THE EFFECTS OF PREGNANCY ON SERUM CONCENTRATIONS OF TOTAL PROTEIN, ALBUMIN, UREA, CREATININE, SODIUM ION AND POTASSIUM ION:

A CASE STUDY OF NIGER STATE.

BY

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CERTIFICATION

This thesis entitled 'Effect of Pregnancy on Serum Concentration of Total Protein, Albumin, Urea, Creatinine. Sodium ion and Potassium ion' was carried out by Tijjani Maruf under my supervision and has been examined, read and found to meet the regulations governing the award of the Degree of Masters of Technology in Biochemistry of Federal University of Technology, Minna and is approved for its contribution to knowledge and literary presentation.

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DEDICATION

This work is dedicated to my Daughters, Kabirat and Karimat.

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ABSTRACT

From time immemorial, pregnant women are known to have certain physiological 'disturbances' most of which are well tolerated by the expectant mothers. These 'disturbances' are found to be necessary for the well being of the fetus. Blood samples were taken from 96 pregnant women, 42 non-pregnant women and 25 menopausal women from Minna, Suleja, Bida and Kontagora area of Niger State and analyzed for serum total protein, albumin, Urea, creatinine, sodium ion and potassium ion. It was found that the blood serum concentrations of all the biochemical parameters under consideration were lowered during pregnancy and elevated in menopausal women compared to non-pregnant women values. This trend is not true for serum creatinine, though the concentration is lowered in pregnant women. Maternal physiology in pregnancy is often mistaken for disease conditions. The data and findings obtained in the work forms a baseline to distinguish between maternal physiological changes and pathophysiology in pregnancy.

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DEFINITION OF SOME TERMS COMMONLY USED IN THE WORK

ANTENATAL CARE: The care given to pregnant women between the time of conception and childbirth.

CONCEPTUS: The fetus in the womb of the pregnant women

GLOMUMERULAR FILTERATION RATE: Volume of blood filtered by glomerulus per minute.

GLYCOSURIA: A condition whereby the presence of glucose is detected in the urine.

HAEMORRHAGE: Escape of blood from a vessel.

HAEMORRHOIDS: Varicosity of the veins around the anus.

HEMODILUTION: Increase in the plasma volume of the blood.

HYPERINSULINEMIA: Excess amount of insulin in the blood.

HYPERKALEMIA: Physiologically high potassium ion concentration in the blood.

HYPERLAPSIA: Increase in number of cells in tissues

HYPERNATREMIA: Physiologically high sodium iron concentration in the blood.

HYPERTROPHY: Increase in size of cells in the tissue.

HYPOKALEMIA: Physiologically low potassium ion concentration in the blood

HYPONATREMIA: Physiologically low sodium iron concentration in the blood

MENOPAUSE: A period in the life of a woman when she no longer ovulates.

MULTIGRAMIDAE: Pregnancy that is not the first for the woman.

MULTIPLE PREGNANCY: A pregnancy with more than one fetus in the womb.

OEDEMA: Swelling of the tissues under the skin due to retention of water in these tissues.

PERISTALSIS: Wave like movement of food in the oesophagus or gut.

PRIMIGRAVIDAE: First pregnancy.

SINGLETON: A pregnancy with only one fetus in the womb

SPERMATOZOON: The male reproductive cell.

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CHAPTER ONE

INTRODUCTION

A new life begins when a single spermatozoon fertilizes an ovum. Out of the several millions of the spermatozoon deposited in the vicinity of the cervix, only a few thousands manage to negotiate the twisting mucus tunnels of its canal to reach the cavity of the uterus. Furthermore, only a few hundreds get through the narrow cavity of the uterus to enter the oviduct and only a few dozens swim along the oviduct, against the current made by the movement of its lining, to reach the ovum. Only one penetrate (mostly) through the tough, glistering, transparent 'shell' which surrounds the ovum. Once the spermatozoon has penetrated the shell, of the ovum, it alters the shell in some ways so that no other spermatozoon is able to penetrate it. Pregnancy is then said to be conceived. The new life actually begins when the chromosomes of the ovum and those of the spermatozoon fuse together. Under the control of genes, the cell then divide progressively until a human beings is formed (Llewellyn, 1998).

Most women have an idea that they are pregnant before they consult a doctor to confirm their suspicion; arising certain symptoms and physiological changes. While the fetus is developing in the dark confine of the uterus, certain physiological changes take place in the entire body of the mother, making all the functions of the expectant mother's body adjusting to the need of pregnancy and without compromising the mother's health in the process. However, some of the changes may cause discomfort and stress to the mother (Chamberlain, 1991; Leader et al., 1996; Moore, 1991; Miller and Callender, 1989).

All the changes occuring in the mother's body are associated with, and in most cases by, the influence of specific hormones (Case and Waterhouse, 1994). These

changes from the normal non-pregnant state is traditionally described as maternal physiology, but not unconnected with biochemical and anatomic events (Eugene and Sandberg, 1978).

Pregnancy is a 'load', causing pronounced alterations which generally aim to minimize the stresses imposed and to provide the best environment for the growing fetus. The alterations are systematic so that the effect of pregnancy are minimized to the barest minimum (Chamberlain, 1991). The physiological, biochemical and anatomical changes that occur during pregnancy are extensive and may be systemic or local. The changes commonly experienced occur with symptoms like morning sickness (nausea and vomiting), change of taste, pica, constipation, abdominal pain, headache, backache, waist pain, fatigue, heart burn, oedema of lower limb, frequent urination, glycosuria, breathlessness, faster heart beat, heart murmurs, palpitation of part of the body and many others yet to be well defined. Some symptoms of changes are not experienced by some women. Most systems return to pre-pregnancy status between time of delivery and six weeks of post partum (Moore, 1991).

The extent of changes occurring in pregnancy depends on multiple factors. Most important of these factors are health status of the women prior to pregnancy, the number of previous pregnancy (abortion inclusive), size of the body, nutritional status, environmental changes, psychological changes, inheritance, and multiple pregnancy (Moore, 1994). In the past, various believes were attached to changes in the body during pregnancy but most of them have no scientific correlation.

Morning sickness occur in about 70% of pregnant women, at variable degree, in the first 12 – 14 weeks of pregnancy. It occasionally leads to initial loss of weight in

pregnancy and there may be fainting in extreme cases (Sakala, 2000). In the days of Queen Victoria of England, a faint was the way the modest wife announced to her husband that a little stranger was on the way (Llewellyn, 1998).

Ptyalism is the excessive loss of saliva and this is common in pregnancy because the women are unable to swallow the saliva due to nausea. There is no evidence for overproduction of saliva. Gums usually become soft and edematous and may bleed with brushing. Change of taste and pica is also not unusual in pregnancy and is associated with increase in production of sex hormones, particularly progesterone. Pica is dietary craving for non-nutritional substances and is not uncommon in pregnant women. Pregnant women in Southern America often crave for clay and starch while in England and Wales, affected women usually crave for coal. Other substances craved for in Pica affected pregnant women include soap, toothpaste, cement odour, sand, ice, and newspaper, depending on their availability and accessibility to the women (Barber et al, 1990).

Most women experience fatigue in pregnancy and often sleep for longer time, day and night. Backache is a very common phenomenon in the last trimester of pregnancy and this is due to pelvic joint relaxation and the effect of growing weight of uterus on the center of balance, so that the expectant mother has to stand with her shoulder further back than normal. Headache in first trimester of pregnancy is due to increase in size of the pituitary gland and usually subsides as the pregnancy gets older (Chamberlain, 1991).

Frequency of urination is common in early pregnancy and occur again in the last weeks when the fetus head presses into the pelvis, reducing the bladder capacity to contain urine. There may also be glycosuria due to hyper-efficacy of the kidney which

give rise to higher glomerular filteration rate and reduced glucose renal threshold (Case and Waterhouse, 1994).

Heartburn is an annoying and fairly common complaint of most pregnant women and this is more frequent in late pregnancy. It is due to the passage of small amount of stomach contents into the lower part of the osophagus because the valve (muscle) guarding the entrance to the stomach relaxes as the enlarging uterus pushes up against the stomach (Symonds, 1992).

Oedema of the lower limb is observed in 60% of pregnant women and is sometimes followed by leg cramp. It runs in families and its excessiveness was once thought to be related to multiple pregnancy. Constipation in pregnancy is caused by diminished intestinal motility brought about by relaxation of smooth muscles of the gut by the progesterone. There is also increase in water reabsorbtion as well as some useful minerals, making constipation almost inevitable. Constipation aggravate pile which often occur in pregnancy or at child birth. Pile is more common in multigravidae and also seem to occur in families. The usual complaints are of bleeding during a bowel motion, the presence of tender lump noticed during the use of toilet paper and pain around anus or just inside the rectum (Coustan, 1994).

Nearly 75% of all pregnant women experience breathlessness (Dyspnea of pregnancy) on exertion. This condition is mostly experienced in the last 10-12 weeks of pregnancy. Though annoying, breathlessness harms neither mother nor child. Breathlessness is due to hyperventilation drive of progesterone and raising of the diaphragm by the enlarged uterus. There may also be nasal stiffness. Slight nose

bleeding is not unusual in pregnancy, occurring in about 20% of pregnant women. It is due to increase in blood supply and not high blood pressure (Steele, 1985).

In pregnancy, breast becomes fuller, firmer and more tender. Occasionally they throb and the nipples tingle as it becomes larger, darker and more erectile when the pregnancy is advancing. Some physicians are able to guess the age of pregnancy from the observation of breast development. The changes in breast are caused by increased production of female sex hermone, oestrogen and progesterone, by the placenta. These hormones caused growth of the ducts and milk sac of the breasts and lead to fat being deposited around them. The tingling and throbbing occasionally felt is due to increased flow of blood through the blood vessels which supply the breasts (Case and Waterhouse, 1994).

There may be placidity and drowsiness as the pregnancy advances and the expectant mother no longer has the clarity of mind and precision of thought she had before pregnancy. Even small intellectual matters become a trial and to do anything is an effort. She becomes restless and easily annoyed. There is always increased in systolic murmur of the heart and the heart sound may be heard. Skin pigmentation usually occur and is due to high level of melanocite stimulating hormones, oestrogen and progesterone (Hacker and More, 1986).

With general improvement in the knowledge and understanding of changes in pregnancy, coupled with improved ante-natal care, symptoms of maternal physiological changes will no longer be a threat to expectant mothers. However, consideration of the extent of changes is very important to exclude disease development or aggravation situation which is more probable in cases of extreme changes.

It is established that pregnancy brings about changes in concentration of serum biochemical parameters and the extent of the changes have been determined. However, no correlation has been put forward for such changes in concentration nor is there any comparism with the changes in concentration of the same parameters in menopausal Women. The objective of the study therefore is:

1. To determine whether the extent of changes in concentrations of serum biochemical parameters in pregnancy is applicable to the locality under study or not.
2. To compare the changes of concentration of some serum biochemical parameters in pregnant women and menopausal women.
3. To determine the correlation that exists between these serum biochemical parameters.

The significance of this studies is that it will provide baseline data for the interpretation of clinical tests by health workers during antenatal care.

CHAPTER TWO

2.0 LITERATURE REVIEW

All changes occurring during pregnancy are associated with, and in some systems caused by, the effect of specific hormones (Case and Waterhouse, 1994). In fact physiological, anatomical and biochemical changes occurring in pregnancy is caused directly or indirectly by hormonal effects. Some of the underlying causes of changes are themselves caused by hormonal interactions. Hence, hormonal changes are regarded as primary cause of changes while other changes like cardiovascular changes, metabolism, Gastrointestinal changes etc. are regarded as secondary cause of changes (Davey, 1995).

2.1.0 PRIMARY CAUSE OF CHANGES

The primary cause of changes is hormonal level changes and ductless glands function. Hormones are substances, which are released from special glands into the blood stream and stimulate other glands and/or tissues to activity (Dorlands, 1988).These hormones and ductless glands in pregnancy are discussed below:

2.1.1 PITUITARY HORMONES:

Puberty in female is said to commence when the hypothalamus stimulate the anterior pituitary to release increased amount of follicle stimulating hormone (FSH) and leutenising hormone (L.H). The gonadotropic hormones caused maturation of the ovaries which then begin secreting the female sex hormones (oestrogen and progesterone). The maternal FSH ad L.H are suppressed by placental oestrogen and progesterone during pregnancy and this is necessary to halt further follicular growth phase that leads to ovulation. Hence no ovulation takes place during pregnancy. However, prolactin levels rise throughout the pregnancy (Miller and Calendar, 1989). Also adrenocorticotropic

hormone and tyrotropic hormone and melanocyte rise during pregnancy (Case and Waterhouse, 1994). The weight of the anterior pituitary gland increases by 30-50%, which is why some women suffer from headache during pregnancy (Mc Fadyen, 1995; Chamberlain, 1991).

The effect of increased prolactin secretion are suppressed by oestrogen and progesterone during pregnancy (Howie, 1995). Following delievery of the placenta, Serum concentration of prolactin decreases, even in breast feeding women, but prolactin is subsequently secreted in pulsatile burst with suckling to stimulate milk production (Cunningham et al,,1989). Lactation does not occur until after delievery when increased prolactin persist in association with decreased oestrogen (Miller and Callendar, 1989).

The posterior pituitary gland releases Oxytocin in low frequency pulses throughout pregnancy. At term, the frequency of the pulses increase, which stimulates uteric contraction (Fusch and Fusch, 1991.) Secretion of oxytocin may also be stimulated by stretching of lower genital tract (Chamberlain, 1991). Th pituitary growth hormone level are also significantly reduced but are possibly compensated for by the abundant secretion of human placental lactogen (HPL) which has a degree of somatotropic activity. The posterior lobe does not hypertrophy during pregnancy (Eugene and Sandberg, 1978).

2.1.2 **THYROID HORMONE.**

In normal pregnancy, the thyroid gland increases in size by about 13% owing to hyperlapsia of glandular tissues and increased vascularity. There is normally an increased uptake of iodine in pregnancy which may be to compensate for renal clearance

of iodine which doubles with increased Glomerular filteration rate (GFR) leading to a reduced level of serum iodine (Cunningham et al, 1989).

Although pregnancy can give the impression of hyperthyroidism, thyroid function is basically normal. The basal metabolic rate (BMR) is increased mainly because of increased oxygen consumption by the fetus and the work of maternal heart and lungs (Ramsay, 1991). Rising level of thyroxine (T4) and triidothyroine (T3) and many other hormones do contribute, however, to the increased BMR (Guyton, 1991). Total thyroxin levels rise sharply from second month to a plateau which is maintained till term. However, the thyroxine is mainly bound rather than free in the plasma owing to oestrogen stimulated hepatic production of thyroxine binding globulin. As a result, the amount of free (unbound) effective thyroid hormone is not increased in spite of the elevated concentration of total thyroxine (Rodin et al, 1989).

2.1.3 **OESTROGEN**

In early pregnancy, the source is the ovary, Later, oestrogen and oestradiol are probably produced by the placenta and are increased hundred fold. Oestriol, however, is a product resulting from the interaction of the placenta and the fetal adrenals and is increased one thousand fold. The output of oestrogen reaches maximum of atleast 30-40mg per day and Ostriol accounts for 85% of this total. Level of oestrogen increases up to term (Miller and Callendar, 1989).

Functions of oestrogen in pregnancy include the induction of uterus growth and control of its function. They are also responsible for development of breasts, though in conjunction with progesterone. Oestrogen is also known to alter the chemical

constitution of connective tissue, making it more pliable in order to allow stretching of cervix, relaxation of joint capsule and mobility of pelvic joints. It has also been proved that oestrogen reduces sodium excretion in pregnancy (Hanretty and Miller, 1997).

2.1.4 **PROGESTERONE.**

This hormone is produced by corpus luteum in the first few weeks of pregnancy. Thereafter, it is derived from the placenta. Level of progesterone rise steadily during pregnancy with a fall towards term. Progesterone output reaches maximum of at least 250 mg/day (Miller and Calendar, 1989).

Possible actions of progesterone in pregnancy include reduction of smooth muscle tone which results to diminished stomach motility and nausea. Colonic activity is also reduced and may delay emptying. Progesterone also facilitate water reabsorbtion which leads to constipation. Uterine tone of pregnant women is also believed to be reduced by progesterone to bring about diminished uterine activity, in the same way it reduces bladder tone to cause urine stasis.

Vascular tone of pregnant women is not spared by progesterone as it is reduced to bring about reduction in diastolic pressure and more importantly venous dilation. Progesterone is responsible for raised body temperature and fat storage in pregnancy. It induces over breathing and breast development (Hanretty and Miller, 1997).

