Serum Glucose Concentrations of Women on Depo-Provera Contraceptive Attending Family Planning Unit of Jos University Teaching Hospital.

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ABSTRACT

Contraceptives are devices, drug or agents that are used to prevent conception. The serum glucose concentrations of women on Depo-Provera contraceptive were investigated with the aim of establishing whether Depo-Provera can affect glucose metabolism of those who use it as a means of family planning. A total of one hundred (100) women of ages between 19-47 years who came for Depo-Provera administration for the first time were recruited for this study. Ethical clearance was sorted for and obtained from ethical committee Jos University Teaching Hospital before carrying out this study. Parameters such as tribe, occupation, body weight and blood pressure were collected and analysed. Blood samples were collected and analysed for serum glucose concentration before and after Depo-Provera administration using glucose oxidase method. Tribe and occupation were analysed based on percentage, and result obtained for tribal classification indicates that Igbo has the least number of participants while other minor tribes grouped together as others has the highest number of participants. Occupational classification indicates that, health worker have the least number of participants while business women have the highest number of participants. The mean and standard deviation of age, body weight, blood pressure and glucose concentration were calculated. Result indicates that there was no significant change in body weight and blood pressure one month after Depo-Provera administration. Glucose concentration was further analysed using students t-test and result indicates, there was no significant change in serum glucose ($p>0.05$) after comparing glucose value obtained before and one month after Depo-Provera administration.

Key Words: Serum glucose, Contraceptives, Depo-Provera, Family Planning, Tribe, Occupation, Bodyweight, Blood Pressure.

1.0 GENERAL INTRODUCTION

Contraceptives could be described as a device, drug or chemical agents that is used to prevent conception. Contraceptives brings about contraception which can be defined as an intentional prevention of conception or impregnation through the use of various devices, agents, drugs, sexual practices and surgical procedures (Dictionary of English Language, 2007). The use of contraceptives are means of family planning and family planning is the use contraception to limit or space out the numbers of children born to a couple (Concise medical Dictionary, 2003). There are different means of contraception namely:-

1. By the use of condom and diaphragm
2. By the use of oral contraceptive pills
3. By the use of Injectable
4. By the use of contraceptive implant
5. By the use of intrauterine device
6. By voluntary surgical contraception.
7. By natural contraception.

The use of condom and diaphragm, surgical contraception are mechanical means of contraception while oral contraceptive pills are synthetic female hormones containing estrogen and progestin taken either alone or in combination by women in order to prevent pregnancy. Injectable are long-acting contraceptive containing combined estrogen and progestin or progestin only and are given intramuscularly. Implants are progestin-only contraceptive inserted under the skin of a woman's upper arm through a minor surgical procedure. Intrauterine device (IUD) is a small plastic object impregnated with hormones that is inserted in the womb to prevent pregnancy. Voluntary surgical contraception (VSC) such as tubal ligation or conclusion in females and vasectomy in males is a permanent method of contraception which involves a minor surgical procedure performed to prevent pregnancy. Natural contraceptive method is a method in which sexual intercourse is restricted to the safe periods (FMOH, Nigeria 2005). This study will concentrate in progestin only injectable contraceptive; medroxyprogesterone acetate DMPA (Depo Provera) which is injected into users to prevent pregnancy. Glucose is a monosaccharide which is gotten mainly from carbohydrate rich food but can also be synthesized by the body during high demand through gluconeogenesis by the human liver. Glucose is a primary source of

energy for humans. The nervous system including the brain totally depends on glucose from the surrounding extracellular fluid for energy. Nervous tissue cannot concentrate or store carbohydrate, therefore it is critical to maintain a steady supply of glucose to the tissue. For this reason, the concentration of glucose in the extracellular fluid must be maintained in a narrow range. When the concentration falls below a certain level, the nervous tissue lose the primary energy-source and are incapable of maintaining normal function (Michael, *et al.* 2005). Glucose is required by the body to produce a universal energy currency known as Adenosine triphosphate (ATP) needed by the body for its optimum physiological function.

Carbohydrate containing foods when ingested are metabolized to release glucose into the blood which by the action of a hormone: insulin is taken into the cells either for energy production or storage which is determined by the load ingested. The glucose left in the blood after insulin action is referred to as blood glucose or serum glucose and its established reference range is between 3.9-6.mMol/L and values greater or lower than this range is of clinical significance (Spellacy, *et al.* 1972).

1.1 BACKGROUND STUDY

Contraceptives are means of family planning yet their use is not without side effects. It has been reported that high dose hormonal contraceptive will cause glucose intolerance among users (Fahmy, *et al.* 1991). Synthetic steroid hormonal contraceptive are known to affect carbohydrate metabolism by increasing free fatty acids which is associated with insulin resistance state and glucose intolerance (Pouliot, *et al.*1990). Shamma, *et al* (1995) reported in their study that impaired glucose tolerance has been greater in users of birth control pill and are usually reversible after discontinuation of the pill. The insulin resistance induced by hormonal contraceptives is associated with reduced peripheral tissue insulin sensitivity.

In normal subjects, evidence is lacking that hormonal contraceptives can cause true diabetes. It is suspected however that in those with latent diabetes, the disease may be precipitated. There may also be renal glucosuria in subjects taking hormonal contraceptives. It is possible that the incidence of clinical diabetes mellitus may be increased in those women with latent diabetes.

From various literature, it is unknown whether changes in glucose tolerance occur in black women using contraceptives since most of the reports so far centers around Caucasian race {i.e.

white women} and it is also unknown whether age, weight, blood pressure and tribe among the black women using Depo Provera has any effect on glucose tolerance.

There is still a practical concern about the effects of synthetic steroid hormonal contraceptives on glucose concentrations because very little is known about the effects of estrogen and progestin or progestin- only on serum glucose concentration to healthy women. The common consensus on this topic believes that most women using combined oral contraceptive pills have elevated blood glucose (Tankeyoon, *et al.* 1996). Although, only about 3-5% of oral contraceptive pills users are likely to develop significance hyperglycemia (Gaspard, *et al.* 2003), it is still prudent to examine individuals who may be at greater risks, for example, women of child bearing age, women with strong family history of diabetes and obese women, since oral contraceptive pills and Depo-Provera are grouped among hormonal contraceptives which exhibit similar characteristics. This is even more so since there is evidence that hyperglycemia is a major cause of diabetes mellitus which has an increase in mortality rates (Kjos, *et al.* 1998).

