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CORRELATION OF GALL STONE AND ORAL CONTRACEPTIVES IN FEMALES - AN OBSERVATIONAL STUDY

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ABSTRACT

There has been an increase in the diagnosis of gall-stones in recent years and notably an increased incidence of gall-stones in younger females. This has occurred at a time when oral contraceptive use has increased. It is suggested that oral contraceptives may predispose pre-menopausal women to gallstone formation and this is discussed in relationship to the physical and chemical alterations in biliary secretion produced by hormonal changes. The difference between women and men begins during puberty and continues through the child bearing years because of the effects of female sex hormones. Intake of OCP is probably a risk factor for gallstones, especially in younger women. The present study was undertaken to find out the possible association of cholelithiasis with age and intake of OCP. In our study out of total 72 female patients who were diagnosed as cholelithiasis or choledocholithiasis. Among which 66 patients were married and rest unmarried. A detailed history regarding OCP intake was taken from each married female. In this study lower incidence of gallstone was observed in patients taking oral contraceptive pills, as only 9 patients (13.64%) gave history of taking Oral contraceptive pills.

INTRODUCTION

The introduction of Gall Bladder disease to mankind dates back to the 21st Egyptian Dynasty (1085-945 BC), when gall stones were discovered in the mummy of priestess of Amen.¹

The prevalence of Gall stones increases with advancing age and it is due to increase in cholesterol content in Bile. Various studies reveals that Gall stones prevalence rates increases with advancing age with peak age of incidence at 41-50 years. As per gender Female: Male ratio for gall stone disease is 4:1.² Incidences increase with aging in both regarding males and females, advanced age and moreover other factors include family history, sedentary lifestyle, high body mass index (BMI), smoking, dyslipidemia, diabetes mellitus, dietary factor, underlying disease, multipara women, and oral contraceptive user's etc.³ Oestrogenic influences including Oral Contraceptive Pills (OCPs) intake and pregnancies increase the expression of hepatic lipoprotein receptors.⁴ It has long been stated that oestrogens may cause an alteration in the composition of bile.^{5, 6} Various studies show that increased incidence of gall-stones in younger patients. This has occurred at a time when oral contraceptive use is at peak.⁷ Moreover, use of oral contraceptives causes an increase in cholesterol secretion, which promotes gallstone formation via cholesterol super saturation of bile⁸. Oestrogen treatment enhances the risk, both in women when used for anti conception or hormone-replacement and in men with prostatic cancer.^{9,10} The hepatic Oestrogen receptor α , which is activated by Oestrogen, interferes with the negative feedback regulation of cholesterol biosynthesis by stimulating the sterol-regulatory element binding protein-2 pathway, resulting activation of the SREBP-2 responsive genes in the cholesterol biosynthetic pathway. These alterations lead to increased hepatic secretion of newly synthesized cholesterol and super saturation of bile, thereby predisposing to precipitation of solid cholesterol monohydrate crystals and formation of gallstones.¹¹ On the basis of these evidences it was felt that we should examine married female patients prospectively to determine whether there is any increased risk of formation of gall-stones in women on oral contraceptives.

MATERIALS AND METHODS

The study was conducted in department of Jarahat (Surgery), A.K Tibbiya College Hospital AMU, Aligarh. In this study 72 female patients were included who were diagnosed as cholelithiasis or choledocholithiasis. Among which 66 were married and rest unmarried. These patients were of low and middle socio economic groups and the diagnostic criteria were based on ultra sonography report. A detailed history regarding use of OCP was taken from each diagnosed case of cholelithiasis. The association of OCP intake and cholelithiasis was assessed with the percentage cases present in given sample of 66 married female patients.

OBSERVATION AND RESULTS

In our study out of total 72 female patients of cholelithiasis, 66 patients were married and 6 unmarried. According to age wise distribution 5 patients were in age group of 16-20 years. 7 patients were of the age group of 21- 25 years. Maximum numbers of patients i.e., 18 were in age group of 26-30 years. 13 female patients belong to age group of 31-35 years, 12 female patients belong to the age group of 36-40 years, 8 female patients were in age group of 41-45 years, 2 patients were in age group of 46-50, 2 patients were in age group of 51-55 years, and 3 patients belong to age group of 56-60 years. There was no patient in age group of 61-65 years. There were only 2 patients above 65 years. As shown in Table 1 and figure 1.