2.1.5 **CORTISOL**:

The maternal adrenals are the sole source in early pregnancy. But later, considerable quantities are thought to be produced by the placenta. About 25 mg are

produced each day. Much of this is protein bound and therefore may not be generally active. Possible actions of cortisol include

(i) Increase of blood sugar

(ii) Modification of antibody activities (Moore, 1994).

2.1.6 ALDOSTERONE:

The hormone is wholly derived from maternal adrenals. The amount produced during pregnancy are much increased. It promotes retention of sodium and water (Ramsay, 1991).

2.1.7 HUMAN CHORIONIC GONADOTROPIN (HCG).

It is produced by the trophoblast and peak levels are reached before 16 weeks of gestation. From 18 weeks onward, levels remain relatively constant. Apart from the early maintenance of the corpus Luteum, the physiological role of HCG remains unclear. It appears to have thyrotropic action and to initiate testosterone secretion from the leydig cells (Miller and Calendar, 1989).

2.1.8 HUMAN PLACENTAL LACTOGEN (HPL)

This hormone is lactogenic and antagonistic to insulin. Its level rises steadily, with the growth of placenta, throughout the pregnancy (Hanretty and Miller, 1997).

2.1.9 RELAXIN:

This hormone is produced by corpus luteum. It can be detected throughout the pregnancy but highest levels are found in the first trimester. Its physiological role is uncertain but it has been used clinically for cervical ripening (Hansen et al, 1996).

2.1.10 INSULIN:

The maternal islet of langerhans are enlarged and there is hyperinsulinemia in normal pregnancy which is particularly accentuated in the last trimester. Fasting blood sugar level are some what diminished but essentially stable throughout, demonstrating the well known reduced sensitivity to insulin, especially in late pregnancy (Davey, 1995).

It has been suggested that extra insulin is secreted in response to increasing amount of HPL (human placental lactogen) which is known to be antagonistic to insulin (Ralph and Win, 1974). Additionally, peripheral tissues may loose their ability to use insulin during pregnancy. Regardless, it is apparent that homeostasis require significantly increased insulin secretion and patients with minimal pancreatic reserve, adequate for non-pregnant stresses, may develop a diabetic glucose tolerant curve during pregnancy or even frank diabetes. Glycosuria during pregnancy, however, is more commonly the result of increased glomerular filteration rate (GFR) couple with a reduction in tubular reabsorbtion (reduced renal threshold for glucose) than it is of diabetes. Nonetheless, it should be investigated in each instance (Eugene and Sandberg, 1978).

The relative level of hormones in pregnancy is shown in fig. 1 below.

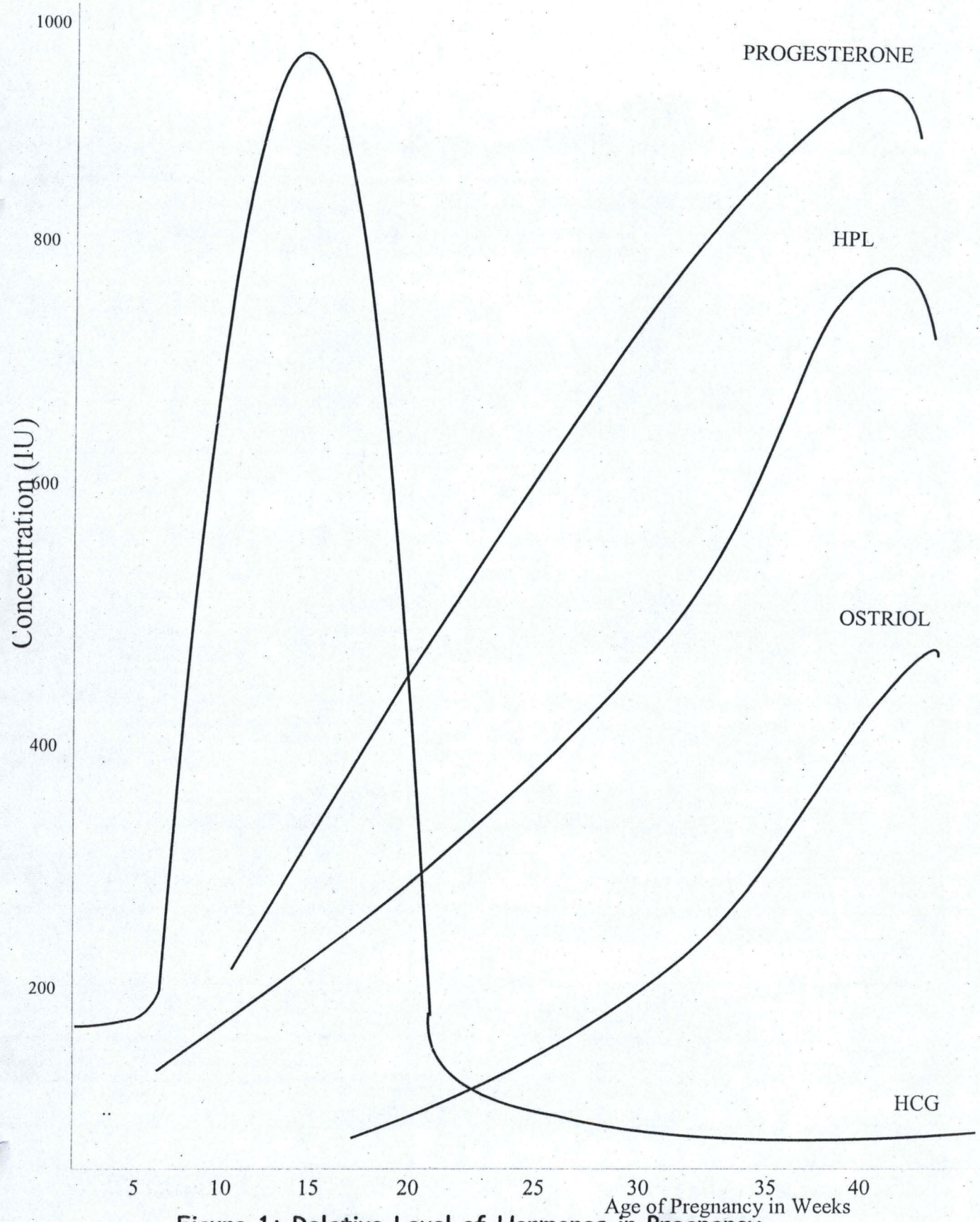

Figure 1: Relative Level of Hormones in Pregnancy

2.2.0 SECONDARY CAUSES OF CHANGES

These include non-hormonal changes that results from hormonal interactions and can themselves cause changes in the body of the pregnant woman. Secondary changes that affect the parameters under consideration are discussed below.

2.2.1 CHANGES IN THE CARDIOVASCULAR SYSTEM

Marked demands are made in this system, mainly as a result of the growth of the conceptus and increase in metabolism (Miller and Callendar, 1989). The changes can be described in various dimensions, namely the blood volume, the heart, the cardiac output, effects on the blood pressure and blood flow (Letsky, 1991).

2.2.11 THE BLOOD VOLUME:

The increase in blood volume in pregnancy may be as little as 20% or as much as 100% and varies according to the size of the woman, the number of pregnancy she has had, her parity and whether the pregnancy is singleton or multiple. The increase begins at about 10 weeks of gestation and is progressive until about 20 – 34 weeks of gestation after which a plateau is reached (Cruikshank and Hays, 1991).

A higher circulating volume is required to provide extra blood flow for placental perfusion at the choriodecidual interface, to supply extrametabolic needs of the fetus, to provide extra perfusion of kidneys and other organs, to counterbalance the effect of increased arterial and venous capacity, and to compensate for blood lost at delivery. Raised level of aldosterone, oestrogen and progesterone during pregnancy are thought to contribute to the increased blood volume (Moore, 1994).

The increase in plasma volume corresponds to the increase in blood volume (Cunningham et al, 1989). This helps to compensate for the increased blood flow to the uterus and other organs, reduce viscosity of the blood and improve capillary flow. A normal increase in plasma volume is correlated to fetal well being and birth weight (Mc Fadyen, 1995).

The mechanism by which higher blood volume is achieved is not well understood but may be as a result of increased aldosterone secretion and also placental steroids secretion which lead to reduced excretion of water and salts by the kidney, hence fluid retention (Miller and Callendar, 1989). The peripheral vascular dilation, uterine vascular diltation, and low pressure circulation in placental lead to reduced peripheral resistance which in turn causes lower diastolic pressure. The later then stimulates the adrenal cortex to secrete the aldosterone (Chamberlain, 1991).

In pregnancy, intracellular water tends to be unchanged, but both blood and interstitial fluids are increased. The plasma volume starts to increase early in pregnancy and reaches a peak around the 32nd week. Thereafter it is maintained until towards term when a slight fall occurs. The increase varies from individual to individual, but is marked in multigravidae women.

Average non-pregnant plasma volume is about 2,600ml. In primigravidae pregnancy, the peak volume reaches about 3,850ml or 41% increase while the peak volume in multigravidae pregnancy reaches about 4,100ml or 57% increase (Hanretty and Miller, 1997)

2.2.1.2 **THE HEART.**

Owing to an increase in workload, the heart muscle hypertrophies, particularly in the left ventricle, leading to the enlargement of the heart. The growing fetus pushes the heart upwards and to the left. The great vessels are unfolded and so the heart is rotated upwards and outwards, producing electrocardiographic and radiographic changes similar to those in ischaemic heart disease but which are considered normal in pregnancy. Heart sounds are changed and systolic and other murmurs are common (Chamberlain, 1991).

2.2.1.3 **CARDIAC OUTPUT**

During pregnancy, there is an increase in the heart rate as early as 4th week from 70 to 85 beats per minute. There is also increase in stroke volume (The amount of blood pumped by heart in each beat) from 64 – 71 ml. These results in raised cardiac output (rate at which blood is pumped by the heart) from 5 – 7 liters per minute i.e about 40% increase. This is in order to perfuse the growing fetus. The raised cardiac output (c/o) is due to increased blood volume and increased oxygen requirement of all maternal tissues as well as growing fetus (Symonds, 1992). It subsequently became apparent, however, that c/o increases markedly by the end of first trimester when uterine blood flow has not yet increased significantly (De swiet, 1991). This is demonstrated most conclusively by a study by Robson et al, 1989 which showed that the c/o had risen by 40% above pre-pregnant values by the 12th week and by 50% by the 34th week. The increase does, however, appear to vary among individuals. Furthermore, little inconclusive evidence exists about cardiac output in the third trimester. A fall in c/o was previously considered to be due to compression of the inferior venacava by the uterus, irrespective of posture, causing reduced venous return and decrease stroke volume. A rise, fall, or no change at

all has more recently been shown to occur, depending on individual variations (Vanoppen et al, 1996; Robson et al, 1989).

2.2.1.4 EFFECTS ON THE BLOOD PRESSURE

Although the Cardiac output (c/o) is increased in pregnancy the blood pressure does not rise because of the reduction in peripheral resistance to about 50% of non-pregnant values. The capacity of veins and venules can increase by a liter. The most obvious cause for this is progesterone which relaxes smooth muscle, causing arterial walls to relax and dilate (Cruikshank and Hays, 1991). It may also be due to increased production of vasodilator prostaglandins (Cunningham et al, 1989).

While the systolic pressure remains almost constant, the diastolic pressure drops slightly in the first trimester, reaches its lowest level at 16-20 weeks and towards term returns to the level of the first trimester (De swiet, 1991). During the mid trimester, changes in blood pressure may cause fainting. In late pregnancy, the unsupported supine position should be avoided as this causes profound hypotension to occur in 10% of pregnant women, known as supine hypotensive syndrome. The pressure of the gravid uterus compresses the vena cava, reducing venous returns. Cardiac output is reduced by 25 – 30% and the blood pressure may fall by 10 – 15%, which gives rise to feelings of dizziness, nausea, and even fainting (Cruikshank and Hays, 1991).

Poor venous return in late pregnancy along with increased distensibility and pressure in the veins of the legs, vulva, rectum and pelvis can lead to oedema in lower leg, varicose veins, and haemorrhoids (Case and Waterhouse, 1994).

2.2.1.5 **BLOOD FLOW**

While blood flow increases to the uterus, kidneys, breasts, and skin, there is no increase in blood flow to brain and liver (Mc Fadyen, 1995). Much of the increased cardiac output is directed to the uteroplacental circulation whose blood flow increased by 10 – 15% to about 750ml per minute at term (Bissonette, 1991). This is due to the vascular resistance within the uteroplacental circulation being lower than that of the systemic circulation. In maternal systole, blood flows through the spiral arteries into the choriodecidosal space and spurts upwards towards the chorionic plate, allowing exchange of gasses, excretion of waste products from the fetus and providing nutrition (Coustan, 1994).

Regulation of uterine blood flow is of clinical importance to the welfare of the fetus. Hemorrhage, uterine contraction, adrenaline and nor-adrenaline, and lying in supine position in late pregnancy can all reduce uterine blood flow. Chronic impairment can lead to intrauterine growth retardation and ultimately fetal death. Conversely, uterine blood flow is increased physiologically by the effect of angiostesin II on placental tissue causing local release of vasodilator prostaglandins (Symonds, 1992).

Renal blood flow increases by as much as 70-80% by the end of the first trimester which helps to enhance excretion (Davidson and Dunlop, 1995). Increased blood flow to the capillaries of the skin and mucus membranes, and, in particular, to hands and feet, reaches maximum of 500ml per minute by the 36th week and is thought to eliminate extra heat generated by fetal metabolism. The associated peripheral vasodilatation explains why pregnant women, feel the heat and sweat profusely at times and often suffer from nasal congestion (Llewellyn, 1994). A greatly increased blood flow to the breasts

throughout pregnancy is suggested by the dilated veins on the surface of the breasts, as well as enlargement and tingling from early pregnancy (De swiet, 1991).

2.2.2 CHANGES IN THE URINARY SYSTEM.

By the second trimester renal blood flow has increased by as much as 70-80% and it remains at that level until 30th week, after which it declines slowly, although it is still above non-pregnant value at term (Mc Fadyen, 1995). As a result, the kidneys enlarge and glomerular filtration, which is assessed by measuring creatinine clearance, increases by about 45% by 8 weeks. This is maintained throughout the second trimester but decrease significantly during the last weeks of pregnancy (Davidson and Dunlop, 1995).

Changes in glomerular filtration rate GFR are partly responsible for the increased clearance of creatinine, urea, and uric acid which are also less efficiently reabsorbed in early pregnancy (Davidson and Dunlop, 1995). As a result, plasma levels of urea, uric acid and creatinine fall, although uric acid levels return to non-pregnant levels in late pregnancy (Cunningham et al, 1989).

Protein and amino acids are less efficiently reabsorbed, but while amino acids and vitamins are found in much greater amounts in the urine of pregnant women, proteinuria does not usually occur in normal pregnancy (Cunningham et al, 1989).

Glucose excretion increases as a result of the increased GFR of glucose rather than diminished reasorbtion (Baylis and Davidson, 1991). Glycosuria is therefore quite common in pregnancy and is not usually related to a high blood sugar level. It should,

however, be carefully monitored to exclude diabetes mellitus. Glycosuria can be a cause of urinary tract infection (Moore, 1994; Davidson and Dunlop, 1995).

Although 100 extra litres of fluid pass into the renal tubules each day, the urinary output is diminished because of enhanced tubular reabsorbtion of water. An accompanying increase in the reasorbtion of sodium is promoted, possibly by hormones aldosterone, progesterone, oestrogen and deoxy corticosterone (Hanretty and Miller 1997).

The urine of pregnant women is more alkaline owing to alkalemia of pregnancy, which is compensated for by renal bicarbonate excretion (Coustan,1994).

In early pregnancy, increased production of urine causes frequent micturition, but in later pregnancy, increased frequency is caused by pressure of the growing uterus on the bladder (Chamberlain , 1991).

Renal handling of water is more sensitive to maternal posture in pregnancy (Mc Fadyen, 1995). Excretion of water is reduced in the upright position or when the woman changes from the recumbent to supine position (particularly in late pregnancy) possibly owing to reduced renal perfusion subsequent to reduced venous return to the heart (section 2.2.1.4). Other theories accounting for reduced sodium and water excretion in the supine position relate to the release of antidiuretic harmone (ADH) and to the elevated pressure in the ureters (Cunningham et al, 1989).

Posture also affects the circadian rhythms of sodium excretion. The woman who rests by day in the recumbent position excretes maximum amounts of urine in the middle of the day. The women who is active by day, however, accumulates water in the form of

dependent oedema. At night this is then mobilised and the increased excretion results in nocturia (Mc Fadyen, 1995).

Under the influence of progesterone, the ureters become relaxed, and are dilated, enlongated and curved above the brim of the pelvis, particularly on the right side because of the dextrorotation of the uterus. This, along with compression of the ureters against the pelvic brim, can result into stasis of urine in the ureters with subsequent bacteriaurea and infection of the urinary tract (Moore, 1994). Hydroureter and hydronephrosis may be associated with stasis of urine, pyelonephritis and difficulty in interpreting intravenous pyelography during pregnancy.

