in Groups

		No.	Mean	SD	Mini.	Maxi.	Median	p-Value
TC 6 m	TAH	10	170.5000	12.2406	152.0000	189.0000	168.0000	<0.0001
	TAH BLS	16	178.5333	19.6936	152.0000	216.0000	178.0000	
	TAH BSO	19	232.2105	21.1123	200.0000	270.0000	226.0000	

Table 14. Distribution of Mean TC 6 m in Groups

Statistical Analysis

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS (Version 24.0; SPSS Inc., Chicago, IL, USA). Data had been summarized as mean and standard deviation for numerical variables.

RESULTS

We found that in TAH, the mean age (mean ± S.D.) of patients was 42.7000 ± .9487 years. In TAH BLS, the mean age (mean ± S.D.) of patients was 42.5625 ± 2.9205 years. In TAH BSO, the mean age (mean ± S.D.) of patients was 47.4211 ± 3.6563 years. Difference of mean age vs. group was statistically significant ($p < 0.0001$).

It was found that in TAH, 6(60.0%) patients had Dub and 4(40.0%) patients had fibroid. In TAH BLS, 3 (18.8%) patients had adenomyosis, 12 (75.0%) patients had fibroid and 1 (6.3%) patient had menorrhagia. In TAH BSO, 1 (5.3%) patients had adenomyosis, 5 (26.3%) patients had Dub, 3 (15.8%) patients had fibroid and 10 (52.6%) patients had menorrhagia. Association of indication in three groups was statistically significant ($p < 0.0001$).

Among TAH, the mean pre op TG (mean ± S.D.) of patients was 101.4000 ± 21.4900. In TAH BLS, the mean pre op TG (mean ± S.D.) of patients was 119.1250 ± 25.1843. In TAH BSO, the mean pre op TG (mean ± S.D.) of patients was

165.7368 ± 12.7360. Difference of mean pre op TG vs. group was statistically significant ($p < 0.0001$).

It was seen that in TAH, the mean total glyceride at 3 months (mean ± S.D.) of patients was 113.8000 ± 17.0542. In TAH BLS, the mean total glyceride at 3 months (mean ± S.D.) of patients was 127.8750 ± 25.0197. In TAH BSO, the mean total glyceride at 3 months (mean ± S.D.) of patients was 190.4737 ± 15.2584. Difference of mean total glyceride at 3 months vs. group was statistically significant ($p < 0.0001$).

We noticed that in TAH, the mean TG at 6 months (mean ± S.D.) of patients was 137.3750 ± 14.2120. In TAH BLS, the mean TG at 6 months (mean ± S.D.) of patients was 152.3125 ± 27.6350. In TAH BSO, the mean TG at 6 months (mean ± S.D.) of patients was 202.1579 ± 13.4340. Difference of mean TG at 6 months vs. group was statistically significant ($p < 0.0001$).

In TAH, the mean HDL pre op (mean ± S.D.) of patients was 53.1000 ± 8.1302. In TAH BLS, the mean HDL pre op (mean ± S.D.) of patients was 46.3125 ± 6.1179. In TAH BSO, the mean HDL pre op (mean ± S.D.) of patients was 41.8421 ± 7.5811. Difference of mean HDL pre op in three groups was statistically significant ($p = 0.0011$).

We gathered that in TAH, the mean HDL at 3 months (mean ± S.D.) of patients was 44.2000 ± 11.0131. In TAH BLS, the mean HDL at 3 months (mean ± S.D.) of patients was 41.3125 ± 6.2580. In TAH BSO, the mean HDL at 3 months (mean ± S.D.) of patients was 34.6842 ± 7.2958. Difference of mean HDL at 3 months in three groups was statistically significant ($p = 0.0067$).

In TAH, the mean HDL at 6 months (mean ± S.D.) of patients was 47.1000 ± 14.2552. In TAH BLS, the mean HDL at 6 months (mean ± S.D.) of patients was 38.6250 ± 6.2597. In TAH BSO, the mean HDL at 6 months (mean ± S.D.) of patients was 33.4211 ± 8.2146. Difference of mean HDL at 6 months in three groups was statistically significant ($p = 0.0022$).

It was found that in TAH, the mean Pre op LDL (mean ± S.D.) of patients was 78.0000 ± 26.7291. In TAH BLS, the mean Pre op LDL (mean ± S.D.) of patients was 93.8750 ± 18.0217. In TAH BSO, the mean Pre op LDL (mean ± S.D.) of patients was 121.5789 ± 23.0562. Difference of mean Pre op LDL in three groups was statistically significant ($p < 0.0001$).