1.2 LITERATURE REVIEW

1.3 DEFINITION OF CONTRACEPTIVES

Contraceptives are devices, drugs or chemical agents that are used to prevent conception or are capable of preventing pregnancy.

Contraceptive brings about contraception; which is intentional prevention of conception or impregnation through the use various devices, agents, drugs, sexual practices and surgical procedures.

According to Concise Medical Dictionary (2003), family planning is the use of contraception to limit or space out the number of children born to a couple.

1.4 Forms of Contraception

Federal ministry of Health Nigeria, National Family Planning /Reproductive Health (service protocols) in conjunction with United States agency for international development (USAID) (2005), states that there were different forms of contraception such as,

A. The use of oral contraceptive pills

B. Injectable

C. Contraceptive implant

D. Intrauterine Device

E. Voluntary Surgical Contraception

F. The use of Condom and diaphragm

G. By natural contraception

Oral contraceptive pills, injectable, contraceptive implants, intrauterine device are classified as hormonal contraceptives; voluntary surgical contraception and use of condom and diaphragm are classified as mechanical contraceptive while Natural contraception is classified as fertility awareness method.

Oral contraceptive pills are synthetic female hormones, estrogen and progestin taken alone or in combination by women in order to prevent pregnancy. Oral contraceptive pill types are:

a) Combined oestrogen and progestin contraceptive pills (COCs)

b) Progestin -only pills (mini pills)

c) Emergency contraceptive pills (ECPs).

Injectable are long acting contraceptives containing combined estrogen and progestin or progestin only and are given by intramuscular injection.

Injectable types are:

a) Progestin - only which comprises

(i) Norethisterone Enanthate (Noristerat)

(ii) Depot-Medroxy-progesterone Acetate (DMPA, Depo Provera).

b) Combined injectable contraceptive which comprises

(i) Cyclofem

(ii) Mesigyna (FMOH, Nigeria, 2005).

Contraceptive implants are progestin-only contraceptive inserted under the skin of a woman's upper arm through a minor surgical procedure. Contraceptive implant types are:

a) Norplant (containing 36mg levonorgestrel)

b) Jadelle (containing 75mg levonorgestrel) it is an improved version of Norplant.

c) Uniplant (containing nomegestrol acetate)

d) Implanon (containing progestin- 3- ketodesogestrel).

Intrauterine devices (IUD) also called intra uterine contraceptive device (IUCD) is a small plastic object impregnated with hormones that is inserted in the womb to prevent pregnancy. There are two types of intrauterine device- medicated and non-medicated.

A) Non-medicated IUDS are made of inert plastic material e.g. Lippes loop.

B) Medicated IUDS are made of plastic with copper wound round the sleeve or impregnated with hormones which are released in small amounts over time, these include

1) Copper T (Cu-T 380A)
2) Multiload (Cu - 250 and Cu - 375)
3) Progestasert - contains progesterone
4) Norgestrel - T, contains Levonorgestrel (FMOH, Nigeria, 2005).

Voluntary surgical contraception (VSC) is a permanent contraceptive which involves a minor surgical procedure performed on the client to prevent pregnancy. There are two types of surgical contraception - Vasectomy and Tubal Occlusion.

A) Vasectomy is the tying and cutting of the male tubes (vas Deferens) to prevent passage of spermatozoa into the seminal fluid. Methods of tying or blocking the vas deferens are:

1) Ligation - removal of segment of vas deferens and simple ligation

2) Coagulation - electro coagulation of the mucosa at both ends

3) Fascia barrier- removal of a segment of vas deferens and closing of fascia over one end of the vas deferens.

B) Tubal occlusion is the blocking or cutting and tying of fallopian tubes to prevent the passage of ovum through the fallopian tubes to the womb. Methods of occlusion are:

1) Pomeroy
2) Parkland
3) Clips e.g. Filschie clip
4) Yoon/Fallopian rings (FMOH, Nigeria, 2005).

The use of condom and Diaphragm; Diaphragm is a dome shaped rubber cup with a flexible rim. It is inserted into the vagina before intercourse so that the posterior rim rests in the posterior fornix and anterior rim fits snugly behind the pubic bone. The dome of the diaphragm covers the cervix. It is best used with a spermicidal cream which is poured inside the dome so that it is in

contact with the cervix when the diaphragm is in place. This barrier prevents sperm from reaching the woman's ova during intercourse.

Condoms are barriers to the passage of sperm between the genital tracts of sexual partners. They are divided into two types - male and female condoms. The male condom is a thin latex rubber sheath that is worn over the erect penis before penetration into the vagina. It acts as a barrier preventing semen from entering the vagina during intercourse.

Natural contraception comprises of:

A) **Rhythm method:** A contraceptive method in which sexual intercourse is restricted to the safe period at the beginning and end of the menstrual cycle. The safe period is calculated either on the basis of the length of the menstrual cycle, for example minus 18 days from the shortest period and 11 days from the longest period and the fertile period starts from the remainder of the shortest period to the remainder of the longest period, or by-reliance on the change of body temperature that occurs at ovulation.

B) **Billings's method:** This is the change that occurs with ovulation in the stickiness of the mucus at the cervix of the uterus. The method depends for its reliability on the women having regular periods and its failure rate is higher than with other methods. Other natural methods that exit are sympto-thermal, Lactational Amenorrhoea Method (LAM) (FMOH, Nigeria, 2005).

1.5 Hormonal Contraceptives

Pincus, G, (1958) defined hormonal contraceptives as an agent which contains synthetic female hormones estrogen and/or progesterone (progestin) that inhibit ovulation and alter the body's metabolism. Hormonal contraceptives come in different forms such as pills or oral contraceptive agents, Injectable, implants and intrauterine devices.

1.6 General Principles of Hormonal Contraceptives

Hormonal contraceptives interfere basically with the production of hormones; the early-cycle increase in follicle stimulating hormone (FSH) and the mid-cycle luteinizing hormone (LH) surge are absent preventing ovulation (Pincus, G, 1958). In women, FSH stimulates the growth of ovarian follicles and in the presence of LH promotes secretion of estrogens by the maturing follicles. LH in females causes release of the ovum from the ovarian follicle which previously has

matured under the influence of FSH and induces the formation of the corpus luteum from the ruptured follicle. The corpus luteum then secretes progesterone and estradiol under the influence of pulsatile LH release (Carl & Edward, 2001).

