ASSESSMENT OF THE RELATIONSHIP BETWEEN WORKING MEMORY AND SOME REPRODUCTIVE HORMONES IN SELECTED PATIENTS OF AHMADU BELLO UNIVERSITY MEDICAL CENTRE

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DECLARATION

I declare that the work in this dissertation entitled, **'**Assessment of the relationship between Working Memory and some reproductive hormones in selected patients of Ahmadu Bello University Medical Centre' has been carried out by me. The information derived from literature has been duly acknowledged in the text and a list of references provided. No part of this thesis was previously presented for another degree or diploma at this or any other institution.

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Name of Student	Signature	Date

CERTIFICATION

This thesis entitled,'Assessment of the relationship between Working Memory and some reproductive hormones in selected patients of Ahmadu Bello University Medical Centre' by BisolaAke meets the regulations governing the award of the degree of Master of Science of the Ahmadu Bello University, Zaria, and is approved for its contribution to knowledge and literary presentation.

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This dissertation is dedicated to my Father and Friend, the Maker of Heaven and Earth.

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ABSTRACT

Working memory is a central construct in cognitive neuroscience that is responsible for the orchestration of daily activities. Serum concentrations of some reproductive hormones are known to vary in the pregnant and non-pregnant state. There are conflicting reports about the effect of pregnancy on working memory. It is yet to be ascertained whether the change in the concentration of some reproductive hormones during pregnancy affects working memory. The aim of the study was to assess the relationship between working memory and some reproductive hormones(estrogen, progesterone and prolactin) in pregnant and non-pregnant women.A total of 67 participants, comprising 29 non-pregnant and 38 pregnant women were involved in the study.The N-back task was used to assess Working Memory while the Mini-Mental State Examination was used to assess global cognitive functions. Blood samples were collected and assayed for hormonal concentrations of estrogen, progesterone and prolactin. Data obtained were expressed as mean ± SEM. Students t-test was used to analyse the significance of difference between serum levels of Estrogen, Progesterone, Prolactin, MMSE and N-back task between pregnant and non-pregnant women. Pearson's correlation analysis was used to determine the relationship between the serum hormonal concentration (Estrogen, Progesterone and Prolactin) and global cognition(MMSE) and also between the serum hormonal concentration (Estrogen, Progesterone and Prolactin) and WM(N-back task).In the MMSE, the pregnant group had a mean of 27.45 ± 0.57 while the non-pregnant group had 29.55 ± 0.13. In the N-back task, the mean values for the pregnant group was 70.32 ± 0.73, while that of the non-pregnant group was 74.41 ± 0.45. The pregnant group significantly outperformed the non-pregnant group in both the MMSE and the N-back task. Concentrations of estrogen, progesterone and prolactin were 1125 ± 75 pg/ml, 67.70 ± 7.9 ng/ml, 134.3 ± 12.04 ng/ml respectively for pregnant women and 20.90 ± 1.9 pg/ml, 3.0 ± 0.6 ng/ml and 11.6 ± 1.8 ng/ml for non-pregnant women. The pregnant women had significantly higher concentrations of all these hormones compared to the non-pregnant women. The correlation of the N-back task with estrogen, progesterone and prolactin was -0.0232, 0.0902 and -0.029 respectively in pregnant women and -0.2536, 0.03494 and -0.0864 respectively in non-pregnant women.The correlation of the MMSE with estrogen, progesterone and prolactin was -0.171, 0.0998 and 0.717 respectively in pregnant women and 0.1756, 0.251 and-0.0277 respectively in non-pregnant women. There was no significant statistical relationship between either of the neuropsychological tests and any of the reproductive hormones. The study certified that there was poorer global cognition and working memory in pregnancy. However, the study alsoshowed that the hormonal concentrations did not account for the poorer global cognition and working memory observed during pregnancy.