The muscle of the bladder is relaxed owing to raised level of progesterone (Chamberlaion, 1991). Bladder vascularity increases and bladder capacity is reduced. To compensate for this, urethral length is increased. Towards the end of pregnancy, as the head engages, the entire bladder may be displaced upwards (Cunningham et al, 1989).

2.2.3 CHANGES IN THE GASTRO INTESTINAL TRACT

The changes in the gastrointestinal tract (GIT) appear to be of minor degree but may have a marked cumulative effect in some cases (Miller and Calendar, 1989). The main change is one of decreased motility which may be due to the effect of increased circulating progesterone. Many other alterations take place in the GIT (Hytten, 1990).The gums become edematous, soft and spongy during pregnancy, probably owing to the effect of estrogen, which can lead to bleeding when mildly traumatized as with a tooth brush . There is no good evidence that pregnancy caused tooth decay. Dental problems are more likely to occur because of gingivitis (Cunningham et al, 1989).

Increased salivation, ptyalism is a common complaint in pregnancy, but there is no evidence that more saliva is produced. The problem seems to be associated rather with nausea which prevents women from swallowing their saliva (Hytten, 1990). Nausea and vomiting complicates about 70% of pregnancies. It usually begins around 4-8 weeks and continues until about 14-16 weeks. Relaxation of the smooth muscle of the stomach and hypomotility in addition to raised levels of estrogen or HCG may all contribute to the problem. Although distressing and at times quite debilitating, and sometimes causing weight loss in early pregnancy, it rarely causes nutritional or electrolyte inbalance and is associated with satisfactory out come for the pregnancy (Cruishank and Hays, 1991). Occasionally vomiting may become excessive. Although the cause is still not clear, rising hormone levels are implicated by the fact that the condition is common in multiple pregnancies or hydatidiform mole (Hanretty and Miller, 1997).

A change in the sense of taste can occur early in pregnancy. It can be either a metallic taste in the mouth, distaste for something usually enjoyed or craving for a food not usually eaten (Mc Fadyen, 1995). An increase in appetite is also noticed by most women during pregnancy. It is probably related to the signals sent by progesterone to the center in the brain which controls fat storage through energy balance. It may also be due to the fall in plasma glucose and amino acids in early pregnancies. Many women notice an increased thirst in pregnancy. This is probably due to the fall in plasma osmolality, although it may also be related to rising levels of prolactin (Hytten, 1990). Resetting of osmotic threshold for thirst contributes towards the increased water retention which is a normal physiological alteration of pregnancy (Cunningham et al, 1989).

As pregnancy progresses, the stomach and intestines are displaced by the enlarging uterus (Cunningham et al, 1989). Raised intragastric pressure without an accompanying increase in tone of the cardiac sphincter causes reflux of acid mouthfuls with epigastric or retrosternal pain. The resulting symptom of heartburn is said to be so common that women do not complain of it (Mc Fadyen, 1995). Reduced intraoesophageal pressure and peristalsis with raised intragastric pressure also contribute to the reflux of acid into the oesophagus (Cunningham et al, 1989). Gastric tone and peristalsis are reduced, probably owing to reduced levels of the hormone, motilin. Gastric secretion of hydrochloric acid is also reduced, suggesting reduced vagal activity, which may account for the reduced incidence of peptic ulcer (Case and Waterhouse, 1994). There are now conflicting opinions about whether pregnancy causes a delay in gastric emptying time, which is of particular relevance if general anaesthesis is required. It appears that a glucose meal may cause a delay in stomach emptying related to the greater osmolality of its contents, which explains the nausea often experienced after a glucose tolerance test (Hytten, 1991).

Passage of food through the intestines may be so much slower that there is increased absorption of water from the colon, probably as a result of raised levels of aldosterone and angiotensin, which contributes to the tendency of constipation. A higher residue diet which helps to hold water in its passage through the colon will help to relief this problem (Hytten, 1990). Constipation may also be caused by mechanical obstruction by the uterus and by the relaxing effect of progesterone on smooth muscle (Cruikshank and Hays, 1991). Constipation may exacerbate hemorrhoids, which are caused by the

increased pressure in the veins below the level of the enlarged uterus (Cunningham et al, 1989).

The gall bladder increase in size and empties more slowly during pregnancy. Cholestasis which is almost physiological in pregnancy is probably a hormonal effect and can lead to pruritus or gallstone formation (Mc Fadyen, 1995). The once widely accepted belief that pregnant women are predisposed to gall stone formation is now considered to be lacking in evidence (Hytten, 1991).

Although hepatic blood flow is unchanged in pregnancy, there are many changes in liver function that mimic liver disease, therefore liver function test in pregnancy should be interpreted with caution. Serum albumin levels fall progressively throughout pregnancy and at term are 30% lower than the non-pregnant level; serum alkaline phosphates levels rise progressively during pregnancy and at term are two to four times non-pregnant values. Serum cholesterol levels are raised two fold by the end of pregnancy while many liver proteins are raised in response to estrogen and fibrinogen levels are increased 50% by the end of the second trimester (Cruikshank and Hays, 1991).

2.2.4.0 **CHANGES IN METABOLISM**.

Demand for energy can be partitioned into several component. One of the main component is energy required for basic physiological processes like respiration, circulation, digestion, secretion, maintenance of body temperature, growth and repair; all these account for 66% of total energy requirement in the non-pregnant female, i.e 1,440 kcal/day. Another component of energy requirement is the energy for everyday activities like walking, maintaining posture, speech and eating; they are equivalent to 17% of total

energy requirement in the non-pregnant state i.e about 360 kcal/day. Energy requirement for occupational work varies greatly and depends on occupation. It is probably 7 – 10 % of the total energy requirement i.e. 150 – 200 kcal/day. Relatively small amount of energy is required for specific dynamic action of food as metabolism appears to be stimulated by the food intake, they account for about 7% of the total in non-pregnant female i.e 144 kcal/day. The total energy required in non-pregnant female is about 2,100 kcal/day.

In pregnancy, there is a marked increase in energy requirement for basic physiological process due to the development of the fetus. A slight decrease in Energy requirement for every day activity may occur as pregnancy advances and it is assumed that occupational energy requirement will play only a minor role, at least in the last trimester. There ought to be an increased intake of food and therefore an increase in energy required for specific dynamic action of food. The total energy required by a woman in advanced pregnancy will be around 2,500 kcal/day. During lactation a further increase is required for milk production and the total requirements will be in the region of 3000 kcal/day (Miller and Calendar, 1989).

To attain the additional energy requirement, there is the need for an increase in the rate of metabolism in pregnant woman. The increased dietary intake in addition to the gastro intestinal changes in pregnancy are accompanied by characteristic alterations in the metabolism of carbohydrate, protein and fat (Case, 1985).

2.2.4.1 CARBOHYDRATE METABOLISM

The changes in carbohydrate metabolism is brought about, mainly, by human placental lactogen to ensure that glucose is readily available for body and brain growth in the developing fetus, and protect the mother against nutritional deficiencies (Case, 1985).

In the non-pregnant state, ingested glucose is dealt with in four ways. Under the influence of insulin it may be deposited in the liver as glycogen. Some escape into the general circulation and a proportion of this is metabolised directly by the tissues. Some are converted to depot fat, and a further portion is stored as muscle glycogen, again with the aid of insulin. The blood sugar is maintained between 4.5 and 5.5 mMol/l (80-100 mg/dl). Sugar which passes out in the glomerular filtrate is never in excess of the amount which can be reabsorbed by the tubules, and none appears in the urine (Fraser, 1991) except in disease condition.

A marked alteration in carbohydrate metabolism occurs in pregnancy. There is a demand on the part of the fetus for an easily convertible source of energy. At the same time there is need to store energy for future demands such as lactation and the steadily increasing growth of the pregnancy and also to provide a more steady source of energy in the form of a high energy fuel. This the maternal body achieves by storage of fat. The major portion of the diet is carbohydrate and this requires to be redirected to satisfy the above requirements. The first noticeable change occurs in the blood glucose and this can be demonstrated by an oral glucose tolerant test. It can be seen from this that the blood glucose, after a meal, remains high thus facilitating placental transfer (Case and Waterhouse, 1994). Mechanism governing this may be as follows: In pregnancy there is

an increase in antagonists to insulin. These are the raised level of steroids, corticoids and human placental lactogen (HPL) produced by the placenta. Less glycogen is deposited in the maternal liver and muscles. More sugar circulates for a longer time in the maternal blood. The placenta is able to pass more to the fetus. At the same time rather more passes the glomerulus than can be reabsorbed by the renal tubules and a small amount appear in the urine of many pregnant women. This is diabetogenic effect of pregnancy (Cruikshank and Hays, 1991).

2.2.4.2 **PROTEIN METABOLISM.**

The overall aim of protein metabolism changes is directed towards positive nitrogen balance and this reaches its peak at 28th week. By the end of pregnancy about 500g have been retained (Miller and Calendar, 1989). A more recent studies show that during normal pregnancy, approximately 1kg of the weight gain is attributable to protein (Moore, 1991). In either case, half of the gain is found in the fetus and the placenta. The remaining half is being distributed as uterine contractile protein, breast glandular tissue, plasma protein and hemoglobin. The positive nitrogen balance is achieved by a complicated series of interlocking mechanisms. Increase in appetite leads to increase in the intake of food. Diminished intestinal motility with accompanying improved absorption of amino acid raises the amino acid and nitrogen content of the liver. The liver also uses the amino acid for plasma protein synthesis and blood amino acid, from where the fetus is nourished. For the liver amino acid to be adequate for its function, its

deamination is greatly inhibited by both human chorionic gonadotrophin and human placental lactgogen. As a result output is reduced (Miller and Calendar, 1989).

Cortisol, estrogen, progesterone, aldosterone and other steroids are greatly increased in pregnancy, so also is the transport of iron. This may account for some of the protein changes, the excess of which is probably retained in preparation for lactation (Stewart and Taylor, 1976).

2.2.4.3 FAT METABOLISM

Fat appears to be the main form of maternal stored energy during pregnancy. Most of this is in the form of depot fat in the abdominal wall, back and thighs, and perhaps retroperitoneally. Despite the enlargement only some 12-20g are deposited in the breasts out of about 4000g stored by 30 weeks of gestation. Blood fat increases from third month with the total lipoid increasing from about 700 mg/dl to 1,050 mg/dl (50% increases). The cholosterol in the blood increases from 120 mg/dl to 280 mg/dl (133.33%) (Miller and Calendar, 1989).

The high blood levels of fat and increased deposition of fat are due partly to increased intake and partly to increased conversion of glucose to fat which is facilitated by insulin antagonists action (Moore, 1991).

Three facts have to be related. The total metabolism and demand for energy are increased in pregnancy, glycogen stores are diminished and therefore energy obtained directly from carbohydrate will be reduced and although blood fat is greatly increased, only a moderate amount is laid down in fat stores.

Energy demand in pregnancy when glycogen is lacking in both liver and muscle, results to mobilisation of fat in the fat depot into the blood. Fat metabolism hence increases in the muscle which easily induce ketosis. This takes place whenever there is any strain, such as labour, imposed in pregnancy.

It is therefore recommended that no carbohydrate restriction diet should be given to the pregnant women. Also fasting should be discouraged, except with the medical supervision by medical experts, particularly in the first and third trimester. The main danger to the fetus possibly being from dehydration rather than from malnutrition (Athar, 1990).

2.2.5 **WEIGHT GAIN**

There is an increase in weight during pregnancy equivalent to 25% of non-pregnant weight: approximately 12.5 kg in an average woman. There is marked variation in normal women but the main increase occurs in the second half of pregnancy and is usually about 0.5kg per week. Towards term, the rate of weight gain diminishes and weight may fall after 40 weeks. The increase is due to growth of the fetus, enlargement of maternal organs, maternal storage of fat and protein and increase in maternal blood volume and interstitial fluid (Miller and Callendar, 1989).

Continuing weight increase in pregnancy is considered to be a favorable indicator of maternal adaptation and fetal growth. Analysis of many studies investigating weight gain in pregnancy demonstrate the wide range that is compatible with normality but suggests the following figures for the primigravida

Expected total increase is 12500g

i. 4000g in first 20 weeks.

ii. 8,500g in second 20 weeks (400g/week in the last trimester).

It is also suggested that the average multigravida gains about 1000g less than the primigravidae (Hytten, 1991).

Many factors influence weight gain. The degree of maternal edema, maternal metabolic rate, dietary intake, vomiting or diarrhea, smoking, amount of amniotic fluid, and size of the fetus must all be taken into account. A recent study suggests that maternal age, pre-pregnancy body size, parity, race, ethnicity, hypertension and diabetes also influence the pattern of maternal weight gain (Abrams et al, 1995).

The table below shows the distribution of the average increase in weight.

Table 1. **AVERAGE INCREASE IN WEIGHT.**

BODY COMPONENT	**WEIGHT INCREASE(g)**
Breasts	400
Fat	3,500
Placenta	600
Fetus	3,400
Amniotic Fluid	600
Uterus Increase	1000
Blood volume increase	1,500
Extracellular fluid	1,500
Total	12,500

Hytten, 1990.

Wide range of normal weight gain has suggested that the routine practice of only weighing pregnant women is of doubtful value in the provision of quality antenatal care (Hytten, 1990).

2.3.0 PHYSIOLOGICAL ROLE OF SOME BLOOD CHEMICAL PARAMETERS IN PREGNANCY

2.3.1 TOTAL PROTEIN

The plasma protein biosynthesis takes place in the liver with higher turnover rate in pregnancy. The desire for protein reserve; increase in basal metabolic rate, hence need for increase hemoglobin to transport more oxygen; increase in various pregnancy hormones and antibodies biosynthesis justifies the physiological increase in total amount of protein in pregnant women. Pathologically low total amount of protein, on the other hand, upsets the normal distribution of water between the tissues and the blood particularly as pregnancy progresses and greatest in lower limbs causing odema. Moreover, the liver, kidney and pancreas undergo severe degeneration, situation that threatens life of expectant mother (Peter, 1982.)

With increase in appetite and consequent increase in intake, coupled with diminished intestinal motility and considerable improvement in absorbtion, more amino acids are absorbed by the gut of pregnant women into the liver. The hormone, human placental lactogen, inhibits the deamination activity in the liver to form urea, hence most of the amino acids find their way into the blood plasma as serum protein and serum amino acids which are used for fetal growth and development. The elevated serum total protein is, however, masked by hemodilution occasioned by the combined action of oestrogen, progesterone and aldosterone (Miller and Callendar, 1989). This makes the concentration of the total protein in the serum of pregnant women apparently low.

The reduction in the serum total protein in pregnancy is reported by Case and Waterhouse, 1994 to lead to lower osmotic pressure, contributing to oedema of the lower

limbs seen in late pregnancy. In the absence of disease, moderate oedema is considered as physiological and an indicator of favourable outcome of pregnancy (Davey, 1995.)

The reduced concentration of serum total protein in pregnancy is, however, reported not to be a major factor causing water retention in oedema (Eugene and Sandbery, 1978).

2.3.1 ALBUMIN:

Albumin is the main fraction of protein that is stored in the body from where the fetus derive their nutritional need, its concentration in the serum of pregnant women is therefore reduced (Case and Waterhouse, 1994). The serum albumin concentration in pregnancy is further reduced by hemodilution, making it fall progressively as the pregnancy advances. The maximum percentage decrease is approximately twice that of the total protein. The reduction in the serum albumin is sufficient to account for the fall in the serum total protein of pregnant women (Stewart and Taylor, 1976). Thus a decrease in albumin/globulin ratio occur normally in pregnancy.

Low concentration of serum albumin in pregnant women is physiologically compensated for by increase in other fractions of the serum protein notably immunoglobulin (defense protein) and hemoglobin (transport protein). This minimize the effect on osmotic pressure of the plasma and moderate the consequence of odema (Peter 1982). Major function of serum albumin is regulation of blood volume and transport of fatty acids (Keller, 1963).

2.3.3 UREA

Serum urea concentration in pregnancy is greatly lowered and this may be attributed to hemodilution, however, the reduction in concentration is greater than can be

explained by hemodilution alone. The inhibitory effect of the hormone, human placenta lactogen, on deamination of amino acids (in liver) to form urea, lower the output of urea in the hepatic cells. This is believed to be a major factor in the marked reduction of serum urea concentration in pregnancy (Miller and Callendar, 1989).