Pregnancy is also prevented by an alteration in the cervical mucus which becomes thick and viscous to inhibit sperm penetration into the uterus during intercourse. Changes in the endometrium occur so the glands do not produce sufficient glycogen to support the embryo in the endometrium prior to implantation. Finally, the ovaries are less responsive to the same amount of gonadotropins (LH, FSH), so it does not release an egg (Pincus, G, 1958). At the beginning of the menstrual cycle, follicle stimulating hormone increases stimulating ovarian follicular growth and maturation. As a result, level of estrogen and progestin increases. When estrogen reaches a critical level, it stimulates the hypothalamus- pituitary axis to produce more luteinizing hormone with a smaller surge of follicle stimulating hormone. The increased levels of luteinizing hormone and follicle stimulating hormone cause the release of an ovum. Progesterone and estrogen secretion increases at this time to allow the uterus to prepare for the ovum implantation when fertilized by a sperm. When no fertilized egg is present for implantation, the estrogen and progesterone levels decrease and mucosal lining is sloughed off. The fall in estrogen and progesterone levels, stimulates the hypothalamus and pituitary gland to secrete follicle stimulating hormone (FSH) and the cycle repeats itself (Abma, *et al.* 1997).

1.7 Risks and Benefits of Hormonal Contraceptives.

There are benefits and risks of hormonal contraceptives. Some health benefits include a decreased risk of anemia from less bleeding, correcting menstrual disorders, reducing the incidence of some diseases that occur due to reduced immunity and protecting against other diseases such as hypertension and certain cancers (Risser, *et al.* 1999). Risser, *et al.* (1999) also stated that some of the negative side effects of hormonal contraceptives, which include nausea, vomiting, breakthrough bleeding, weight gain, headache, dizziness, fatique, nervousness, mood changes, decreased Libido, scanty periods, amenorrhea, breast tenderness and facial pigmentation.

Lewis, *et al* (1996) stated that serious health problems such as venous thromboembolic disease (a blood clot that blocks a vein) and cardiovascular disease specifically stroke and myocardial

infarction may occur with use of hormonal contraceptives. Martins, *et al* (2006) in their study highlighted that hormonal contraceptives prevent bone mineral loss, a risk factor for Osteoporosis. The increased estrogen in hormonal contraceptives decreases the body's ability to use the calcium stored in the bones thereby protecting against bone loss. But other studies by Scholes, *et al* (2005) and Cromer, *et al* (1996) showed mixed results with some showing that hormonal contraceptives prevents loss of bone mineral density (BMD) while others showed an increased loss of bone mineral density.

1.8 Nutritional Implications of Hormonal Contraceptives.

The estrogen and progesterone in hormonal contraceptives induces changes in body's metabolism both directly and indirectly (Machado, *et al.* 2004). Indirectly, they cause the adrenal cortex to produce the stress hormone cortisol. The increase in cortisol has an effect on protein, carbohydrate and fats metabolism (Machado, *et al.* 2004). In fat metabolism, the increase in serum triglycerides and very low density lipoprotein (VLDL) is related to the estrogen level in hormonal contraceptives. The increase in production has not been shown to promote atherosclerosis and in many cases the levels are within normal ranges (Gaspard, *et al.* 2004). The good news is that hormonal contraceptive use does not seem to affect mortality related to cardiovascular diseases (Gaspard, *et al.* 2004). The increased cortisol appears to have an effect on lipid metabolism independent of the effect of estrogen and progesterone. Cortisol mobilizes fatty acids from adipose tissue and cells increasing circulating free fatty acids (FFA) which has a ketogenic effect. This effect is reduced in the low dose hormonal contraceptives (Pelkman, *et al.* 2001). Pelkman, *et al.* (2001) also stated that any woman with a family history of heart diseases or elevated blood lipids is at increased risk for plaque buildup, a risk factor in coronary heart disease. These women should be monitored during hormonal contraceptives use and encouraged to make dietary changes to decrease the amount of fat and cholesterol in their diet.

1.9 Hormonal Contraceptives and Carbohydrate Metabolism

Glucose intolerance and hyperinsulinemia are caused by changes in carbohydrate metabolism associated with hormonal contraceptives. Progesterone has more of an effect on carbohydrate metabolism than estrogen by increasing insulin secretion and insulin resistance of cells. Not all progesterone has the same effect on carbohydrate metabolism. Those that are more androgenic,

19-nortestosterone and norgestrel derivatives have a more profound effect than the less androgenic progestogens - desogestrel, and norgestimate. Estrogen may impair the initial secretion of insulin by the pancreas but does not have a sustained effect on carbohydrate metabolism (Nessa, *et al.* 2005). Nessa, *et al,* (2005) found some slight changes in fasting insulin and glucose levels but they were not statistically significant and had no clinical relevance. Average increase in blood glucose are approximately 0.56mMol/L in their study and in normal individuals, this is not enough to cause problem as the body can utilize it. In individuals susceptible to diabetes, the change in glucose tolerance may pose a slight risk of causing diabetes to surface or may impact present treatment in a person with diabetes.

The newer progesterone (ethinylestradiol combined with drospirenone) did not seem to alter carbohydrate metabolism and have a less pronounced effect on carbohydrate metabolism than nortestosterone and levonorgestrel (Gaspard, *et al.* 2003).

2.0 Hormonal Contraceptives and Vitamin B6 Metabolism.

Vitamin B6 (Pyridoxine) is required for functions in the body that involve amino acids and proteins. The conversion of tryptophan to niacin and serotonin requires vitamin B6 and in vitamin B6 deficiency the body cannot complete this conversion to the end product possibly causing changes in behavior. It then excretes compounds that are not fully metabolized indicating that a deficiency exists. Masse, *et al.* (1996) in their study found out that women using hormonal contraceptives may have inadequate vitamin B6 because there is an increased excretion of intermediary tryptophan metabolites involved in the conversion of tryptophan to niacin indicating insufficient vitamin B6 to complete the metabolic process. Altered tryptophan metabolism due to a vitamin B6 deficiency may explain behavioral changes in women using hormonal contraceptives such as complaints of anxiety, lethargy, depression, irritability and emotional instability as indicated in the study conducted by Masse, *et al.* (1996).

Masse, *et al.* also investigated the effect of newer hormonal contraceptive (ethinylestradiol combined with Triphasil) on 23 young women and found out that all had adequate vitamin B6 intake and their plasma and erythrocyte vitamin B6 levels were adequate, but a disturbance in vitamin B6 metabolism was detected. However, Lussana, *et al.* (2003) did find significantly lower vitamin B6 levels in women using hormonal contraceptives compared with nonusers.