We have seen that in TAH, the mean LDL at 3 months (mean ± S.D.) of patients was 82.8000 ± 26.4146. In TAH BLS, the mean LDL at 3 months (mean ± S.D.) of patients was 107.0000 ± 20.2748. In TAH BSO, the mean LDL at 3 months (mean ± S.D.) of patients was 148.8947 ± 22.5509. Difference of mean LDL at 3 months in three groups was statistically significant ($p < 0.0001$).

In TAH, the mean LDL at 6 months (mean ± S.D.) of patients was 110.4000 ± 12.3935. In TAH BLS, the mean LDL at 6 months (mean ± S.D.) of patients was 116.4375 ± 21.2539. In TAH BSO, the mean LDL at 6 months (mean ± S.D.) of patients was 160.9474 ± 22.2398. Difference of mean LDL at 6 months in three groups was statistically significant ($p < 0.0001$).

It was found that in TAH, the mean TC pre op (mean ± S.D.) of patients was 145.4000 ± 20.4081. In TAH BLS, the mean TC pre op (mean ± S.D.) of patients was 160.3125 ± 16.9380. In TAH BSO, the mean TC pre op (mean ± S.D.) of patients was 190.4211 ± 25.1359. Difference of mean TC pre op in three groups was statistically significant ($p < 0.0001$).

We have seen that in TAH, the mean TC at 3 months (mean ± S.D.) of patients was 150.0000 ± 19.8886. In TAH BLS, the mean TC at 3 months (mean ± S.D.) of patients was 171.6250 ± 19.1551. In TAH BSO, the mean TC at 3 months (mean ± S.D.) of patients was 217.0526 ± 22.7241. Difference of mean TC at 3 months in three groups was statistically significant ($p < 0.0001$).

In TAH, the mean TC at 6 months (mean ± S.D.) of patients was 170.5000 ± 12.2406. In TAH BLS, the mean TC at 6 months (mean ± S.D.) of patients was 178.5333 ± 19.6936. In TAH BSO, the mean TC at 6 months (mean ± S.D.) of patients was 232.2105 ± 21.1123. Difference of mean TC at 6 months in three groups was statistically significant ($p < 0.0001$).

DISCUSSION

Our study shows patient with mean age of 42.70 ± 0.95 yrs. (TAH), 42.56 ± 2.92 (TAH + BLS), 47.42 ± 3.65 (TAH + BSO), this difference of age is statistically significant.

In this study the preoperative and postoperative total cholesterol, triglycerides, LDL, levels showed significant increment from preoperative to 3 months and 6 months postoperatively.

HDL value decreased successively in each patient undergoing TAH, TAH + BLS, TAH + BSO postoperatively compared to preoperative values.

To the best of our knowledge this is the only study comparing lipid profile changes in bilateral salpingectomy (Ovaries preserved) to hysterectomy with and without oophorectomy. Total cholesterol changes in bilateral salpingectomy group (TAH + BLS) increased from preoperative value 160.31 ± 16.94 to 176.63 ± 19.16 (At three months postoperative period), 178.53 ± 19.69 (Six months postoperative) significantly ($p < 0.001$). Similarly changes in LDL value was significant from 93.87 ± 18.02 (Preoperative) to 107.00 ± 20.27 (3 months postoperative) & 116.43 ± 21.25 (6 months postoperative).

Several cohort studies have reported the relationship between hysterectomy and risk of developing hyperlipidaemia.¹⁶⁻¹⁸ An Iran study found increased levels of triglyceride, total cholesterol and low-density cholesterol in 31 women six months after their hysterectomy and bilateral salpingo-oophorectomy¹⁹.

Based on the result analysis, its suggestive that the lipid profile changes in each group of TAH, TAH+BLS, TAH+BSO is significant. TAH + BLS, a ovarian preserving procedure significantly affects the preoperative and postoperative lipid changes ($p < 0.001$). This allows us to rethink whether sacrificing the fallopian tubes while decreasing the chances of serous ovarian tumours may increase the morbidity due to deranged lipid profile. Most of the patients undergoing BLS where in their reproductive life and subsequent increase in lipid profile will only increase their cardiovascular morbidity.

To be more sure, the study needs to be carried out for a longer duration in order to differentiate whether the changes are in response to stress induced due to surgery or a dysfunctional ovaries.

CONCLUSIONS

There is significant alteration in lipid profile in all the three groups which leads us to rethink the benefit of ovarian preserving procedure and should motivate the patients for regular follow-up and proper life-style modification and

appropriate counseling both preoperatively and postoperatively. This allows us to rethink about other conservative approaches in favour of uterus conserving management. We suggest long term follow up pertaining to cardiovascular health including lipid profile. Still, there is a paucity of studies which include the outcome following bilateral salpingectomy; hence more studies are needed in this regard.

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