Pregnant women are known to have very high turn-over rate for serum protein and liver proteins, this necessitate the inhibitory action of hpl to regulate the deamination process to a physiological level, so that deamination will commensurate with urea synthesis and excretion (Davidson and Dunlop 1995). The hormone, hpl, is present only in pregnant women and this is why there is elevated serum urea in non-pregnant diabetic patient whose reserved protein is excessively catabolized to form urea (Peter, 1991).

The increase in renal plasma flow as well as increase in glomerular filteration rate are also important factors partly responsible for increased clearance of urea which are also less efficiently reabsorbed in pregnancy and as a result serum level of urea fall (Davidson and Dunlop, 1995; Cunningham et al, 1989).

2.3.4 **CREATININE:**

Creatinine is the end product of phosphocreatinine metabolism mostly formed by the muscle cells. The muscle mass of individual determines the rate and amount of creatinine formed. Pregnancy does not affect muscle mass, hence has no reported effect on creatinine. Creatinine is not reabsorbed by the tubules of the kidney and gradually increase in concentration as urine passes down the tubules (Davidson and Dunlop, 1995).

Though increase in renal plasma flow and glomerular filteration rate is expected to increase the clearance of creatinine during pregnancy, the serum concentration is not

affected by pregnancy. The serum creatinine concentration remain same throughout pregnancy (Stawart and Taylor, 1976).

2.3.5 SODIUM ION

The total amount of sodium in a woman weighing 60kg is 53.6g out of this 20g is in bone and is virtually immobile, taking little or no part in the daily exchanges of sodium throughout the body. The fatty tissues of the body contain almost no sodium and each 100g of fat free body weight contains 0.109g of sodium.

The intake of sodium varies widely according to habit, climatic and working conditions with a range 5-15g /day. In healthy body, the daily loss of sodium exactly matches the intake so that a steady state is preserved. In climatic or working conditions where sweating is excessive, a considerable amount of sodium may be lost through the skin, and the urinary loss of sodium is correspondingly reduced, though under these conditions the amount of sodium conserved in this way may be insufficient to maintain normal plasma concentration consequently hyponatremia sets in causing miners' cramp, unless steps are taken to increase the intake appropriately. In average healthy woman, the urinary output of sodium is 4 – 6g/day and random specimens of urine should contain not less than 3g/l.

When excessive sodium is lost, its intravascular concentration is at first maintained by withdrawal of sodium from the extravascular interstitial spaces into the vascular pool. If sodium depletion continues the total sodium content of the plasma is reduced and the plasma osmotic pressure falls. As a result water escapes from the plasma

into the interstitial space so that plasma volume reduces which is detrimental to pregnant women (Keller, 1963, Mc Fadyen, 1995).

The increase in production of the hormone aldosterone in pregnancy promotes the retention of sodium (Ramsay, 1991). There is gain in total amount of sodium ion. About 850 millimole of sodium ion are retained during pregnancy and this is divided in almost equal proportion between the mother and the conceptus (Davey, 1995) and in the same proportion as in the extra water retained. Sodium is retained at steady rate of about 0.5g per week (Keller, 1963).

2.3.6 POTASSIUM ION

This is the main intracellular cation and it is present in concentration of 0.265g per 100g of lean body weight. A woman weighing 60kg contains 130g of potassium, the total amount of potassium available for exchange being 102g, as some is fixed.

The average intake of potassium is 2 – 6g/day and the output is approximately the same. Four-fifths of the normal daily potassium loss occurs in the urine and one fifth through the faeces. Vomiting or diarrhea may cause serious potassium loss resulting in weakness of musclar action, this is particularly evident in cardiac muscles (Keller, 1963).

Like sodium, there is retention of potassium in pregnancy in excess of the normal non-pregnant level. About 3.6 millimole are reported to be stored during pregnancy and the conceptus receives almost twice as much as the mother (Miller and Callendar, 1989). It is probably that, like sodium, all the extra potassium so retained is utilized in the formation of new tissues in connection with the pregnancy.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 MATERIALS

3.1.1 APPARATUS

Colorimeter: Screen master hospitex diagnosis colorimeter, assembled by Transworldmedical system, group 27, chemin pre-bouvier, 1217 Meyrin Switzerland. P. O. Box 433. Geneva.

Weighing Balance: Orma electronics, Bc, Paris.

Flame photometer: PFP 7, S/No 6907, Jenway Gransmore, Fested, Dunmow, Essex CM6, 3L England.

water bath: Gallenkamp equipments limited, England.

Centrifuge: ALC, 4217, England.

Micropipette: Kent Industrial Measurement limited, Chertsey, Surrey, England.

Hot plate: OHAUS electronics corporation. Florham Park, N. J., West Germany.

Refrigerator: LEECOOL equipments, Japan.

3.1.2 CHEMICALS AND REAGENTS:

All chemicals used were of General purpose grade except where otherwise stated. They were all obtained from BDH chemicals Ltd, poole, England.

Biuret reagent: Approximately 9g of sodium potassium tartarate was dissolved in 500 ml of 0.2N sodium hydroxide (AR). Then 3g of copper(II) sulphate was added and dissolved by stirring, then followed by addition of 5g of potassium Iodide before the

volume was made up to a litre with 0.2N sodium hydroxide (AR). The Biuret reagent was stored in a polythene bottle, away from strong direct light.

0.2 N sodium hydroxide: Exactly 8g of sodium hydroxide pallets AR was dissolved in about 700 ml of distilled deinonized water. It was shaken vigorously to completely dissolve and the volume made to a litre with distilled water.

0.3 M Succinate buffer (4.2): 11.9g of succinic acid AR was dissolved in 800 ml of distilled deionised water and pH adjusted to 4.2 using 0.1N sodium hydroxide AR. The volume was made to mark with distilled deionised water in 1 litre volumetric flask.

Bromocresol green solution: 0.419g of bromocresol green was dissolved in 100ml of 0.1 N sodium hydroxide AR and diluted to 1 litre with the 0.10 N sodium hydroxide AR.

Albumin working solution: Obtained by adding 1 volume of bromocresol green solution to 3 volume of succinate buffer and 4ml of brij – 35 per litre and adjusting the pH to 4.2 $\pm$ 0.05 using 0.1 N sodium hydroxide AR.

Acid stock reagent A: 5g of ferric chloride was dissolved in 20ml of distilled deionised water, 100ml of 85% phosphoric acid AR was added and cooled. It was made up to 250ml mark with distilled deionised water.

Acid stock reagent B: 300ml of concentrated sulphuric acid AR was slowly added to 700ml of distilled deionised water in a 2 litre conical flask. It was cooled in a cold water bath.

Urea working acid reagent: Exactly 0.5ml of acid stock reagent A was added to 1 litre of acid stock reagent B.

Urea colour reagent A: 20g of diacetyl monoxime was dissolved in 1 litre of distilled deionised water and filtered.

Urea colour reagent B: 5g of thiosemicarbazide was dissolved in 1 litre of distilled deionised water.

Urea working colour solution: 67 ml of urea colour reagent A and 67 ml of urea colour reagent B were added & then made to 1 litre with distilled deionised water.

Saturated aqueous picric acid solution: 20g picric acid AR was dissolved in 1 litre of distilled deionised water. It was well shaken and allowed to settle before use.

10% sodium tungstate: 10g of sodium tungstate was dissolved in 100ml of distilled deionised water.

2/3 N sulphuric acid: 18ml of concentrated sulphuric acid AR was mixed with 900ml of distilled deionised water carefully and made to 1 litre with the water.

0.75N sodium hydroxide: This reagent was prepared from 1N sodium hydroxide commercial stock by mixing 75ml of the stock with distilled deionised water to make 100ml.

Albumin standard: Commercial grade, 5 g/100ml. Randox laboratories limited, Actmore, Diamond road, Crumtin,Co-antrim, UK BT29 4QY.

Creatinine standard: Commercial stock 530 UMol/l Randox laboratories limited, Actmore, diamond road, Crumtin Co-antrim. UK BT29, 4QY.

Standard protein: Commercial grade, 8 g/100ml, Texas International Laboratories Inc. Housten–Texas.

Urea standard: Commercial stock, 10 mMol/l Randox Laboratories Limited, Actmore, Diamond road. Crumtin, Co.datrin, UK BT29, 4QY.

Sodium standard (1,000 ppm): Commercial stock, Jenway, Felsted, Gt Dunmow, Essex, England.

Potassium standard (1,000 ppm): Commercial stock, Jenway, Felsted, Gt Dunmow, Essex, England.

3.1.3 SAMPLING

Sampling was carried out in four well equipped general hospitals in Niger state. The state is divided into four zones, such that each of the zone has one of the general hospitals. These zones are Minna, Bida, Suleja, and Kontagora as indicated in the map (fig. 2).

Niger state is located in the North-West part of Nigeria. The state is bounded in the North by Kebbi and Kaduna state and in the South by Kwara and Kogi state. The state also share boundary with Federal Capital Territory. With a population estimate of about 3.2 million people, the power state, as it is tagged, is inhabited by Nupe, Gwari, Hausa, Kambari, Koro, Kadara and Wawa tribes. There are also large number of Yoruba and Ibo settlers, mostly traders and civil servants, dispersed around the state. The major occupation of the indigenous people is farming and fishing along the river Niger and its tributaries .

Table 2: Sample size (Different zones).

	Minna			Bida	Suleja	Kontagora
	General Hospital	IBB specialized Hospital	FUT Clinic	Federal Medical Centre	General Hospital	General Hospital
Pregnant	38	7	19	11	15	6
Non Pregnant	12	5	3	9	5	8
Menopausal	9	4	0	4	3	5

More samples were obtained from Minna zone and in each zone, only pregnant women with their pregnancy above five months were sampled. The non-pregnant women samples were taken from those apparently healthy (Mostly volunteers) and all the menopausal women sampled were above 55 years of age.

MAP OF NIGER STATE

FIGURE 2

SOURCE: Department of Budget & Planning
Statistics Division,
P.M.B. 115,
Minna, Niger State.

3.2.0 METHOD

AUTOCALIBRATION OF THE COLORIMETER

The Screen master hospitex diagnosis colorimeter used for the analysis is automated and readily programmed for each parameter. However, revalidation and, if necessary calibration, is necessary before each set of test is carried out.

The following are the calibration procedures:

1. The colorimeter was allowed to warm-up for ten minutes.
2. The concentration mode was selected using the mode button.
3. The wavelength for thc parameter was selected using wavelength knob.
4. The blank (as prepared in each parameter) was then placed in the colorimeter and the instrument was zeroed.
5. The standard (as prepared in each parameter) was then placed in the colorimeter. If it did not read the appropriate concentration, it was set to read the concentration of the standard.
6. Blank was checked again and re-zeroed.
7. It was used immediately to estimate the samples prepared.

3.2.1 TOTAL PROTEIN

The Biuret method was used for determination of protein as reported by (Peter et al, 1982). 0.10 ml of serum was added to 4.90ml of Biuret reagent and incubated at 37°C for 10 minutes. The standard protein was treated in the same way . Their absorbance was measured at 540nm using water in place of sample as blank. The concentration was read directly on the colorimeter.

3.2.2 ALBUMIN

Albumin concentration was determined by the method of Batholomew and Delaney (1966) which was modified by Doumas et al, (1971) as reported by Peter et al (1982), 0.05 ml of serum was added to 5ml of albumin working solution. The standard was treated in the same way.

Their absorbance was quickly measured at 628nm using bromocresol green solution to zero the colorimetre. The concentration was read directly on the colorimeter.

3.2.3 UREA

Urea concentration was determined by diacetyl monoxime method (Peter et al, 1982). Two ml of distilled deionised water was transferred into testubes containing 0.2 ml of serum, standard and blank (Water). Each testube was thoroughly mixed. Then 2 ml of urea working acid reagent was added, followed by 2 ml of urea working colour solution. The testubes were thoroughly mixed and placed in a boiling water for 20 minutes, cooled and measured at 520 nm in the colorimeter. The concentration was read directly.

3.2.4 CREATININE

Creatinine was determined by Rebery-Folin method of 1971 as reported by Peter et al,(1982). The procedure was carried out in two stages. In the first stage, 0.6 ml of distilled deionised water was transferred to labeled testubes containing 0.1 ml of serum samples and blank, followed by addition of 0.2 ml of 10% sodium tungstate solution and 0.2 ml of 0.67Nsulphuric acid. The testubes were then centrifuged at 500 rpm for 10 minutes. In the second stage, 0.6ml of supernatant from the first stage were transferred to

appropriately labeled cuvettes. Exactly 0.6 ml of standard was also transferred to a separate cuvette. Then 0.20 ml of 0.75N sodium hydroxide and 0.20 ml of picric acid were added to each cuvette. The mixture was allowed to stand for about 10 minutes and the absorbance measured at 520nm using the colorimeter which gave the concentration directly

3.2.5 SODIUM ION/POTASSIUM ION

In each case, the sample was prepared by dissolving 0.2 ml of blood serum in 100ml of distilled deionised water and shaken vigorously to allow for thorough mixing.

Preparation of Caliberation curve for Na^+ estimation:

From the sodium standard stock solution, a range of concentrations from 2 ppm to 10 ppm were prepared by dissolving 0.2, 0.4, 0.6, 0.8 and 1.0 ml of the stock respectively in 100 ml of distilled deionised water

A calibration curve was prepared by plotting the emission intensity of the standards against their respective concentrations in ppm. The concentration of the sample was then extrapolated from the curve using its emission intensity (figure 3)

Preparation of calibration curve for K+ estimation:

From the potassium standard stock solution, a range of concentrations from 2 ppm to 10 ppm were prepared by dissolving 0.2, 0.4, 0.6, 0.8 and 1.0 ml of the stock respectively in 100ml of distilled deionised water.

A calibration curve was prepared by plotting the emission intensity of the standards against their respective concentrations in ppm. The concentration of the sample was then extrapolated from the curve using its emission intensity (figure 4)