2.1 Hormonal Contraceptives and Metabolism of other Vitamins and Minerals.

VITAMIN B12: Vitamin B12 levels are decreased in the plasma but not in erythrocytes. Green, *et al.* (1998) found that adolescent girls using hormonal contraceptives had a 33% reduction in serum vitamin B12 levels. The question remains whether the changes seen in vitamin B12 are caused by a redistribution of vitamin B12. Intake of vitamin B12 is important due to its essential role in fetal development, so any woman who gets pregnant after discontinuing prolonged hormonal contraceptives use should pay attention to her vitamin B12 status and ensure adequate intake or consider a supplement of vitamin B12. Sources include dairy products such as liver, milk, beef and pork meat, others are chicken, eggs, mollusks and yoghurt.

FOLIC ACID; Folic acid levels in the serum and red blood cells have been determined to be low in hormonal contraceptives users. Whether it is a problem of absorption, uptake or utilization by the tissue is unclear (Steegers-Theunissen, *et al.* 1993). Folic acid is critical for normal fetal development especially between the 18^{th} and 27^{th} day of pregnancy when a woman may not know she is pregnant. During this time, the neural tube develops and then closes. It is within this structure that the central nervous system (CNS) develops.

Centers for disease control and prevention (2004) conducted a study in United States and stated that if a woman has been using hormonal contraceptives and has low serum folic acid levels, there could be a problem during the first trimester from inadequate folic acid. In 1992, the United States public health service recommended that all women of child bearing age who are capable of becoming pregnant should consume 400 micrograms of folic acid per day for the purpose of reducing their risk of having a pregnancy affected with spina bifida or other neural tube defects.

IRON: Iron status in women using hormonal contraceptives improves because of temporarily stoppage or scanty monthly menstrual flow. Any increase in transferrin, the protein carrier for iron increases the amount of iron in the blood (Steegers-Theunissen, *et al.* 1993). Total iron binding capability increases significantly as well. Decreased menstrual blood loss decreases the monthly iron loss. These factors decrease the likelihood of iron deficiency anemia in women using hormonal contraceptives (Steegers -Theunissen, *et al.* 1993).

2.2 Hormonal Contraceptives and Bone Mineral Density.

The effect of hormonal contraceptives on bone mineral density in women appears to be related to the type of hormonal contraceptives used; depot- medroxyprogesterone acetate (Depo-Provera or DMPA) injections, levonorgestrel (Norplant) sub dermal implants or hormonal pills. Researchers are looking to see how each type of hormonal contraceptives impacts bone density in the short term and what if any, are the long term clinical consequences. Cromer, (1999) stated that many of studies done to date are contradictory due to differences in design, techniques for measuring bone density, age of the participant and type of hormonal contraceptives in use. With that in mind, it does appear that hormonal pills and Norplant implants have a positive effect on bone mineral density (BMD), while DMPA or Depo-Provera injection may have a slightly negative effect on bone mineral density, although the effect is reversible once the injections are stopped (Wanichsetakul, *et al.* 2002). In young women, it appears that the use of DMPA also causes a loss of bone mineral density in the hip and spine that is greater than in older women and was reversible when the contraceptive was discontinued (Scholes, *et al.* 2005).

In a review of the literature from (1996) through (2005), by Martins, *et al.* (2006) they concluded that the results of the combined studies investigating combined hormonal contraceptives with bone mineral density are inconclusive. However, there did appear to be a trend based on age; - Adolescents and young women had generally lower bone mineral density compared with girls who were not using hormonal contraceptives. Peri-menopausal and post-menopausal women hormonal contraceptive users had same bone mineral density as compared to non-users of the same age bracket. Regardless of the choice of hormonal contraceptive, adequate calcium intake is essential. Increasing calcium intake to recommended dietary allowance of 800mg/day in adult female is able to protect young women from loss of bone mineral density while using hormonal contraceptives (Martins, *et al.* 2006).

2.3 ORAL CONTRACEPTIVE PILLS AND ITS METABOLIC/CARDIO-

VASCULAR EFFECTS.

Oral contraceptive pill is a class of hormonal contraceptives. The possibility that oral contraceptive pills (OCP) may have adverse metabolic/cardiovascular effects was raised as long ago as (1969) when Wynn & Doar, performed oral and intravenous glucose tolerance tests in 91 normal women before and during oral contraceptive pill therapy. Both tests showed

deterioration of glucose tolerance and increased insulin concentrations in the women studied and 13% developed clinical diabetes. In their discussion, the authors commented that the important question of all, namely whether the impairment of glucose tolerance and increased plasma insulin levels, will accelerate the rate of development of clinical diabetes and also of atherosclerosis requires careful consideration. The metabolic impact of current commonly used oral contraceptive pill (ethinylestradiol) was discussed and highlighted in a comprehensive review by Godsland, (1996). He showed that oral contraceptive pills were generally associated with reduced glucose tolerance, hyperinsulinemia and insulin resistance. He also concluded that the estrogen component was primarily responsible for this change. It was also shown that more androgenic progestin in oral contraceptive pills could further impair insulin action. Oral contraceptive pills increase plasma triglycerides and may increase plasma high density lipoprotein (HDL) cholesterol which is beneficial for the heart, especially oral contraceptive pill containing, progestin of low androgenicity (Baillargeon, et *al.* 2005). The relationship of oral contraceptive pill with myocardial infarction, stroke and venous thromboembolic diseases was reviewed by the practice committee of the American society of reproductive medicine and the risks were considered to be low in young patients and non-smokers. However, a more recent meta-analysis of the association of current use of low-dose oral contraceptive pill and cardiovascular arterial disease demonstrated increased risk of cardiac and vascular arterial events including a significant risk of vascular arterial complications even with less androgenic oral contraceptive pill (Baillargeon, *et al.* 2005).

2.4 Emergency Contraceptive and its Mechanism of Action

Emergency contraceptive pills (ECPs) are an important option for women who have recently had unprotected intercourse or a contraceptive failure and who do not want to become pregnant. Mifepristone, the generic name of RU468 is a new class of drugs known as anti-progesterone that can be used as an emergency contraceptive. The anti-progesterone drug, Mifepristone is a synthetic steroid that prevents progesterone and glucocorticoids from binding to hormone receptors because mifepristone can block ovulation (Von look and Von Hertzen, 1993). It seemed probable that the compound would be effective in emergency contraception. This was confirmed by two randomized trials from World Health Organization (WHO) about post-coital contraception

with mifepristone and alternative treatments in post-coital contraception (WHO, 1998). Progesterone is involved before ovulation, in follicular maturation and the process leading to ovulation. Helena and Paul (1996), in their study stated that progesterone is a major constituent of follicular fluid and may be the component responsible for inducing the movement of spermatozoa into the ovum for fertilization. It may also produce structural changes that facilitate the entry of spermatozoa into the ovum. It influences the transport of the fertilized egg through the fallopian tube and causes endometrial changes that are required for successful implantation and establishment of pregnancy. Data from Helena and Paul, (1996) suggest that for mifepristone to exert a blocking effect on ovulation, the mifepristone has to be given before the onset of the Luteinizing hormone (LH) surge, if the surge has already started, it may be too late to inhibit ovulation with mifepristone.