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LIST OF ABBREVIATIONS

CE	Central Executive
EB	Episodic Buffer
ELISA	Enzyme Linked Immunosorbent Assay
IQ	Intelligence Quotient
MMSE	Mini-Mental State Examination
PL	Phonological Loop
PS	Performance Scores
VSS	Visuo-Spatial Sketchpad
WM	Working Memory
WMC	Working Memory Capacity

CHAPTER ONE

1.0 INTRODUCTION

Working memory (WM) is a multi-component system that is responsible for temporary concomitant storage and manipulation of information in the face of ongoing processing and/or distraction. WM serves as a mental workspace that is used in many important daily activities like learning, remembering short driving instructions, mental rearrangement of furniture to create space and calculating the right tip. These activities involve multiple steps with intermediate task results that need to be kept in mind temporarily to successfully accomplish the task at hand (Shelton *et al.*, 2007, Harden, 2011, Baddeley, 2012).

Research is highlighting the importance of WM in academic, professional and social settings. WM has been implicated in ability to do arithmetic, learn languages and is a better test of intelligence than the regular intelligence quotient (IQ) tests. WM is compromised in Alzheimer's disease, Parkinsonism and Schizophrenia. WM is a viable tool for investigating and understanding other research areas like psychiatry.learning and language. (Perry *et al.*, 2001; Huntley *et al.*,2011;Baddeley,2012).

The prefrontal cortex is one of the parts of the brain that are responsible for working memory functions. It has been observed that the prefrontal cortex is larger in women and contains more estrogen receptors than other cortical areas(Kane and Engle, 2002).

1.1 STATEMENT OF STUDY PROBLEM

Hormones can alter cognitive functions. Estrogen, progesterone and prolactin have been implicated in cognition. Working Memory is a central construct in cognitive neuroscience.Some studies indicate a relationship between exogenous estrogen and working memory. (Maki *et al.*, 2002; Shelton *et al.*, 2007). No study is known to analyze the relationship between working memory, serum estrogen, progesterone and prolactin levels of pregnant and non-pregnant women in Zaria.

1.2 JUSTIFICATION

Estrogen is a hormone that mediates several feminizing features in women. The serum Estrogen, Progesterone and Prolactin levels vary with reproductive phases. However, estrogen has also been implicated in cognitive functions. It has been established that the prefrontal cortex, which is a key area of the brain in working memory is larger in females and has relatively higher estrogen receptor levels compared to other parts of the brain. Hormones can alter cognitive functions. Working Memory is a central construct in cognitive neuroscience (Maki *et al.*, 2002; Shelton *et al.*, 2007). Some studies indicate a relationship between exogenous estrogen and working memory. Given the pivotal dais that Working Memory occupies in cognition, it has become rather imperative to investigate the relationship between working memory and endogenous serum Estrogen, Progesterone and Prolactin levels of pregnant and non-pregnant women in Zaria.

1.3 AIM AND OBJECTIVES

This study is aimed at evaluating the relationship between working memory, and endogenous serum estrogen, progesterone and prolactin levels of women in Zaria, through the following objectives:

1. Assessment of working memory, concentrations of endogenous serum Estrogen, Progesterone and Prolactin in pregnant women.

2. Assessment of working memory, concentrations of endogenous serum Estrogen, Progesterone and Prolactin in Non-pregnant women.

3. Correlation of working memory and concentrations of endogenous serum Estrogen, Progesterone and Prolactin in Pregnant women.

4. Correlation of working memory and concentration of endogenous serum Estrogen, Progesterone and Prolactin in Non-pregnant women.

1.4 HYPOTHESIS

There is no relationship between working memory, serum estrogen, Progesterone and Prolactin levels of women in Zaria.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1. WORKING MEMORY

2.1.1. Introduction

Mental rearrangement of furniture to create room for more, comparing attributes of apartments to decide which to rent, mental calculation of an appropriate tip, remembering a phone number until you can put it down are examples of daily cognitive tasks that involve multiple steps with intermediate results that need to be kept in mind temporarily to accomplish the task at hand successfully. These activities are accomplished by working memory which is necessary to stay focused on a task, block out distractions and keep aware of environmental occurrences (Harden, 2011).

Working memory can be defined as a limited capacity multi-component system in the brain that is responsible for temporary storage, active maintenance, manipulation and rapid accessibility to information in the face of frequent updating, ongoing processing and or distraction, necessary for such complex cognitive tasks as language, comprehension, learning, reasoning and guiding behavior (Baddeley, 1992; 2012).