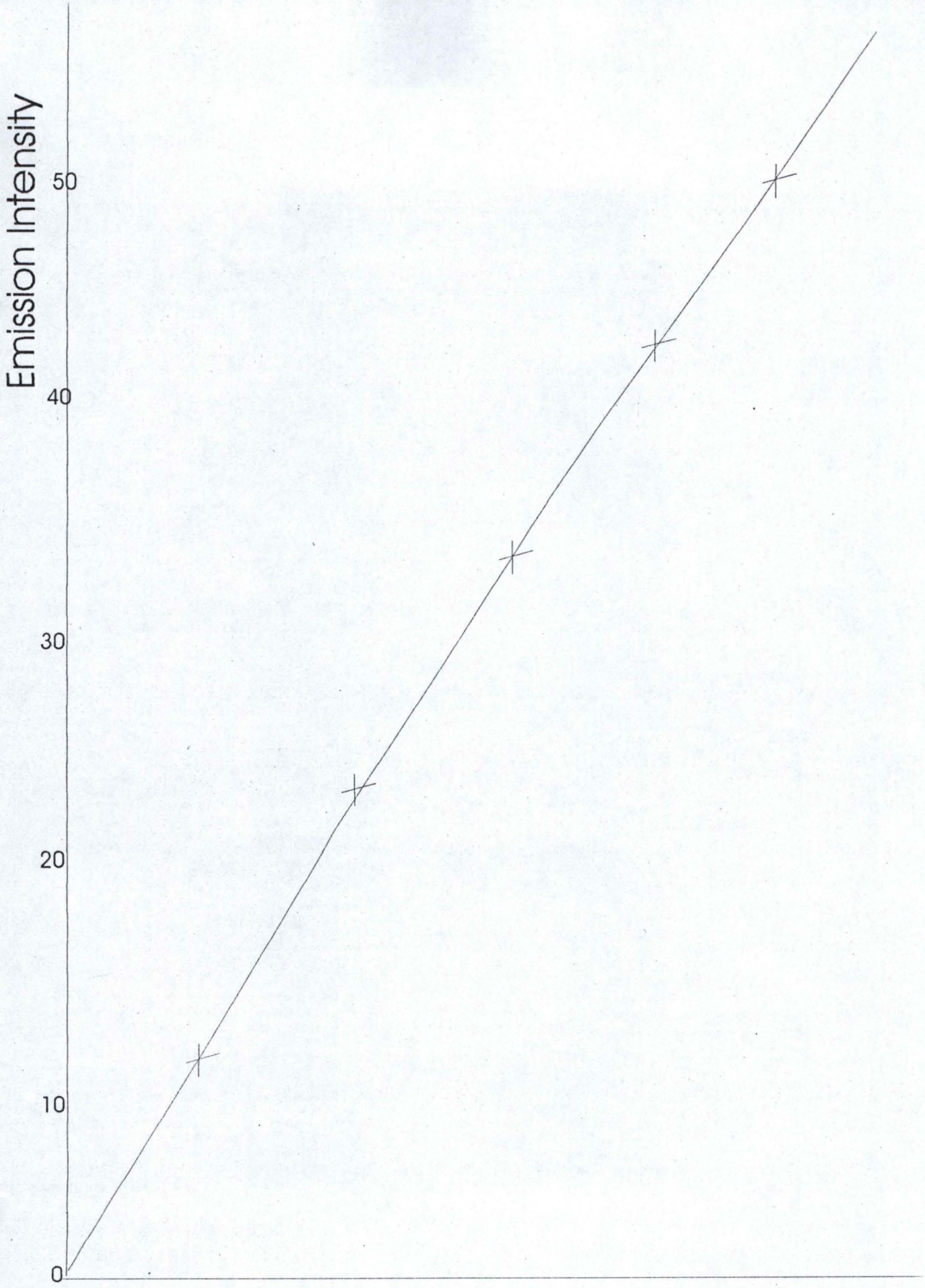

Figure 3: Calibration Curve For Na^+ Estimation

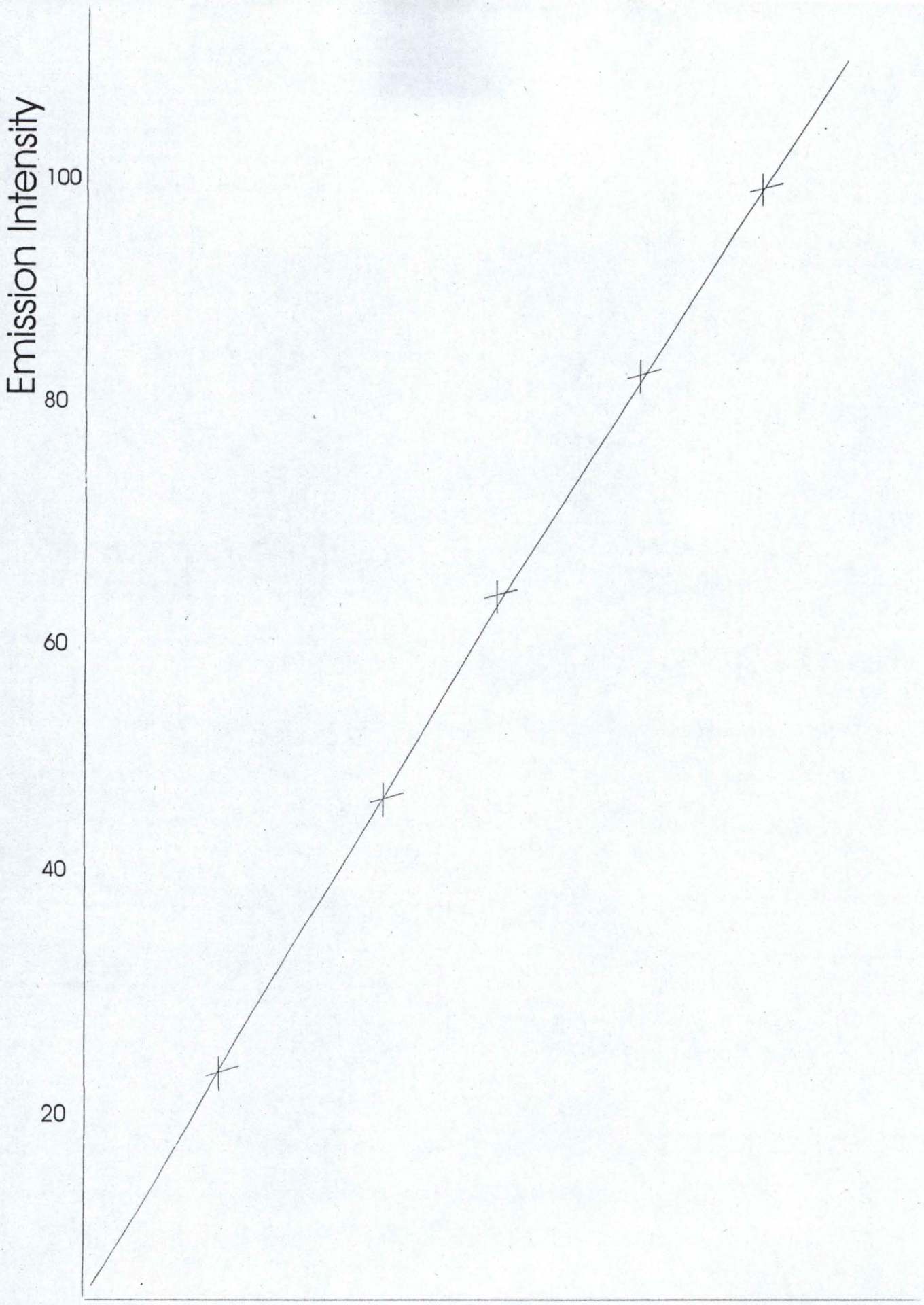

Figure 4: Calibration Curve For K^+ Estimation

3.3.0 HYPOTHESIS AND STATISTICAL ANALYSIS

3.3.1 HYPOTHESIS

The null hypothesis which means that there is no significant difference in the means of the variables was used. These means were therefore subjected to statistical analysis to accept or reject the set hypothesis.

3.3.2 STATISTICAL ANALYSIS

Analysis of variance was used to compare and evaluate the degree of difference for different parametres in the pregnant, non-pregnant, and menopausal women, using statographic computer software package.

CHAPTER FOUR

4.0 RESULTS

4.1 SERUM TOTAL PROTEIN

The mean serum total protein concentration was significantly lowered in pregnancy (7.29 ± 0.21g/100ml) from the normal non-pregnant mean concentration of 7.99 ± 0.30 g/100ml (P>0.05). In the menopausal women the mean serum total protein concentration (8.75 ± 0.39 g/100ml) was significantly higher than the mean concentration in both pregnant and non pregnant women (p<0.05) (Table 3 and figure 5).

4.2 SERUM ALBUMIN

There was a significant difference in the mean serum albumin concentration of pregnant women (3.28 ± 0.22 g/100ml) and non-pregnant women (4.07 ± 0.17 g/100ml) (P>0.05). The mean serum albumin concentration in pregnant women (3.28 ± 0.22 g/100ml) and non-pregnant women (4.07 ± 0.17 g/100ml) are significantly lowered than the mean serum albumin concentration in menopausal women (4.30 ± 0.31 g/100ml) (P>0.05). (Table 3 and figure 6).

4.3 SERUM UREA.

Significant difference exist between the mean serum urea concentration of pregnant women (1.66 ± 0.29mmol/l) and non-pregnant women (3.72 ± 0.31mmol/l) (P>0.05). Furthermore, the mean serum urea concentration in pregnant women (1.66 ± 0.29mmol/l) and non-pregnant women (3.72 ± 0.31 mmol/l) are significantly lowered than the mean serum urea concentration in menopausal women (4.90 ± 0.64mmol/l) (P>0.05). (Table 3 and Figure 7).

4.4 SERUM CREATININE

The mean of serum creatinine concentration in pregnancy (95.25 ± 5.70 μmol/l is significantly lowered than the mean serum creatinine concentration in non-pregnant women (99.78 ± 3.64 μmol/l} (P>0.05). In the menopausal women, the mean serum creatinine concentration (98.17 ± 4.69 μmol/l} is insignificantly higher than the mean serum concentrations in pregnant women (95.25 ± 5.70 μmol/l) (P<0.05) but not statistically different from the mean serum creatinine concentration in non-pregnant women (99.78 ± 3.64 μmol/l} (P>0.05) (Table3 and figure 8).

4.5 SERUM SODIUM ION

The mean serum sodium ion concentration in pregnant women (137.25 ± 5.64 mmol/l} is significantly lowered than the mean serum sodium ion concentration in non-pregnant women (153.11 ± 8.94 mmol/l) (P>0.05). The mean serum sodium ion concentration in menopausal women (156.43 ± 8.25mmol/l) is insignificantly higher than the mean concentration in non pregnant women (153.11 ± 8.94mmol/l) but significantly higher than the mean serum sodium ion concentration in pregnant women (137.25 ± 5.64 mmol/l} (P<0.05) (Table 3 and figure 9).

4.6 SERUM POTASSIUM ION

There is a significant difference between the mean serum potassium ion concentration in pregnant women (4.05 ± 0.61 mmol/l and non-pregnant women (4.60 ± 0.45mmol/l) (P>0.05). In menopausal women, the mean serum potassium ion concentration (4.75 ± 0.35mmol/l) has no significant difference with the mean concentration in non-pregnant women (4.60 ± 0.45mmol/l) (P<0.05), however there is significant difference with the mean concentration in pregnant women (4.05 ± 0.62 mmol/l) (P<0.05) (Table 3 and figure10).

Table 3:

Mean and standard deviation of serum total protein, albumin, urea, creatinine, sodium ion and potassium ion concentrations in pregnant, non-pregnant and menopausal women in Niger state.

	NON-PREGNANT	PREGNANT	MENOPAUSAL
	N= 41	N= 96	N = 25
TOTAL	7.99	7.29	8.75
PROTEIN (g/100ml)	± 0.30	± 0.21	± 0.39
ALBUMIN	4.07	3.28	4.30
(g/100ml)	± 0.17	± 0.22	± 0.31
UREA	3.72	1.66	4.90
(mmol/l)	± 0.31	± 0.29	± 0.64
CREATININE	99.78	95.25	98.17
(umol/l)	±3.64	± 5.70	± 4.69
SODIUM ION	153.11	137.25	156.43
(mmol/l)	± 8.94	± 5.64	± 8.25
POTASSIUM ION	4.60	4.05	4.75
(mmol/l)	± 0.45	± 0.61	± 0.35

Table 4
Sample correlations

	Total protein	creatinine	Urea	Albumin	Sodium	Potassium
Total Protein	1.0000	0.1839	0.7646	0.8600	0.6407	0.4574
	(75)	(75)	(75)	(75)	(75)	(75)
	.0000	.1142	.0000	.0000	.0000	.0000
creatinine	.1839	1.0000	.2650	.2512	.2786	.1950
	(75)	(75)	(75)	(75)	(75)	(75)
	.1142	.0000	.0216	.0297	.0155	.0937
Urea	.7646	.2650	1.0000	0.8050	.6580	.4696
	(75)	(75)	(75)	(75)	(75)	(75)
	.0000	.0216	.0000	.0000	.0000	.0000
Albumin	.8600	.2512	.0850	1.0000	.6620	.4789
	(75)	(75)	(75)	(75)	(75)	(75)
	.0000	.0297	.0000	.0000	.0000	.0000
Sodium	.6407	.2786	.6580	.6620	1.0000	.5872
	(75)	(75)	(75)	(75)	(75)	(75)
	.0000	.0155	.0000	.0000	.0000	.0000
Potassium	.4574	.1950	.4696	.4789	.5872	1.0000
	(75)	(75)	(75)	(75)	(75)	(75)
	.0000	.0937	.0000	.0000	.0000	.0000

Coefficient (sample size) significance level.

CORRELATION OF THE PARAMETERS

All the parameters are positively correlated to one another ($P<0.05$) and the correlations are strong, except with creatinine which is not strongly correlated with any of the parameters. In fact the positive correlation of creatinine with total protein and potassium ion is very insignificant and weakly significantly correlated with all other parameters ($P<0.05$). This confirm the fact established by Stewart and Taylor (1976) (Table 4).

CHAPTER FIVE

DISCUSSION

The results confirm the claim by Chamberlain, 1991 and Llewellyn, 1998 that pregnancy causes alterations all over woman's body systems. These alterations are similar for the parametres under consideration, suggesting that the factors responsible for the changes have common origin. However, the changes are more pronounced in serum albumin and serum urea probably due to other additional factors (Miller and Calendar, 1989).

TOTAL PROTEIN

The mean serum total protein concentration obtained for pregnant women (7.29 $\pm$ 0.13 g/100ml) and that obtained for non-pregnant women (7.99 $\pm$0.30 g/100ml) agree with values reported by Hacker and Moore (1986) (5.50 – 7.50g/100ml) and (6.50 – 8.50 g/100ml) respectively.

The significant difference between the mean serum total protein for pregnant women (7.29$\pm$0.21g/100ml) and non-pregnant women (7.99 $\pm$ 0.30g/100ml) {P>0.05} could be attributed to hemodilution. Though there appears to be lower concentration per milliliter of plasma in pregnancy, the total amount of protein is increased considering the increase in plasma volume caused by increased plasma volume stimulating hormones concentration in circulation in pregnancy (Moore, 1994). The actual gain in total protein concentration in pregnancy accounts for about 18% at term (Guyton, 1991). Similarly, the significant difference between the mean serum total protein in menopausal women (8.75 $\pm$ 0.39 g/100ml) with that of pregnant women (7.29 $\pm$ 0.21 g/100ml) ($p<0.05$) and non pregnant women (7.99 $\pm$ 0.30 g/100) ($p<0.05$) is due to reduction of plasma volume stimulating hormone concentration in circulation in menopausal women and its

elevation in pregnant women (Case 1985; Moore, 1994). Reduced total protein level has been reported in cases of malnutrition, liver diseases and renal impairment wherein excess water is inadequately excreted by the kidney (Cunningham et al,1989).

ALBUMIN

The estimated mean serum albumin concentration for pregnant women (3.28 ± 0.22g/100ml) and for non-pregnant women (4.07 ± 0.17g/100ml) conform with values obtained by Miller and Calendar (1989) (2.50 – 3.80 g/100ml) and (3.50 – 4.80 g/100ml) respectively.

The significantly lowered mean serum albumin concentration for pregnant women (3.28 ± 0.22 g/100ml) compared with the value for non-pregnant women (4.07 ± 0.17 g/100ml) { P>0.05} may be attributed to hemodilution as in total protein. However, unlike total protein, the actual amount of albumin is not increased in pregnancy, rather it is reduced as it is the main fraction of the total protein supplied to the fetus by the mother. The albumin concentration is only further lowered by hemodilution, making it fall progressively as pregnancy advances, the maximum percentage decrease being approximately twice that of the total protein. The reduction in the mean serum albumin concentration in pregnancy is sufficient to account for the fall in total protein (Stewart and Taylor, 1976). Thus a decrease in albumin/globulin ratio occur normally in pregnancy. In the non-pregnant women, such a decrease could be an indication of liver disease (Moore, 1991). The significant difference in the mean serum albumin concentration in menopausal women (4.30 ± 0.31 g/100 ml) when compared with that of pregnant women (3.28 ±0.22g/100ml) {P<0.05} and non-pregnant women (4.07± 0.17 g/100ml) {P<0.05} is due to reduction of circulating plasma volume stimulating

hormones concentration in the menopausal women. This is the more reason why protein diet must be controlled to match requirement at old age, to avoid renal impairment (Case and Waterhouse, 1994).

UREA

The mean serum urea concentration estimated in pregnant women (1.66 $\pm$ 0.29 mmol/l) and that of non-pregnant women (3.72 $\pm$ 0.31mmol/l} fall within the range obtained by Moore (1991) in pregnant women (1.5-4.5mmol/l) and in non-pregnant women (2.5-7.0mmol/l).

The dietary protein level, health status of the liver and renal function are known to be some of the factors affecting serum urea concentration (Bortollussi et al, 1996). The significantly lowered mean serum urea concentration in pregnancy (1.66 $\pm$ 0.29 mmol/l) compared with that in non pregnant women (3.72 $\pm$ 0.32 mmol/l) ($p>0.05$) may be due to hemodilution. However, the reduction in concentration is greater than what can be explained by hemodilution alone. The marked reduction in this studies could be due to inhibitory effect of the hormone, human placental lactogen, on deamination of amino acids (in Liver) to form urea (Miller and Calendar, 1989). Increased renal plasma flow and glomerular filteration rate are also important factors partly responsible for increase clearance of urea which are less efficiently reabsorbed in pregnancy; as a result, serum urea level falls (Davidson and Dunlop, 1995; Cunningham et al, 1989).

The mean serum urea concentration of the menopausal women (4.90 $\pm$ 0.64 mmol/l) is significantly higher than the mean serum urea concentration for both pregnant women (1.66 $\pm$ 0.29mmol/l) ($P<0.05$) and non-pregnant women (3.72 $\pm$ 0.23 mmol/l) ($P<0.05$). This can be traced to reduced plasma volume in menopausal women

occassioned by reduced plasma volume stimulating hormones (Case and Waterhouse, 1994). Elevated serum urea concentration has also been reported in severe uncontrolled diabetes mellitus (Peters, 1991) and nephropathy (Guyton, 1991; Lewis, 1990). It is also reported in any condition associated with increase in protein breakdown such as pneumonia, malaria, meningitis, typhoid and surgical operations (Case, 1985). Low serum urea concentration, on the other hand, is one of the early symptoms of liver disease as well as protein deficiency disease.