2.5 Depo Provera and its Mechanism of Action

Depot- medroxyprogesterone acetate (DMPA) also known as Depo-Provera is an injectable synthetic hormonal contraceptive popularly used in family planning unit of Jos University Teaching Hospital for intentional prevention of conception or pregnancy. It is injected intramuscularly into users for every 12 weeks in order to maintain its effective contraception. Depo-Provera acts by inhibiting the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) that stimulate the ovarian follicular growth and maturation thereby inhibiting ovulation. It has been reported that high dose hormonal contraceptive will cause glucose intolerance among users (Fahmy, *et al.* 1991) and synthetic steroid hormonal contraceptive which Depo-Provera belongs to are known to affect carbohydrate metabolism by increasing free fatty acids which is associated with insulin resistance state and glucose intolerance (Pouliot, *et al.* 1990).

Depo-Provera also causes an alteration in the cervical mucus which becomes thick and viscous thereby inhibiting sperm penetration into the uterus. With continuous use of Depo-Provera, there is less than 1% chance of experiencing a contraceptive failure (Rock, *et al.* 1957).

2.6 COMPOSITION OF DEPO PROVERA (MEDROXY PROGESTERONE ACETATE).

Depo-Provera is available in 1ml vials and each vial contains; medroxy progesterone acetate (150mg), preservatives which include methylparaben 0.014%m/v and propylparaben

0.015%m/v. The recommended dose is 150mg of Depo-Provera every three months administered by deep intramuscular injection. To increase assurance that the patient is not pregnant at the time of the first administration, it is recommended that this injection be given during the first 5days after the onset of a normal period or before the sixth week postpartum (Pharmacia South Africa, 2005).

The side effects of Depo-Provera are usually not so serious; some of the side effects include thromboembolic diseases: thrombophlebitis and pulmonary embolism, nervousness, insomnia, fatique, depression, dizziness, headache, urticarial, acne, nausea, abdominal discomfort, diarrhoea, breast tenderness, amenorrhea, prolonged irregular bleeding, loss of Libido, dysmenorrhoea and delay in ability to become pregnant (Pinkston and Miller, 1995). Other side effects include slight increased risk of breast cancer especially for women under age 35, Osteoporosis-decrease in the amount of calcium in their bones which can increase their chance of bone fractures (Cromer, *et al.,* 1996). The rate of calcium loss from the bones is greatest in the early years of use but adequate calcium in the diet or a calcium supplement can help prevent Osteoporosis in all women (Cromer, *et al.* 1996). As has been stated by Rock, *et al.* (1957) and Pharmacia South Africa (2005), Depo-Provera is an effective hormonal contraceptive which can ensure non contraceptive failure when in use.

2.7 MATERIALS AND METHOD

2.8 RESEARCH DESIGN:

This study was planned and conducted with the approval of the ethical committee of Jos University Teaching Hospital and aimed at finding out the serum glucose concentration of women on Depo-Provera contraceptive. A total number of one hundred (100) women aged between 19-47 years were used for the study. Their serum glucose concentrations were analysed before and one month after Depo-Provera administration and results compared to find out whether Depo-Provera injectable have any significant alteration on glucose concentration of users. Confirmed diabetics patients were excluded from this study. Relevant information such as age, tribe, occupation, body weight and blood pressure of participants were also obtained.

2.9 STUDY SUBJECTS

The subjects used for this study were women aged between 19-47 years who came for Depo-Provera contraception for the first time and were willing to participate in the study. They were informed of the study while attending family planning unit of Jos University Teaching Hospital (JUTH) and their consent obtained.

3.0 APPARATUS

Spectrophotometer (TRSP – 721), incubator (memmert), centrifuge (Cel-tech), weighing balance, refrigerator and freezers, Automatic pipettes, Pasteur pipette, 1ml pipette, test tubes, test tubes racks, plain tubes, 5ml syringes and needle, medicated cotton wool, tourniquet, sphygmomanometer.

3.1 COLLECTION OF BLOOD SAMPLE

Blood (5ml) was drawn from fasting test subjects via the antecubital vein by venepuncture using sterile needle and syringes for the collection. The blood was allowed to cloth in a clean plain tube and then centrifuged at 3000rpm for 10minutes to obtain serum sample which was transferred into a clean plain labelled tube prior to analysis. All sera samples were analysed immediately after separation from the whole blood using the glucose oxidase method.

3.2 REAGENTS

Glucose reagent used in this study was of standard quality, commercially prepared by Randox Laboratories, United Kingdom which comprises buffer and phenol reagent labelled as solution A, enzyme reagent labelled as solution B and working glucose standard solution labelled as solution C, Distilled water. All reagents used were of analytical grade.

3.3 REAGENT PREPARATION

Reagents were commercially prepared by the manufacturer Randox Laboratories, ready for use.

3.4 SERUM GLUCOSE DETERMINATION: GLUCOSE OXIDASE METHOD (TRINDER 1969, MOD. BAU MINGER 1974)

PRINCIPLES: Glucose in the presence of glucose oxidase is converted to gluconic acid and hydrogen peroxide. The hydrogen peroxide is converted to molecular oxygen and water by peroxidase and in the presence of oxygen acceptor (a chromogen) such as 4-amino phenazone, a coloured compound is formed whose intensity is proportional to the concentration of glucose present in the sample. The coloured compound was measured spectrophotometrically at 510nm.

$$\text{Glucose} + 2H_2O + \text{glucose} \xrightarrow[\text{Oxidase}]{} \text{Gluconic acid} + 2H_2O_2$$

$$\text{4-amino phenazone} + H_2O_2 \xrightarrow{\text{peroxidase}} \text{Oxidized amino phenazone (coloured)} + H_2O$$

PROCEDURE

Reagents	**Test**	**Standard**	**Blank**
Phenol reagent (mL)	2.50	2.50	2.50
Enzyme reagent (mL)	2.50	2.50	2.50
Serum sample (mL)	0.05	-----	-----
Glucose standard (10mMoL/L) (mL)	-----	0.05	-----
Distilled water (mL)	-----	-----	0.05

Mix and incubate at 37oC for 20mins, cool and read spectrophotometrically at 510nm, zeroing with the reagent blank.