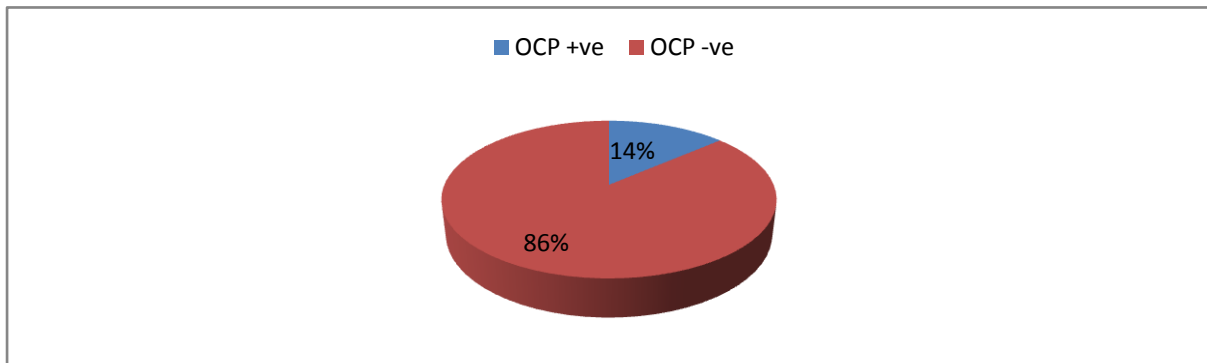
Further in our study, correlation between gall stone disease and oral contraceptive intake was observed to be non significant. Out of 66 married female patients of gallstone disease 9 patients were taking oral contraceptive pills and 57 patients (86.36%) were not taking oral contraceptive pills. The observations are summarised in table 2 and figure 2.

Table 1: Incidence of gallstones in different age wise groups:

Age group	No. of patients	Percentage
16-20	5	6.94
21-25	7	9.72
26-30	18	25
30-35	13	18.06
36-40	12	16.67
41-45	8	11.11
46-50	2	2.78
51-55	2	2.78
56-60	3	4.16
61-65	-	-
66-70	2	2.78
Total	72	100

Table 2: Incidence of gallstones in patients taking oral contraceptive pills.

Total No. of married Patients	Oral contraceptive +ve patients		Oral contraceptive -ve patients	
	No. of patients	Percentage	No. of patients	Percentage
66	9	13.64	57	86.36

Fig 1: Incidence of gallstones in patients taking oral contraceptive pills (Total Married Female- 66)

DISCUSSION

The present study was undertaken to find out the possible association of cholelithiasis with age and use of OCP.

The occurrence of gall-stones is substantially higher in women than in men but the sex difference decreases after the menopause.¹²

Administration of Oestrogen to postmenopausal women and Oestrogen therapy to men with prostatic carcinoma has similar lithogenic effects. Therefore, Oestrogen has been proposed to be an important risk factor for the formation of cholesterol gallstones.¹³ Increases in serum cholesterol and serum triglycerides have been reported frequently in pre-menopausal women taking oestrogen preparations.¹⁴

As per literature, so far females have been the easiest victim of Gall Stone Disease .It was documented that human Gall Bladder wall have oestrogen and progesterone receptors.¹⁵

One study having sample size of 121 female gallstone patients, reveals that 78 respondents were taking OCPs containing oestrogens and 43 were not taking OCPs .This result is supported by other studies also which also concludes that bile becomes more lithogenic when women are placed on OCPs containing oestrogen.¹⁶

Another study that researched on oestrogen receptors and cholesterol biosynthesis found that oestrogen in particular stimulates the HMG-Co-A reductase enzyme causing increased synthesis of cholesterol and thus putting women at an increased risk of supersaturation. Further supporting the link between Oestrogen and gallstones, it was determined that postmenopausal women on oestrogen replacement therapy were found to have an increased incidence of gallstone.¹⁷

Estrogens appear to influence several key steps in gallstone formation. One study of postmenopausal women found that exogenous conjugated equine oestrogen (CEE) given orally or oestradiol given transdermally, decreased nucleation time in vitro, increased cholesterol saturation index and increased biliary arachidonate and prostaglandin E2 levels. The pattern of findings resulted in both an increased propensity to form cholesterol crystals and an excess saturation of biliary cholesterol, which along with hypo motility of the gallbladder are thought to be key requirements for gallstone formation.¹⁸

CONCLUSION

In conclusion, the study shows that there is a slight preponderance of the incidence of gall stone in 2nd half of the 3rd decade of life. The Percentage of incidence of stones in this decade is 25%. Moreover the study shows lower incidence of gallstone in patients taking oral contraceptive pills, in contrary to previous studies reporting the higher incidence in such cases.

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