CREATININE

According to Stewart and Taylor (1976) the mean serum creatinine concentration in pregnant and non-pregnant women fall within the same range of 88 – 176 μmol/l. This established normal range for creatinine in both pregnant and non-pregnant women is wide. In this studies, the creatinine level obtained for pregnant women (95.2480±5.70 μmol/l) and non-pregnant women (99.28 ± 3.64 μmol/l) fall within this range, agreeing with findings of earlier researchers that pregnancy has no significant effect on serum creatinine concentration.

Though the values are within the same range, as reported in 1976 above, there is significant difference when the mean serum creatinine concentration in pregnant women (95.25 ± 5.70μmol/l) is compared with that of non-pregnant women (99.78 ± 3.64 μmol/l) {P>0.05}. However, the increase is not strongly correlated with any of the parameters. (Table 4).

The difference in these means could be attributed to increase renal plasma flow and subsequent increase in glomerular filteration rate in pregnant women, consequently,

there is increase in creatinine clearance which results into lower serum concentration in pregnancy (Davidson and Dunlop, 1995; Robson et al, 1989).

Creatinine is a product of muscle breakdown and is excreted by the kidney at a regular rate, it is therefore used in renal function assessment. In the presence of normal renal plasma flow, elevated serum creatinine concentration is suggestive of moderate to severe kidney damage. Diseases associated with Muscle wasting reduce the level of creatinine in the blood. Therefore serum creatinine concentration could be used for diagnosis of muscle wasting diseases (Peter et al, 1982).

SODIUM ION

The estimated mean serum sodium ion concentration for pregnant women (137.25 $\pm$ 5.64 mmol/l) and non-pregnant women (153.11 $\pm$ 8.94mmol/l) are within the range reported by Keller (1963) and Peter et al., (1982) in pregnant women (125-140 mmol/l) and in non-pregnant women (136-155 mmol/l).

The significantly lowered mean serum sodium ion concentration in pregnancy (137.25 $\pm$ 5.64 mmol/l) ($P>0.05$) could be linked with hemodilution. However, the total amount of sodium ion concentration is increased considering the plasma volume increase. About 850 Millimole are retained during pregnancy and this is divided in almost equal proportion between mother and conceptus. This is due to increase in aldosterone, renin and angiotesin I & II (Miller and Calendar, 1989). The mean serum sodium ion concentration for menopausal women (156.43 $\pm$ 8.25mmol/l) is significantly higher than the concentration for pregnant women (137.25 $\pm$ 5.64 mmol/l) but not that of non-pregnant women (153.11 $\pm$ 8.94 mmol/l) ($P<0.05$).

Hypernatremia is not a common disorder unless there is dehydration or administration of sodium containing infusion. This is because the Osmoregulatory activity of the kidney will always take care of the excess. More common hyponatremia, on the other hand, may accompany any severe illness including viral and bacterial infection, malaria, heart attack, stroke, tumour of the brain and Lungs. Other causes are surgery, drug effects and inadequate dietary intake. Hyponatremia can also be caused by Addisons disease wherein adrenal steroid is absent; sodium ion loosing nephropathy which may be staged in chronic glomerular nephritis (pyelonephritis), manifested by abnormal renal function test (Guyton, 1991); loss of gastrointestinal secretions by vomiting, diarrhea or tube drainage with replacement of fluid but not electrolyte (Goodman and Gilma, 1985); loss of sodium from skin through burns and metabolic loss through starvation, acidosis and antidiuretic hormone deficiency (Tiez, 1973). In fact excessive sweating could also lead to hyponatremia.

POTASSIUM ION

The mean serum potassium ion concentration obtained for pregnant women (4.05 $\pm$0.61 mmol/l) and non-pregnant women (4.60 $\pm$ 0.45 mmol/l) conform with the range established by Miller and Calendar (1989) that is, the mean serum potassium ion concentration in pregnant women is in the range 3.80-4.20 mmol/l while that of the non-pregnant women is 4.50-5.20 mmol/l.

The significant difference in the mean of serum potassium ion concentration in pregnant women (4.05 $\pm$ 0.61 mmol/l) when compared with that of non-pregnant women (4.60 $\pm$ 0.45 mmol/l) ($p>0.05$) could be attributed to hemodilution. However, as in serum sodium ion concentration, it is found that there is gain in total amount of serum potassium

ion concentration in pregnant women. About 316 Millimole is gained during pregnancy and the conceptus receives almost twice as much as the mother (Miller and Calendar, 1989). The mean serum potassium ion concentration for menopausal women (4.75 $\pm$ 0.35 mmol/l) is significantly higher than the mean serum potassium ion concentration for pregnant women (4.05 $\pm$0.61 mmol/l) ($P<0.05$), but there is no significant difference from the mean serum potassium ion concentration for non-pregnant women (4.60 $\pm$ 0.45 mmol/l) at the same p value.

Incidence of hyperkalemia is rarely encountered because any potassium ion absorped by the gastrointestinal tract causes only a slight and temporal increase in the serum since it is rapidly excreted by the kidney (Tiez, 1973). The common cause of hyperkalemia is renal failure and could lead to sudden fatal disorder of heart rythm. Other causes of hyperkalemia include shock, over consumption of potassium, administration of potassium ion containing infusion. Tissue breakdown or hemolysis which release potassium ion from cells to blood can also lead to hyperkalemia. Potassium ion concentration is normally low in the blood (Guyton, 1991).

CORRELATION OF PARAMETERS

The nearly strong correlation existing between all parameters ($P<0.05$) may be attributed to increase in circulation of plasma volume stimulating hormone concentration which brings about hemodilution, affecting the parameters in the same way. The secondary causes of changes in pregnancy, fetal dependence and hormonal effects (other

than plasma volume stimulating hormone) may be responsible for the very slight difference in degree of the correlation {Table 4}.

CONCLUSION

The reported changes in concentration of serum biochemical parameters in pregnant women is applicable to pregnant women in Niger state, having their mean serum biochemical parameter concentrations significantly lower than the mean serum concentration in non-pregnant women ($P>0.05$). On the other hand, the mean serum concentrations of the biochemical parameters in menopausal women are significantly higher than the mean serum concentrations in non-pregnant women ($P<0.05$) except for serum concentrations of sodium ion , potassium ion and creatinine. Mean serum concentrations of the biochemical parameters in menopausal women are also significantly higher than the mean serum concentrations in pregnant women {$P<0.05$} except for serum concentrations of creatinine.

There is a positive correlation between all the parameters under consideration ($P<0.05$) and the correlations are strong, except with serum creatinine concentrations.

SUGGESTION

Since it has been established that the Primary cause of changes in pregnancy is hormonal level dynamism, estimation of hormones level in individuals, before and during pregnancy, will be worth doing. The level of the various pregnancy related hormones could then be compared to level of changes in such individuals.

APPENDIX A I

TABLE OF RESULTS OF THE BIOCHEMICAL PARAMETRES FOR PREGNANT WOMEN

T/PROTEIN g/100ml	CREATININE µMol/l	UREA mMol/l	ALBUMIN g/100ml	Na^+ mMol/l	K^+ mMol/l
6.7	94.3	2.4	3.1	130.5	3.58
7.8	88.7	1.2	3.5	137.0	3.58
7.4	92.5	1.5	3.4	139.5	4.60
7.5	88.3	1.6	3.5	130.5	3.58
6.8	90.7	2.0	3.2	145.7	4.60
7.2	92.3	1.7	3.1	145.7	4.60
8.0	95.9	1.1	3.4	130.5	3.58
7.1	89.7	1.9	2.9	141.0	3.58
7.7	94.4	1.4	3.7	130.5	4.60
7.3	93.0	1.6	3.6	137.0	3.58
7.6	98.3	1.5	3.3	130.5	4.60
6.8	94.4	2.0	3.1	145.7	3.58
7.1	98.5	2.0	3.2	141.0	3.58
7.4	91.9	1.6	3.6	141.0	3.58
6.9	100.3	2.1	3.4	130.5	3.58
6.7	88.9	2.2	3.3	150.1	4.60
8.1	90.4	1.2	3.4	130.5	4.60
6.5	111.2	2.2	3.0	137.0	3.58
7.4	90.0	1.3	3.3	145.7	4.60
7.9	99.3	1.2	3.5	137.0	5.12
8.0	96.4	1.4	3.8	130.5	4.60
7.3	100.7	1.7	3.4	137.0	3.58
7.6	100.1	1.4	3.0	130.5	4.60
6.9	101.4	2.3	3.0	141.0	5.12
7.2	104.0	1.7	3.3	137.0	5.12
7.9	96.3	1.2	3.7	141.0	4.60
7.1	92.8	1.9	3.2	130.5	5.12
7.0	90.2	1.8	3.4	141.0	3.58
7.2	89.0	2.0	3.0	130.5	3.58
6.6	91.6	2.2	3.1	141.0	4.60

7.3	89.4	1.8	3.4	137.0	4.60
7.7	93.7	1.2	3.5	150.1	4.60
6.4	106.2	2.3	3.2	130.5	3.58
6.8	102.4	2.2	3.2	130.5	3.58
8.3	101.4	1.2	3.5	137.0	4.60
7.8	99.8	1.4	3.4	130.5	4.60
7.0	92.4	1.9	3.2	141.0	3.58
7.2	102.3	1.8	3.6	137.0	3.58
7.7	97.7	1.5	3.5	141.0	4.60
6.5	108.6	2.1	3.2	130.5	5.12
7.3	107.5	1.9	3.0	141.0	3.58
7.6	79.9	1.2	3.7	130.5	3.58
7.8	94.8	1.3	3.5	137.0	3.58
7.6	100.2	1.6	3.5	145.7	4.60
7.2	99.8	1.4	3.6	130.5	4.60
7.0	100.3	1.8	3.1	130.5	4.60
6.8	90.6	1.7	3.3	137.0	3.58
6.5	93.0	1.2	3.4	141.0	4.60
6.7	98.4	2.1	3.2	130.5	3.58
7.4	102.1	1.1	3.3	145.7	5.12
7.3	88.5	1.5	3.4	137.0	3.58
7.2	102.2	1.3	3.0	145.7	3.58
7.1	88.9	1.5	3.3	130.5	4.60
7.6	101.0	1.4	3.5	137.0	5.12
7.4	97.6	1.8	3.5	141.0	3.58
6.9	103.1	2.0	2.9	141.0	3.58
7.1	88.8	1.6	3.2	145.7	4.60
8.2	88.1	1.2	3.8	150.1	4.60
7.5	92.3	1.7	3.3	130.5	4.60
8.1	90.2	1.2	3.7	141.0	3.58
7.1	89.0	2.0	3.6	141.0	3.58

CONT.

T/PROTEIN g/100ml	CREATININE µMol/l	UREA mMol/l	ALBUMIN g/100ml	Na^+ mMol/l	K^+ mMol/l
6.9	93.9	1.9	3.2	145.7	4.60
7.5	91.8	1.7	3.4	130.5	3.58
6.7	102.0	2.0	3.2	150.1	4.60
7.2	95.6	1.6	3.3	130.5	3.58
6.9	99.8	1.8	3.2	137.0	4.60
7.9	90.0	1.3	3.4	145.7	4.60
7.3	91.1	1.5	3.5	145.7	4.60
7.7	96.5	1.5	3.1	150.1	3.58
7.4	95.2	1.3	3.4	137.0	3.58
7.7	97.7	1.7	3.7	141.0	3.58
6.9	100.0	1.8	3.2	145.7	3.58
8.0	88.0	1.3	3.9	141.0	3.58
7.8	94.2	1.3	3.4	130.5	4.60
6.6	114.6	2.2	3.0	130.5	3.58
7.0	93.6	1.9	3.2	137.0	3.58
7.4	78.3	1.2	3.1	137.0	4.60
7.7	91.1	1.6	3.4	130.5	3.58
6.3	89.2	2.3	3.0	141.0	3.58
7.5	93.4	1.5	3.4	145.7	4.60
7.2	105.8	2.0	3.2	137.0	4.60
6.8	99.4	1.8	3.2	130.5	3.58
7.6	87.6	1.6	3.5	130.5	4.60
7.8	90.5	1.2	3.4	130.5	4.60
6.5	92.8	2.4	3.0	141.0	3.58
8.1	90.1	1.2	3.4	137.0	3.58
6.6	100.4	2.2	3.1	145.7	3.58
8.0	89.9	1.2	3.5	141.0	4.60
7.2	98.8	2.1	3.3	130.5	3.58
7.4	93.2	1.3	3.4	137.0	3.58
7.0	101.6	2.0	3.2	130.5	3.58
6.6	107.1	2.2	2.9	141.0	4.60

7.9	100.5	1.4	3.1	145.7	5.12
7.4	89.1	1.4	3.4	137.0	4.60
7.0	97.9	2.2	3.2	137.0	3.58
7.5	100.9	1.3	3.5	130.5	3.58
x=7.2854	x=95.6229	x=1.6677	x=3.3146	x=137.68	x=4.1227
S.D=0.4636	S.D=6.3298	S.D=0.3629	S.D=0.2142	S.D=6.2230	S.D=0.5738

APENDIX A II

TABLE OF RESULTS OF THE BIOCHEMICAL PARAMETRES FOR NON-PREGNANT WOMEN

T/PROTEIN	CREATININE	UREA	ALBUMIN	Na^+	K^+
g/100ml	µMol/l	mMol/l	g/100ml	mMol/l	mMol/l
7.5	92.4	4.3	3.9	145.7	4.60
8.1	101.5	3.7	3.9	150.1	4.60
8.2	97.3	3.5	4.2	145.7	4.60
7.9	96.6	4.0	3.8	154.4	4.60
8.5	101.1	3.3	4.4	165.3	5.12
8.9	97.7	3.1	4.7	161.0	4.60
8.2	105.6	3.9	4.2	141.0	3.58
7.8	97.5	3.8	3.8	145.7	4.60
8.0	102.2	3.5	3.9	137.0	3.58
8.3	98.2	3.7	4,1	169.7	4.60
7.7	101.3	3.8	3.9	169.7	5.12
8.7	96.3	3.3	4.6	165.3	5.12
7.3	100.6	4.3	3.8	145.7	4.60
8.3	97.8	3.7	4.0	161.0	4.60
7.9	101.2	3.8	4.2	145.7	4.60
7.7	97.9	3.5	3.9	169.7	5.12
8.4	100.9	3.9	4.4	141.0	3,58
8.0	97.4	4.2	4.3	154.4	4.60
8.5	53.4	3.6	4.4	169.7	5.12
7.7	115.4	4.0	3.9	161.0	4.60
8.0	94.4	3.7	4.0	150.1	5.12
8.4	99.4	3.4	3.9	165.3	4.60
7.8	106.0	4.1	4.1	154.4	4.60
8.5	92.9	3.6	4.6	161.0	4.60
7.8	101.2	3.8	4.1	150.1	4.60
7.8	101.7	3.5	4.0	150.1	4.12

8.4	95.1	3.3	4.4	169.7	5.12
8.7	101.5	3.3	4.1	161.0	4.60
8.3	98.3	3.8	4.3	165.3	5.12
7.7	106.4	3.9	3.9	150.1	3.58
8.2	93.2	3.5	4.2	145.7	4.60
7.6	97.6	4.0	3.9	169.7	4.60
8.0	103.7	3.6	4.3	154.4	4.60
7.9	101.4	3.6	4.1	161.0	4.60
8.6	97.1	3.7	4.4	145.7	5.12
8.4	101.0	3.1	4.1	154.4	4.60
7.5	102.5	4.2	3.9	150.1	4.60
8.2	97.1	3.6	4.3	165.3	5.12
8.5	97.6	3.1	4.2	145.7	4.60
8.8	101.7	3.3	4.3	150.1	4.60
7.4	104.4	4.1	4.0	165.3	5.12
X=8.0756	X=99.4268	X=3.6854	X=4.1317	X=155.69	X=4.6526
S.D=0.4037	S.D=4.9412	S.D=0.3237	S.D=0.2360	S.D=9.6272	
S.D=0.4270					

APPENDIX A III

TABLE OF RESULTS OF THE BIOCHEMICAL PARAMETRES FOR MENOPAUSAL

T/PROTEIN g/100ml	CREATININE µMol/l	UREA mMol/l	ALBUMIN g/100ml	Na^+ mMol/l	K^+ mMol/l
8.5	95.3	4.8	4.0	161.0	5.12
9.2	101.1	3.9	4.3	169.7	5.12
8.2	98.0	4.2	4.0	154.4	4.60
8.9	96.0	5.8	4.2	150.1	4.60
8.7	90.1	4.5	3.7	165.3	5.12
8.2	100.4	5.2	3.8	161.0	5.12
8.5	94.8	4.4	4.1	145.7	4.60
8.6	98.2	5.6	4.5	154.4	4.60
9.2	94.2	4.8	4.7	150.1	3.58
8.8	102.2	5.4	4.2	161.	4.60
9.4	93.4	3.9	4.6	150.1	4.60
8.4	95.5	5.6	4.4	165.3	4.60
8.7	106.3	3.9	4.6	169.7	5.12
9.0	101.6	4.7	4.6	161.0	5.12
8.3	94.3	5.3	3.9	161.0	4.60
9.1	90.2	4.6	4.7	154.4	4.60
8.1	95.1	5.6	4.0	150.1	4.60
8.4	100.9	5.4	4.2	141.0	4.60
8.9	103.0	5.9	4.7	154.4	5.12
9.3	106.2	3.9	4.1	150.1	4.60
8.3	98.4	4.9	4.4	145.7	4.60
8.7	102.1	5.6	4.2	150.1	4.60
9.1	103.7	5.2	4.3	165.3	5.12
9.3	92.7	4.8	4.8	169.7	5.12
8.9	101.3	4.7	4.5	150.1	4.60
X=8.7480	X=98.2000	X=4.9040	X=4.3000	X=156.4280	X=4.7464
S.D=0.3896	S.D=4.6175	S.D=0.6361	S.D=0.3069	S.D=8.2514	
S.D=0.3499					

APPENDIX B

Conversions for (Na^+)

Emission Intensity	Concentration (ppm)	Concentration mmol/l
33	6.00	130.50
34	6.30	137.00
35	6.50	141.00
36	6.70	145.70
37	6.90	150.10
38	7.10	154.40
39	7.40	161.00
40	7.60	165.30
41	7.80	169.70

APPENDIX C

CONVERSIONS FOR POTASSIUM ION CONCENTRATION

Emission Intensity	Concentration (ppm)	Concentrations (mmol/l)
3	0.28	3.58
4	0.30	4.60
5	0.40	5.12

One-Way Analysis of Variance

Data: MAURUF.Totalprot

Level codes: MAURUF.des

Labels:

Range test: Tukey Confidence level: 95

Analysis of variance

Source of variation	Sum of Squares	d.f.	Mean square	F-ratio	Sig. level
Between groups	26.512267	2	13.256133	139.148	.0000
Within groups	6.859200	72	.095267		
Total (corrected)	33.371467	74			

0 missing value(s) have been excluded.