CALCULATIONS:

Glucose Conc. (mMoL/L) = Sample Abs x Conc. of Std (10 mMoL/L)

Standard Abs

Normal range = 3.9 – 5.6 mMol/L (JUTH)

Abs = Absorbance
Conc = Concentration
Std = Standard

Results were expressed as mean ± standard deviation (S.D) for the number of different parameters obtained.

Further, the student t-distribution (t-test) was used for the statistical analysis of serum glucose concentration obtained before and one month after Depo-Provera administration. The parameters obtained before Depo-Provera administration served as the control of this study while parameters obtained after Depo-Provera administration served as the test.

Mean (X) = $\sum \chi / n$

Where $\sum$ = Summation of values

χ = Observed value of parameters

n = Number of observed parameters

Standard deviation SD = $\frac{\sum\sqrt{(x-\bar{x})^2}}{n-1}$

Where χ = Observed value of parameter

$\overline{x}$ = Mean of values obtained

n = Number of observations

Standard error mean $S\overline{x}$ = $\frac{S.D}{\sqrt{n}}$

Where S.D = Standard deviation

n = Number of observations

T-test = Observed difference between mean

n = number of observations

$$t = \frac{\bar{x}_1 - \bar{x}_2}{Sx_1x_2\sqrt{2/n}} \qquad \text{where } Sx_1x_2 = \frac{\sqrt{S^2x1 - S^2x2}}{2}$$

Where $\bar{x}_1$ = Mean of glucose value after Depo-Provera administration

$\bar{x}_2$ = Mean of glucose value before Depo-Provera administration

Sx_1 = Standard deviation of glucose value after Depo-Provera administration

Sx_2 = Standard deviation of glucose value before Depo-Provera administration

n = (100) number of women recruited for the study.

3.5 RESULT

Out of one hundred (100) women enrolled for this study, 5(5%) were IGBO, 30 (30%) were Hausa-Fulani, 6(6%) were Yoruba while 59 (59%) of other tribal minorities were classified as others as shown in table 1.

Classifications based on their occupation indicates that 46 (46%) were Business women, 24 (24%) were Students, 15 (15%) were full time Housewives, 10 (10%) were Civil servants, 3(3%) were applicants while 2 (2%) were health workers as shown in table 2.

The mean and standard deviation of parameters such as age, weight, blood pressure, and glucose concentration obtained before Depo-Provera administration were calculated and recorded. The values of age were expressed in years, weight in kilogram and blood pressure in millimetre mercury & glucose in millimole per litre as shown in Table 3.

The mean and standard deviation of parameters obtained after Depo-Provera administration were calculated and recorded as shown in Table 4.

The result of t-test calculation for glucose concentration before and after Depo-Provera administration for test of significance is presented in Table 5.

TABLE 1: CLASSIFICATION OF WOMEN STUDIED BASED ON DIFFERENT TRIBES

Tribes	Number of women	Percentage (%)
Igbo	5	05
Hausa-Fulani	30	30
Yoruba	6	06
Others	59	59

TABLE 2: CLASSIFICATION OF WOMEN STUDIED BASED ON THEIR DIFFERENT OCCUPATIONS

Occupation	Number of Women	Percentage (%)
Business women	46	46
Students	24	24
Full-time housewives	15	15
Civil servants	10	10
Applicants	3	03
Health workers	2	02

TABLE 3: MEAN AND STANDARD DEVIATION OF PARAMETERS BEFORE DEPO-PROVERA ADMINISTRATION

Parameters	Minimum value	Maximum Value	Mean obtained	Standard deviation
Age	19	47	29.4	6.20
Weight	41	95	63.4	12.20
Blood pressure	98/61	140/90	116/77	12/10
Glucose concentration	2.5	9.6	5.2	4.00

TABLE 4: MEAN AND STANDARD DEVIATION OF PARAMETERS, AFTER DEPO-PROVERA ADMINISTRATION

Parameters	Minimum value	Maximum Value	Mean obtained	Standard deviation
Age	19	47	29.4	6.20
Weight	41	95	63.4	12.20
Blood pressure	98/61	140/90	116/77	12/10
Glucose concentration	2.4	9.2	5.2	4.04

TABLE 5: RESULT OF T-TEST CALCULATION FOR GLUCOSE CONCENTRATION

Parameter	t-cal	t-tab	df	P value at 0.05	Remark
Glucose	0.07	1.96	198	P>0.05	Non significant

P value<0.05 = Significant

P value>0.05 = Non Significant

3.6 DISCUSSION, CONCLUSION AND RECOMMENDATION

A total of one hundred (100) women were enrolled to study whether Depo-Provera can affect glucose metabolism of those who use it as a means of family planning. This was due to concerns raised by Fahmy, et *al.* (1991) and Pouliot, *et al.* (1990) that high dose hormonal contraceptive will cause glucose intolerance among users. On the contrary, Nessa, *et al.* (2005) in their study found some slight changes in fasting insulin and glucose levels but according to them, they were not statistically significant and had no clinical relevance. In their study average increase in blood glucose was approximately 0.56mMol/L and in normal individuals, this is not enough to cause problems as the body can easily utilize it. They also stated that in individuals susceptible to diabetes, the changes in glucose tolerance may pose a slight risk of causing diabetes to surface or induce present treatment on the individual.

All these reports centers on Caucasian women and no concrete report so far exist on African women using this synthetic hormonal contraceptive to intentionally prevent pregnancy hence the need for a study like this.

Depo-Provera used for this study is available in 1ml ampoule, each ampoule contains 150mg depot-medroxy progesterone which is the recommended dose in every 12weeks for users. The present study shows that the women who had not entered their menopause were still using Depo-Provera for effective contraception. The classification of women studied based on their tribes shows that 5% were Igbo's, 30% Hausa-Fulani's, 6% Yoruba's and 59% who were minorities in Nigeria tribal classification were grouped as others. The high dominance of the Hausa-Fulani's in this study might be due to the fact that the study was conducted in Plateau State of Nigeria, a state dominated by tribal minorities and the Hausa-Fulani's and even shares boundary with other Northern states of Nigeria where we have the Hausa-Fulani dominance. Their classifications based on their occupation indicates that business women has the highest number of representation of 46% while students has 24%, full-time housewives 15%, civil servants 10%, applicants 3% and health workers 2%. The low representation of civil servants, applicants, and health workers might be that they adopt other means of contraception such as implants, intrauterine contraceptive device which last for five (5) years before losing its contraceptive

potency. This long duration will assist a busy worker who might have no idle time to be going for 12 weekly contraception as in the case of Depo-Provera. From this study, it was found that once a woman reaches her reproductive age and had started her child bearing, can make use of injectable contraceptive such as Depo-Provera since the age recruited for this study ranged from 19-47years.

