CHAPTER – I
INTRODUCTION

Contraception was a topic of discussion among ancient Greek philosophers and poets like Aristotle, Plato, Heriod and others, more than 2400 years ago. The first reference to contraception in China is found 1300 years ago. One of the major development of fertility control in the twentieth century has been the promotion of reproductive choice. This has become particularly important to women especially with regard to their contraceptive choice and to the development of contraceptives.(s.k.chaudhary 2001)

The use of oral contraceptives (OCs) has been growing since the 1970s over 100 million women in the world are using OCs now (WHO, 1998); it is mostly used in the developed countries but is becoming more and more popular in the developing countries as well.

In 1998, in the developed countries, an estimated 14% of married women of reproductive age (MWRA), numbering about 24 million in all, used OC, whereas in the developing countries 6% of MWRA of about 39 million used then.

In India OC use is still very poor (only 3.1% of MWRA is 1998) although this marks an increase from about 2% in 1982 of all methods of contraception, it is next highest is incidence after sterilization of (both males and females). The Government of India has lately beez promoting pills, and has started supplying one type of pill (Mala N) through family welfare clinics and another type of pill (Mala-d) at a subsidized price. The use of pill has increased lately particularly among the elite women.

When oral contraceptives were introduced in the United States in 1960, many women believed they had found the answer to the need for convenient

safe and reliable birth control. By 1965, "the pill" was America's leading contraceptives (WHO, 1998). With the 1970's came disillusionment,, the pill was not perfect while it was highly effective and convenient, it had many minor side effect and a serious ones.(speroff,1996)

Evidence suggesting that oral contraceptives might have effects on health. It is currently believed that the most important effect is an increase in the risk of cardiovascular disease especially the risk of venous thromboembolic disease, stroke, and myocardial infarction. One possible mechanism of increased risk for myocardial infarction is the effect of hormonal contraceptives on lipid metabolism. Some investigators have found that the concentration of Apo A-1 & Apo-B are better predictors of coronary artery disease (Kjeld et al 1976), than are measurements of total plasma lipids or lipoproteins, because the apolipoproteins regulate lipoprotein metabolism, bind the transport lipids, react with tissue receptors and are the agents of genetic disorders. Apolipoproteins A-1 is the best predictor of atherosclerotic risk in patients, undergoing coronary atheriography. Higher levels of apolipoproteins A-1 are associated with a decreased prevalence of obstructive coronary lesions. Indeed, apolipoproteins A-1 is found to be a better coronary artery disease predictor than either total cholesterol or high-density lipoprotein. Recent studies show that plasma apolipoprotein- B concentration may also be indicators of coronary risk.

Oral contraceptives are broadly divided into two groups, combined pills and progestrogen only pills or mini pills. The most popular contraceptives are combined pills, these are combined formulation of two synthetic hormones (an estrogen and a progestrogen) similar to the hormones the ovary normally produces (Wentz 1988). Combined pills are divided into sub groups. Low

dose pills containing ethinyl estradiol (EE) of less than 0.05 mg in each pill and High dose pills containing 0.05 mg ethinyl estradiol in each pill. High dose combined pills, such as were used earlier, have been completely abandoned for regular use due to their greater side effects and major complications. However, they are still being used for 1-3 cycles sometime.

When studies linked the amount of estrogen in birth control pills with serious side effects including blood clot. heart attaks and strokes, researcher developed new pill formula with less estrogen. They also developed a progestogen only pill known as the mini pill **(Internet download NICHD, 2003 and Facts and comparisons, 1999).** Mini pills (low dose progestins) contains even less progestogen than low dose combined pill, which may make the minipill the safest oral contraceptive known.

Today the Food and Drug Administration urges physicians to start patients on combined pills with no more than 50 micrograms of estrogen and if possible, one of the newer "low dose" combined pill with only 30 or 35 µg fo estrogen. **(WHO, Geneva 1987)**

Major studies have concluded that switching from higher doses to pills with 50 micrograms of estrogen cuts the blood clots risk substantially. Recent research suggests that pills with less than 50 µ grams of estrogen cut the risk even further **(WHO, 1998; Wentz 1988)**.

Oesterogen used in OCs are of two types: ethinyl estradiol (EE) or its 3-methyl ester deviation (mestranol) which is promptly metabolized to EE. Mestranol is slightly less potent than the same microgram weight of potent ethinyl estradiol. The risk of thrombolism is greater with mestranol **(Tindall, 1987)** hence nowadays mestranol is much less used in most countries. Progestogens (progestins) or progestational agent are compounds which

produce secretary changes in the oestrogen primed endometrium. But they differ in their biological effect on other organs or systems.

Combined pills including low dose inhibit ovulation by suppressing hypothalmic releasing factors, which in turn leads to inappropriate secretion of FSH & LH, these hormones are maintained at constant low levels similar to those seen in the proliferative phase of the cycle **(Kjeld et al. 1976)**. As a result no LH surge occurs and ovulation is suppressed. The progestogen components preferentially inhibit the preovulatery LH surge, with a lesser effect upon FSH function.

The oestrogen of OCs on the other hand, preferentially inhibits FSH & it is dose dependent **(Wentz, 1988)**. OCs alter maturation of the endometrium, rendering it unsuitable for implantation of the fertilized ovum. These changes which resists implantation are less marked with (multiphasic pills). Both kinds of pills make the cervical mucus thick and "inhospitable" to sperm, discouraging entry to the uterus. Many of the risks of OCs suspected or reported in 1960s and 1970s.

Low dose combined oral contraceptives (COCs) are being used since 1980s and recent reports have established the fact that the risks of low dose pills are much less than those of high dose pills. Information is now available about the risks of the low dose COs used nowadays from recent studies, including the WHO collaboration study of cardiovascular disease and steroid hormone contraception conducted in 21 centres of different countries in Africa, Asia, Europe and Latin America **(WHO, 1998)**.

Women who do not smoke, who have their blood pressure checked, and who do not have hypertension or diabetes, are at no increased risk of myocardial infarction, if they use low dose COCs. There is less risk of

myocardial infarction they use low dose OCs containing desogestral or gestodene than in users containing levonorgestrel is yet to be substantiated. In women who do not smoke and who do not have hypertension, the relative increased risk is about 1.5 in current users of low dose OCs, compared with that of non-users.

Current users of low does COCs have a low absolute risk of UTE mainly because incidence of VTE is very low in non-pregnant women. COCs containing desogestrel and gestodene may carry a slightly greater risk of VTE than COs containing levonorgestrel

Low dose OCs cause modest elevations in blood pressure particularly in women over 35 which may increase the risk of arterial disease **(WHO, 1998)**. This may be effect of the progestogen.

Among COCs users, Cardiovascular complications may mainly due to alternation in coagulation system, brought about by the estrogen component. Progestogens are associated with the increase of low density lipoprotein cholesterol and a decrease of high density cholesterol, which enhance the risk of atheroslerosis, coronary heart disease and cerebral thrombosis but estrogen have the opposite effect, and these actions, seem relatively balanced in low dose COC. To date there is no data of suggest that low dose COCs have clinically significant adverse effects on the lipid profile **(IPPE, 1998)**.

The objective of the present study is comparison between high and low dose hormonal contraceptives on serum lipids and Apolipoproteins in relation to the development of vascular complication risks and effect of oral contraceptives on the levels of serum female sex hormone i.e., Oestrogen, Progestins, LH & FSH and Prolectine hormones.