Sun Apr 14 2002 12:58:07 PM

Table of means for MAURUF.Totalprot by MAURUF.des

Level	Count	Average	Stnd. Error (internal)	Stnd. Error (pooled s)	95 Percent Tukey HSD intervals for mean	
1	25	7.2920000	.0411987	.0617306	7.1875346	7.3964654
2	25	7.9920000	.0605310	.0617306	7.8875346	8.0964654
3	25	8.7480000	.0779145	.0617306	8.6435346	8.8524654
Total	75	8.0106667	.0356402	.0356402	7.9503536	8.0709798

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Multiple range analysis for MAURUF.Totalprot by MAURUF.des

Method: 95 Percent Tukey HSD Intervals

Level	Count	Average	Homogeneous Groups
1	25	7.2920000	*
2	25	7.9920000	*
3	25	8.7480000	*

One-Way Analysis of Variance

Data: MAURUF.Urea

Level codes: MAURUF.des

Labels:

Range test: Tukey Confidence level: 95

Analysis of variance

Source of variation	Sum of Squares	d.f.	Mean square	F-ratio	Sig. level
Between groups	135.03707	2	67.518533	347.119	.0000
Within groups	14.00480	72	.194511		
Total (corrected)	149.04187	74			

0 missing value(s) have been excluded.

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Table of means for MAURUF.Urea by MAURUF.des

Level	Count	Average	Stnd. Error (internal)	Stnd. Error (pooled s)	95 Percent Tukey HSD intervals for mean	
1	25	1.6560000	.0577581	.0882068	1.5067295	1.8052705
2	25	3.7160000	.0618277	.0882068	3.5667295	3.8652705
3	25	4.9040000	.1272111	.0882068	4.7547295	5.0532705
Total	75	3.4253333	.0509262	.0509262	3.3391520	3.5115147

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Multiple range analysis for MAURUF.Urea by MAURUF.des

Method: 95 Percent Tukey HSD Intervals

Level	Count	Average	Homogeneous Groups
1	25	1.6560000	*
2	25	3.7160000	*
3	25	4.9040000	*

One-Way Analysis of Variance

Data: MAURUF.Creatinine

Level codes: MAURUF.des

Labels:

Range test: Tukey Confidence level: 95

Analysis of variance

Source of variation	Sum of Squares	d.f.	Mean square	F-ratio	Sig. level
Between groups	263.8664	2	131.93320	6.037	.0038
Within groups	1573.4968	72	21.85412		
Total (corrected)	1837.3632	74			

0 missing value(s) have been excluded.

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Table of means for MAURUF.Creatinine by MAURUF.des

Level	Count	Average	Stnd. Error (internal)	Stnd. Error (pooled s)	95 Percent Tukey HSD intervals for mean	
1	25	95.248000	1.1179761	.9349679	93.665774	96.83023
2	25	99.780000	.7294518	.9349679	98.197774	101.36223
3	25	98.168000	.9168010	.9349679	96.585774	99.75023
Total	75	97.732000	.5398039	.5398039	96.818501	98.64550

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Multiple range analysis for MAURUF.Creatinine by MAURUF.des

Method: 95 Percent Tukey HSD Intervals

Level	Count	Average	Homogeneous Groups
1	25	95.248000	*
3	25	98.168000	**
2	25	99.780000	*

One-Way Analysis of Variance

Data: MAURUF.Sodium

Level codes: MAURUF.des

Labels:

Range test: Tukey Confidence level: 95

Analysis of variance

Source of variation	Sum of Squares	d.f.	Mean square	F-ratio	Sig. level
Between groups	5251.2843	2	2625.6421	42.840	.0000
Within groups	4412.8712	72	61.2899		
Total (corrected)	9664.1555	74			

0 missing value(s) have been excluded.

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Page 1

Table of means for MAURUF.Sodium by MAURUF.des

Level	Count	Average	Stnd. Error (internal)	Stnd. Error (pooled s)	95 Percent Tukey HSD intervals for mean	
1	25	137.25200	1.1982087	1.5657570	134.60230	139.90170
2	25	153.10800	1.7876420	1.5657570	150.45830	155.75770
3	25	156.42800	1.6502780	1.5657570	153.77830	159.07770
Total	75	148.92933	.9039902	.9039902	147.39953	150.45914

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Multiple range analysis for MAURUF.Sodium by MAURUF.des

Method: 95 Percent Tukey HSD Intervals

Level	Count	Average	Homogeneous Groups
1	25	137.25200	*
2	25	153.10800	*
3	25	156.42800	*

One-Way Analysis of Variance

Data: MAURUF.Potassium

Level codes: MAURUF.des

Labels:

Range test: Tukey Confidence level: 95

Analysis of variance

Source of variation	Sum of Squares	d.f.	Mean square	F-ratio	Sig. level
Between groups	6.748800	2	3.3744000	14.683	.0000
Within groups	16.547328	72	.2298240		
Total (corrected)	23.296128	74			

0 missing value(s) have been excluded.

Table of means for MAURUF.Potassium by MAURUF.des

Level	Count	Average	Stnd. Error (internal)	Stnd. Error (pooled s)	95 Percent Tukey HSD intervals for mean	
1	25	4.0504000	.1215572	.0958799	3.8881444	4.2126556
2	25	4.6024000	.0889143	.0958799	4.4401444	4.7646556
3	25	4.7464000	.0699783	.0958799	4.5841444	4.9086556
Total	75	4.4664000	.0553563	.0553563	4.3727217	4.5600783

Multiple range analysis for MAURUF.Potassium by MAURUF.des

Method: 95 Percent Tukey HSD Intervals

Level	Count	Average	Homogeneous Groups
1	25	4.0504000	*
2	25	4.6024000	*
3	25	4.7464000	*

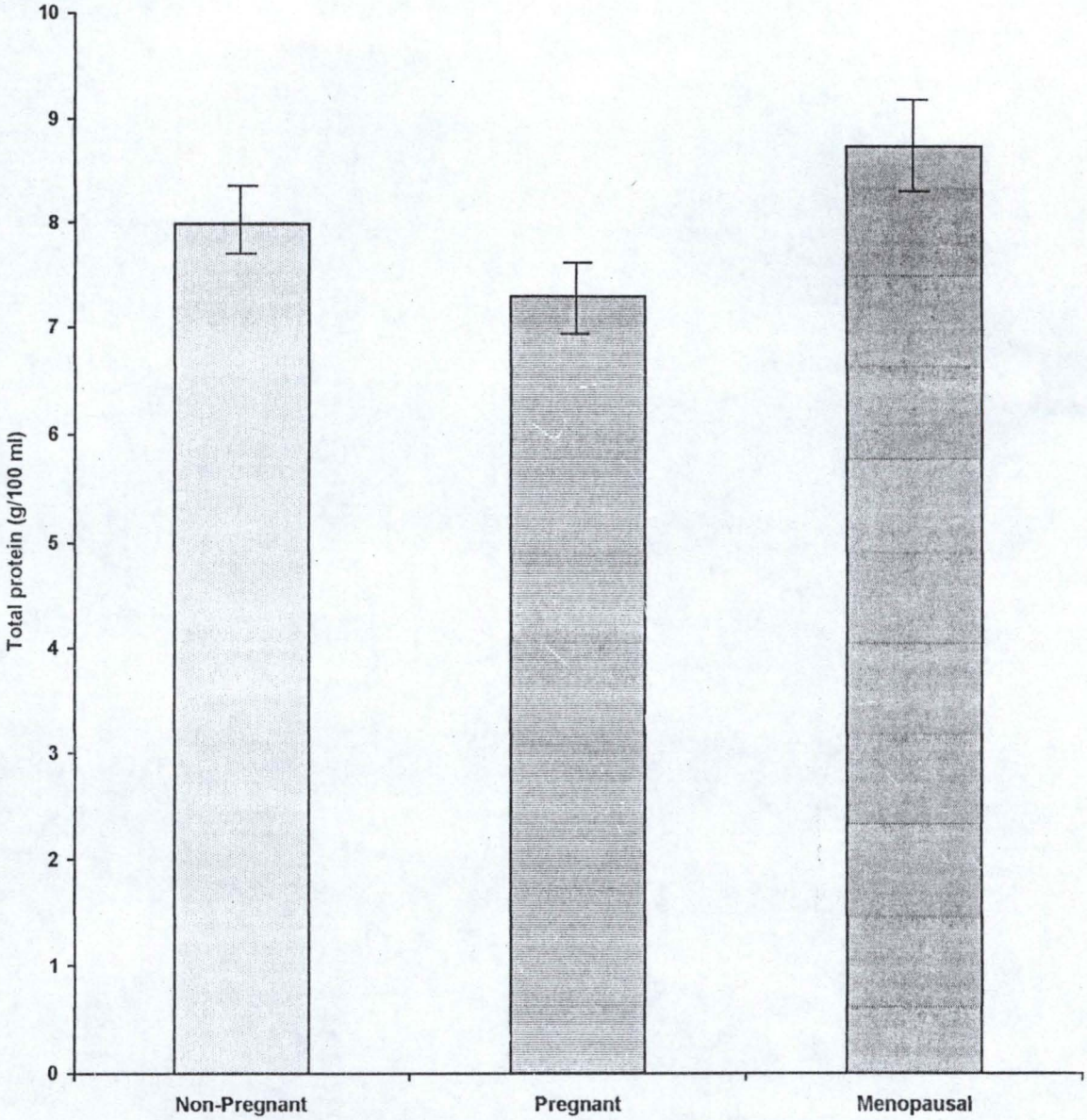
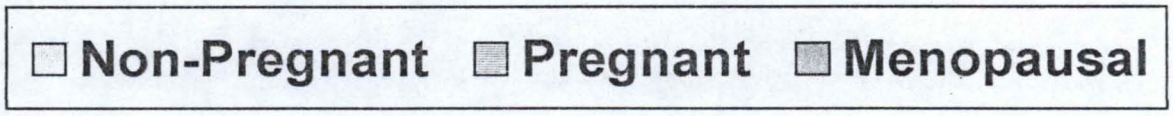


Fig. 5: Mean serum total protein concentrations in g/100 ml of non-pregnant, pregnant and menopausal women in Niger State.