Also, there was no evidence of weight change in the subjects studied one month after Depo-Provera administration. This finding agrees with what was stated by federal Ministry of Health, Nigeria, National Family planning/Reproductive health, service protocols (2005) that any weight gain during injectable contraceptives should either be due to pregnancy, dietary intake or pattern of eating (FMOH, Nigeria 2005).

Results obtained also shows that there was no change in blood pressure of individuals studied. This might be due to that a repeat check of their blood pressure was done just one month after their first injection and their body was getting used to the injectable. There may be a rise in their blood pressure as they continue with the hormonal contraceptive. Federal Ministry of Health Nigeria, Service protocols (2005) advised that any individual who is taking hormonal contraception and has an increase in blood pressure of above 160/100mmHg, should stop the hormonal contraception and non-hormonal contraceptive method be given to such an individual (FMOH, Nigeria 2005).

Also, from the individuals studied, Depo-Provera did not cause any alteration on their carbohydrate metabolism. Their mean glucose concentration before Depo -Provera administration was 5.2 $\pm$ 4.00mMol/L as against their mean glucose concentration one month after Depo-Provera administration which was 5.2 $\pm$ 4.04mMol/L. This study agrees with the study done by Nessa, *et al.* (2005) and Gaspard *et al.* (2003). Gaspard, *et al.* (2003) stated that newer progestogen contraceptive do not seem to alter carbohydrate metabolism and have a less pronounced effect on carbohydrate metabolism than the older progestogen contraceptives which are of a higher dose.

3.7 CONCLUSION

Depo-Provera had no significant alteration on carbohydrate metabolism of individuals' studied. Also, it did not cause a change in their weight or blood pressure one month after administration. It can therefore be concluded that Depo-Provera did not induce insulin resistance nor glucose intolerance one month after exposure among African women studied and may be used as effective contraceptive but diabetic women should be monitored when on this hormonal injectable contraceptive since the individuals examined are non-diabetic patients.

3.8 RECOMMENDATION

I wish to recommend from this study that Depo-Provera should be used as a means of contraception for African women. This is because the parameters (weight, blood pressure and glucose concentration) studied do not show any significant increase or decrease one month after Depo-Provera administration. I also recommend a regular screening of serum glucose concentration of women on Depo-Provera since it is a hormonal contraceptive which can induce glucose intolerance in diabetic women (Pouliot, *et al.* 1990). More work should also be done on women in Depo-Provera to find out whether Depo-Provera can cause any alteration in their serum lipids, liver enzymes, vitamin B6, B12 and folic acid metabolism. The bone minerals such as serum calcium and phosphorus of women on Depo-Provera should also be examined since the reports so far on this were inconclusive. Also, more work should be done on their serum glucose using a larger population say 300 women monitored over a longer period of time e.g. 6 months.

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APPENDIX I

PARAMETERS OBTAINED BEFORE DEPO-PROVERA ADMINISTRATION.

S/NO	NAMES	AGE	WEIGHT (kg)	BLOOD PRESSURE (MMHg)	GLUCOSE CONC. (mMOL/L)
1		27	91	110/80	5.4
2		29	71	100/70	5.4
3		40	80	130/90	4.7
4		30	52	140/80	7.2
5		34	53	110/70	5.5
6		30	71	130/90	2.6
7		31	75	119/78	4.8
8		25	67	126/87	3.4
9		25	85	122/79	5.0
10		29	74	199/98	3.2
11		19	46	98/61	4.5
12		35	70	117/69	4.2
13		28	65	123/82	3.7

14		23	68	100/70	4.4
15		32	73	130/90	4.0
16		30	67	100/70	4.0
17		31	68	120/80	4.8
18		37	49	110/80	5.8
19		22	73	100/60	5.6
20		22	59	110/80	5.9
21		32	62	120/80	4.2
22		27	51	120/60	5.5
23		28	72	130/90	5.6
24		22	43	100/70	6.9
25		37	52	120/60	7.1
26		24	53	120/90	8.6
27		30	60	120/90	6.7
28		34	60	120/70	4.4
29		27	47	110/70	4.9
30		28	48	100/70	4.4
31		47	78	110/70	9.6
32		35	95	140/90	4.4
33		27	50	100/60	4.8
34		25	51	110/70	4.0
35		35	56	120/70	3.9
36		22	66	130/90	4.3

37		22	64	120/80	3.0
38		32	64	110/80	4.0
39		30	79	130/90	3.0
40		36	53	120/80	2.5
41		27	60	110/70	4.8
42		27	43	120/80	4.0
43		25	52	140/90	5.0
44		36	61	110/70	4.8
45		31	85	120/80	4.3
46		30	54	110/80	2.5
47		22	65	110/70	3.9
48		44	70	100/60	4.2
49		28	48	100/70	3.7
50		27	41	100/70	4.4
51		29	76	100/60	4.9
52		39	56	100/70	4.9
53		34	46	120/85	5.6
54		44	70	110/70	5.6
55		33	65	100/70	3.2
56		27	59	140/90	4.0
57		30	73	100/60	3.5
58		37	49	100/60	3.2
59		19	68	110/70	5.0

60		22	73	120/70	3.4
61		36	67	130/90	4.8
62		27	68	120/80	2.6
63		27	72	130/90	5.5
64		42	51	120/80	7.2
65		26	62	110/80	4.7
66		27	43	130/90	5.4
67		47	52	120/80	5.4
68		30	53	110/70	4.8
69		24	78	120/80	5.5
70		32	48	140/90	5.6
71		34	47	110/70	6.9
72		22	53	119/98	7.1
73		29	61	122/79	8.6
74		25	60	110/80	6.7
75		32	74	100/70	4.4
76		23	85	130/90	4.9
77		35	75	110/70	4.4
78		31	67	119/78	4.4
79		27	71	130/90	3.7
80		25	75	110/70	4.2
81		38	45	140/80	3.9
82		28	50	130/80	2.5

83		34	53	98/65	4.3
84		28	79	117/70	4.8
85		36	64	123/80	5.0
86		40	51	100/70	4.0
87		33	56	130/85	4.8
88		24	64	100/70	2.5
89		25	66	120/80	4.5
90		30	64	110/80	4.2
91		27	71	100/60	3.7
92		40	81	110/80	4.4
93		31	52	120/80	4.0
94		26	80	120/60	4.0
95		29	53	120/90	4.8
96		30	71	120/70	5.8
97		28	75	100/70	5.6
98		19	67	110/70	5.9
99		42	85	140/90	9.6
100		38	74	120/80	4.4

APPENDIX II

PARAMETERS OBTAINED AFTER DEPO-PROVERA ADMINISTRATION

S/NO	NAMES	AGE	WEIGHT (kg)	BLOOD PRESSURE (MMHg)	GLUCOSE CONC. (mMOL/L)
1		27	91	110/80	5.6
2		29	71	100/70	5.7
3		40	80	130/90	4.7
4		30	52	140/80	7.0
5		34	53	110/70	5.2
6		30	71	130/90	3.0
7		31	75	119/78	5.0
8		25	67	126/87	3.6
9		25	85	122/79	5.0
10		29	74	199/98	3.4
11		19	46	98/61	4.0
12		35	70	117/69	4.0
13		28	65	123/82	3.9
14		23	68	100/70	4.5
15		32	73	130/90	4.0
16		30	67	100/70	4.2
17		31	68	120/80	4.8
18		37	49	110/80	5.8
19		22	73	100/60	5.4
20		22	59	110/80	5.7

21		32	62	120/80	4.3
22		27	51	120/60	5.3
23		28	72	130/90	5.6
24		22	43	100/70	7.0
25		37	52	120/60	7.0
26		24	53	120/90	8.0
27		30	60	120/90	6.9
28		34	60	120/70	4.5
29		27	47	110/70	5.0
30		28	48	100/70	4.6
31		47	78	110/70	9.2
32		35	95	140/90	4.4
33		27	50	100/60	5.0
34		25	51	110/70	4.0
35		35	56	120/70	4.2
36		22	66	130/90	4.3
37		22	64	120/80	3.2
38		32	64	110/80	4.0
39		30	79	130/90	3.2
40		36	53	120/80	2.4
41		27	60	110/70	4.8
42		27	43	120/80	4.0
43		25	52	140/90	5.0

44		36	61	110/70	4.8
45		31	85	120/80	4.0
46		30	54	110/80	2.6
47		22	65	110/70	3.5
48		44	70	100/60	4.0
49		28	48	100/70	4.0
50		27	41	100/70	4.2
51		29	76	100/60	5.0
52		39	56	100/70	5.0
53		34	46	120/85	5.4
54		44	70	110/70	5.4
55		33	65	100/70	3.6
56		27	59	140/90	4.2
57		30	73	100/60	3.8
58		37	49	100/60	3.4
59		19	68	110/70	5.0
60		22	73	120/70	3.6
61		36	67	130/90	5.0
62		27	68	120/80	3.0
63		27	72	130/90	5.2
64		42	51	120/80	7.0
65		26	62	110/80	4.7
66		27	43	130/90	5.7

67		47	52	120/80	5.6
68		30	53	110/70	4.8
69		24	78	120/80	5.3
70		32	48	140/90	5.6
71		34	47	110/70	7.0
72		22	53	119/98	7.0
73		29	61	122/79	8.0
74		25	60	110/80	6.9
75		32	74	100/70	4.5
76		23	85	130/90	5.0
77		35	75	110/70	4.6
78		31	67	119/78	4.2
79		27	71	130/90	4.0
80		25	75	110/70	4.0
81		38	45	140/80	3.5
82		28	50	130/80	2.6
83		34	53	98/65	4.0
84		28	79	117/70	4.8
85		36	64	123/80	5.0
86		40	51	100/70	4.0
87		33	56	130/85	4.8
88		24	64	100/70	2.4
89		25	66	120/80	4.0

90		30	64	110/80	4.0
91		27	71	100/60	3.9
92		40	81	110/80	4.5
93		31	52	120/80	4.0
94		26	80	120/60	4.2
95		29	53	120/90	4.8
96		30	71	120/70	5.8
97		28	75	100/70	5.4
98		19	67	110/70	5.7
99		42	85	140/90	9.2
100		38	74	120/80	4.4

APPENDIX III

GLUCOSE T-TEST CALCULATION

$$t = \frac{\bar{X}_1 - \bar{X}_2}{Sx_1x_2 \sqrt{2/n}} \quad \text{where } Sx_1x_2 \quad \frac{\sqrt{S2x1+S2x2}}{2}$$

Where $\bar{x}_1 = 5.187$= mean of glucose value after Depo-Provera administration

$\bar{X}_2$=5.183= mean of glucose value before Depo-Provera administration

Sx_1=4.04= standard deviation of glucose after Depo-Provera administration

Sx_2=4.00= standard deviation value before Depo-Provera administration#

n= (100) number of women recruited for the study

$$Sx_1x_2 \quad \frac{4^2.04+\sqrt{4^2.00}}{2} = \frac{\sqrt{16.3216 + 76.00}}{2} = \frac{\sqrt{32.3216}}{2}$$

$$= \sqrt{16.1608} = 4.02$$

$$t = \frac{5.187 - 5.185}{4.02 \times \sqrt{2/100}} = \frac{5.187 - 5.183 = 0.004}{4.02 \times \sqrt{0.02}} = \frac{0.004}{0.569}$$

t=0.07

The degree of freedom for this test is 2n-2 where n is the number of participants.

Degree of freedom = 2 x 100-2 =200-2 =198.

SAMPLE SIZE CALCULATED

$$N = \frac{z^2 x\ p\ x\ q}{d^2}$$

Where N = minimum sample sized desired.

z = score at 95.5 coefficient level = (1.96).

p = prevalent rate of what you desire to study.

q = complementary prevalence of what you desire to study (1-p).

d = level of precision to be adopted (0.05).

N =? z =1.96, p = 20% (0.2), q = 1-0.2, d = 0.05

$$N = \frac{1.96^2 \times 0.2 \times (1-0.2)}{0.05^2} = \frac{1.96^2 \times 0.2 \times 0.8}{0.05^2}$$

$$N = \frac{3.8416 \times 0.2 \times 0.8}{0.0025} = \frac{0.614656}{0.0025} = 246$$

The number of women on injectable contraceptive in Nigeria was 40%, while 20% was allocated to Depo-Provera and calculated out. Thereafter 100 women was recruited in JUTH and was studied.