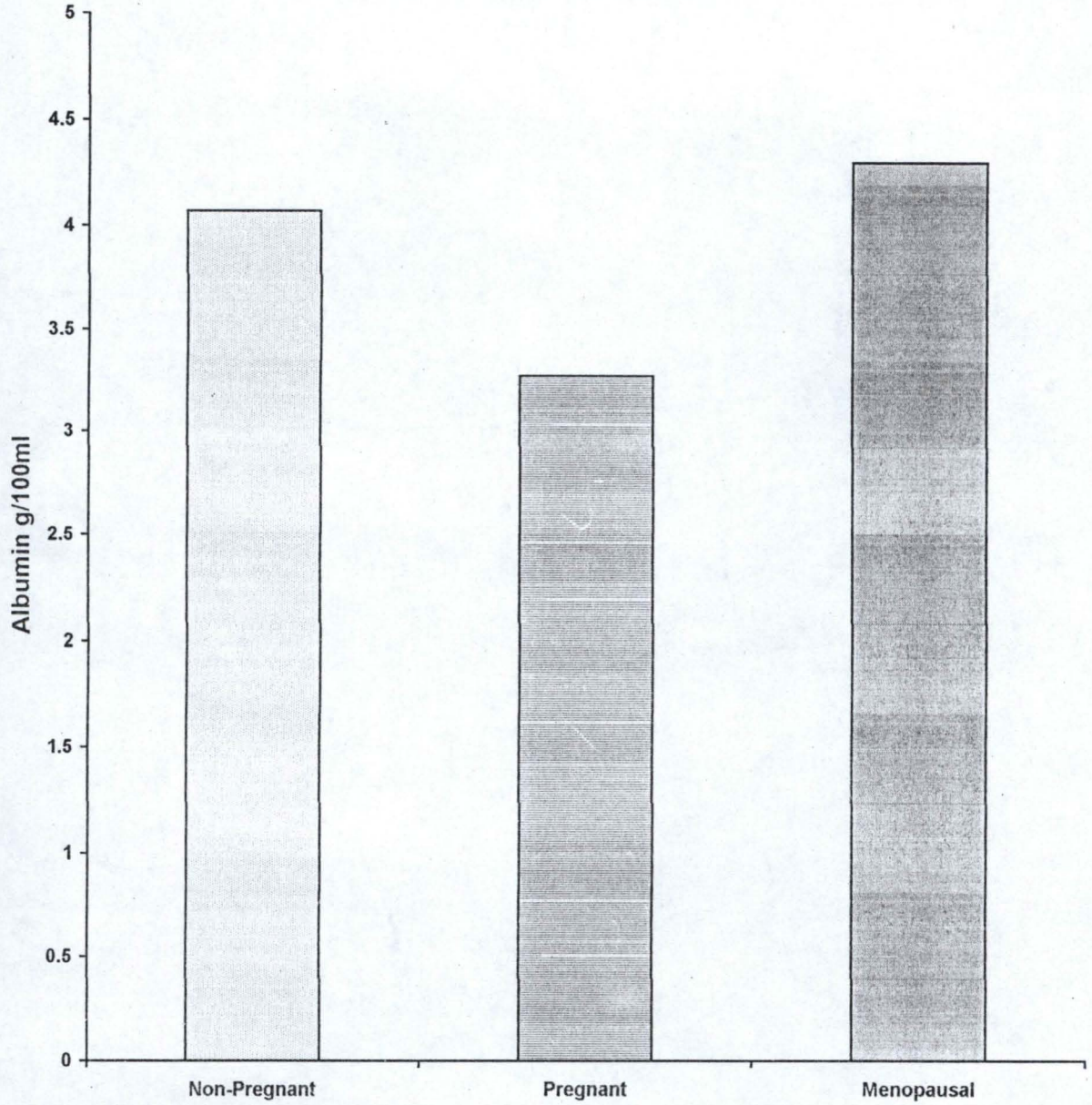


Fig. 6: Mean serum albumin concentartions in g/100 ml

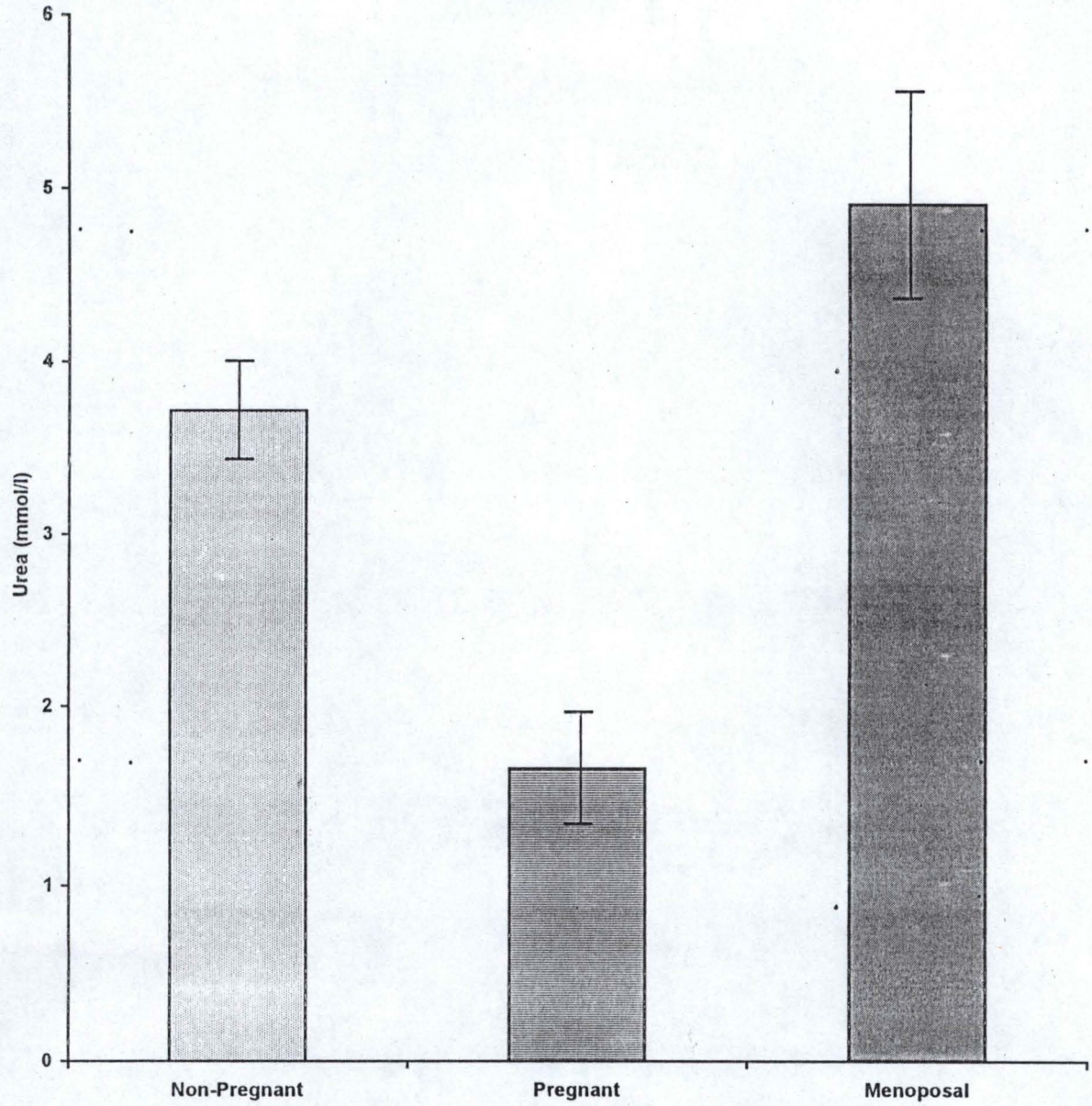


Fig.7: Mean serum urea concentrations in mmol/l

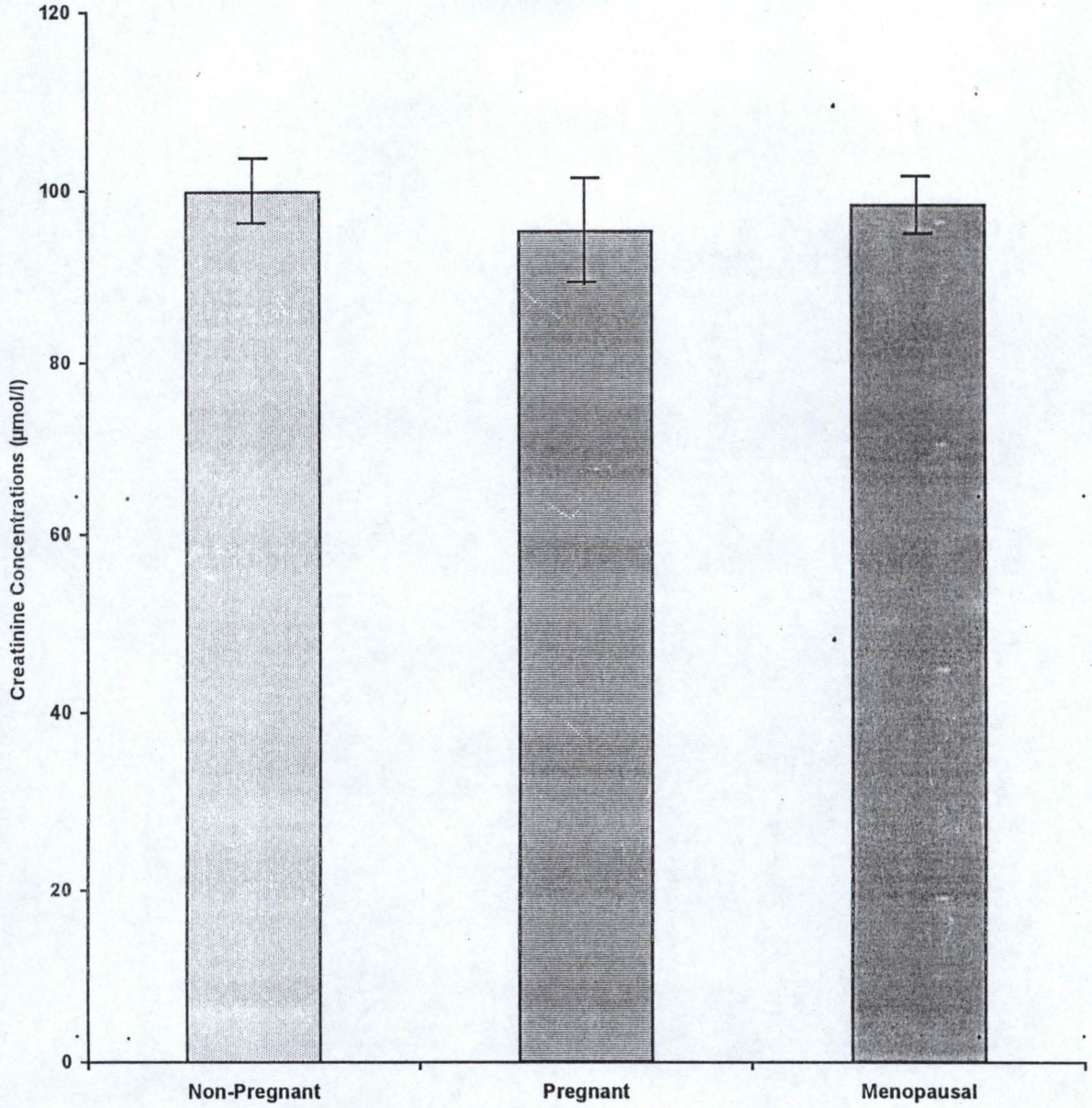
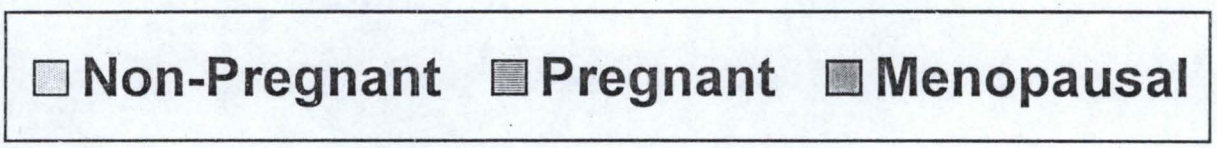


Fig. 8: Mean serum creatinine concentrations in µmol/l



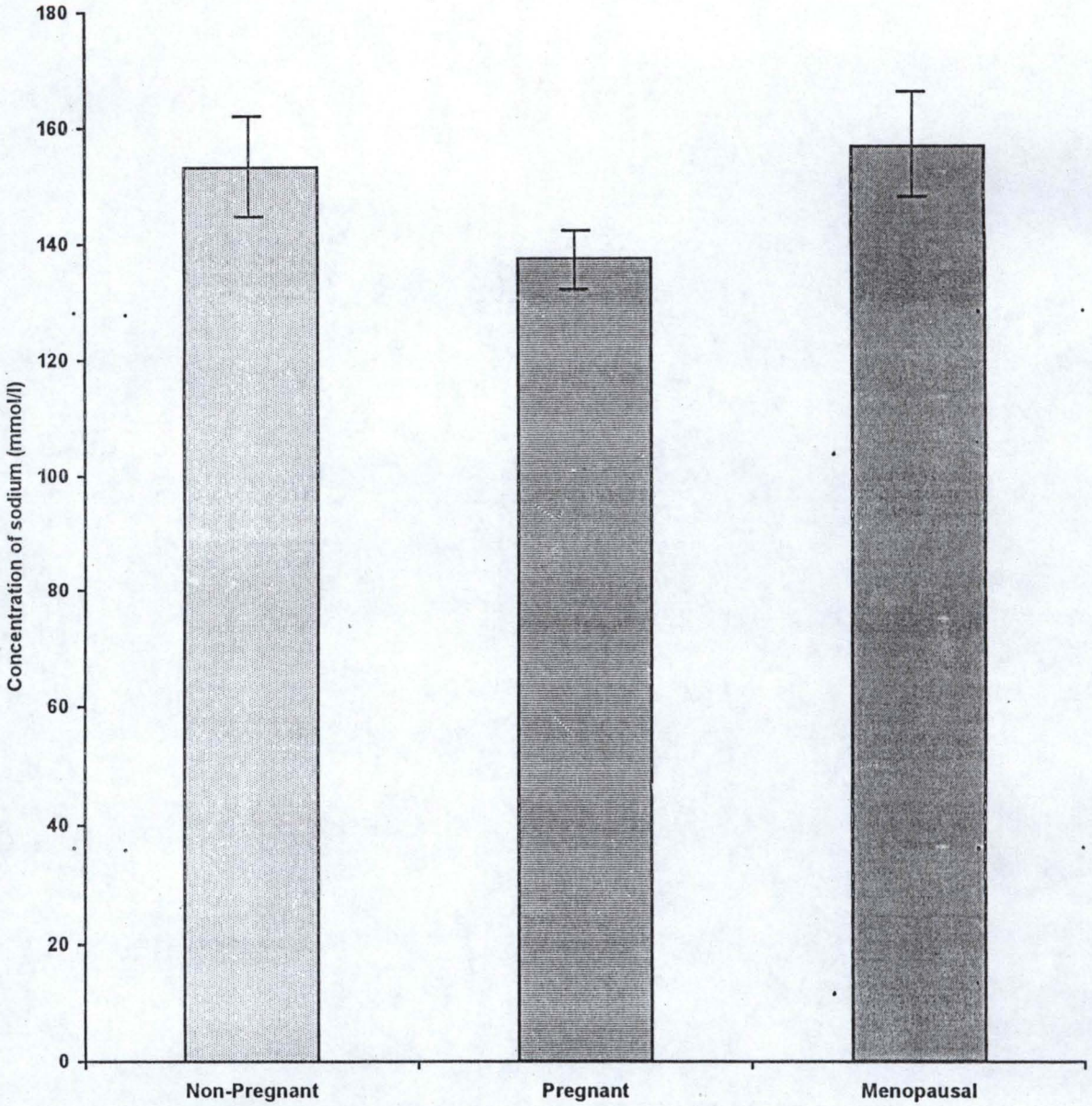
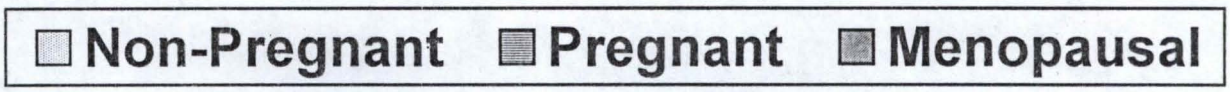


Fig. 9: Mean serum sodium ion concentrations in mmol/l



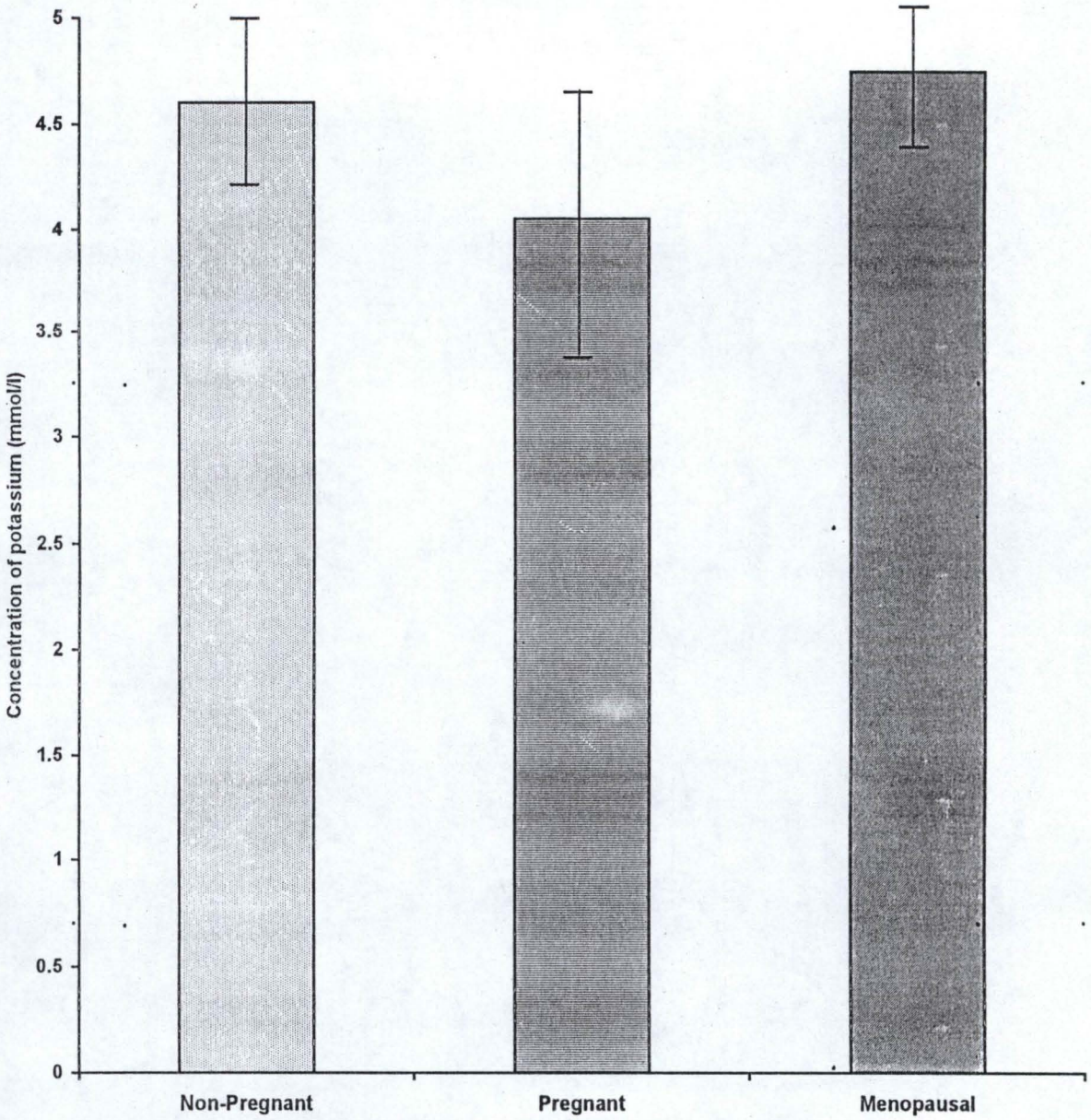
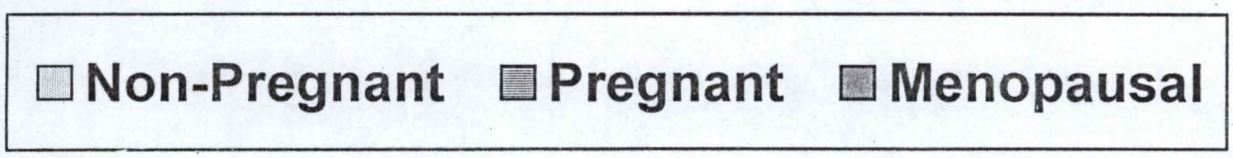


Fig. 10: Mean serum potassium ion concentrations in mmol/l



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