2.1.2. Baddeleys' Multi-component Model of Working Memory

The primal role of working memory in daily, academic, professional and social life has put the concept in the spotlight of research for about four decades (Shelton, 2007). Over the years, many definitions and models of working memory have evolved (Chen *et al.*, 2008). Baddeleys' multi-component model gives a functional description of working memory and is widely embraced (Repovs and Baddeley, 2006).

Baddeleys model of working memory is made up of 4 components- the central executive, the episodic buffer, the phonological loop and the visuo-spatial sketchpad (Baddeley and Jarrold, 2007).

2.1.2.1 The Central Executive

The Central Executive (CE) is the most complex component of WM. The CE is a homunculus that is capable of doing all the ingenious things that are above the competence of the other 3 components. The CE is capable of attentional control, selection, decision making and planning functions. The four fold duties of the CE are:

a. to focus attention

b. to divide attention between 2 important targets or stimulus streams

c. to switch between tasks

d. To interface with long term memory.

(Baddeley, 1996; 2012; Collete and van der Linden, 2002).

2.1.2.2 The Episodic Buffer

The Episodic Buffer (EB) is a fractionated component of CE (Baddeley, 2012). Text comprehension and expert performance in domains like mental calculation, medical diagnosis and chess show that WM is linked to long term memory(LTM) (Ericcson and Kintsch, 1995). The EB forms the link between WM, LTM, perception, semantic meaning and even musical information(Baddeley and Jarrold, 2007).

2.1.2.3 The Phonological Loop

The Phonological Loop (PL) is the simplest, most studied and most understood of all the WM components. PL deals with phonological information. The PL has 2 subcomponents- a storage system and a rehearsal system. The storage system temporarily holds speech based information as memory traces that fade away in about 2 seconds if not refreshed by the rehearsal component. The rehearsal system involves sub vocal articulation to revive the memory trace. PL is crucial for language acquisition and reading skills (Baddeley, 2012). Word length, phonemic similarity, irrelevant speech and articulatory suppression are core factors that come to play in the PL (Baddeley and Hitch, 1994).

2.1.2.4 The Visuo-Spatial Sketch Pad

The Visuo-Spatial Sketchpad (VSS) is greater in complexity to the phonological loop (Baddeley, 1996). The ability to retain and process the identity and spatial location of an object is essential for many daily tasks and is referred to as visual WM. The VSS is responsible for temporary manipulation of visuo-spatial information. The VSS comprises a visual cache which is a temporary visual store and an inner scribe which is a spatial manipulator of visual and spatial information. For example, it is

responsible for the creation and navigation of mental maps (Baddeley and Hitch, 1994 ;Darling *et al*., 2007).

2.1.3. Working Memory Capacity

It is generally accepted that there is a limit to the amount of information that can be handled by working memory per time. The amount of information that can be handled by working memory per time is called working memory capacity (WMC).WMC serves as a mental workspace for concurrent storage and processing of information (Lustig and Hasher, 2002). The exact capacity of WM is controversial (Unsworth and Engle, 2005). There are postulations that WMC is strictly limited to four items while there are counter claims that the quality of information determines WMC (Redick and Engle, 2006). According to Engle (2002), WMC is about using attention to maintain or suppress information. Thus, a greater WMC does not mean a greater storage capacity but rather, greater ability to control attention to maintain information in an active, quickly retrievable state and avoid distraction. Conway *et al.*,(2001), are of the opinion that people with low WMC have a hard time blocking out distracting information.

2.1.4. Measurement of Working Memory

A number of WM tasks are useful in predicting performance on a wide range of cognitive tasks. Generally, in each task, the subject receives items to recall and performs another attention-demanding task that is inter-laced between receiving items for recall. The N- back task is widely accepted and used as a standard in assessment of WM. This task requires a subject to signal when a current stimulus is the same as one that appeared ‘n’ items ago in a series of stimuli(Shelton *et al*., 2007).

2.2 REPRODUCTIVEHORMONES

2.2.1. Estrogen

Estrogenic activity is effected via estradiol-receptor complexes which trigger the appropriate response at the nuclear level in the target sites. There are four estrogen receptors-two ligand activated transcription factors (ERα and ERβ), one G protein coupled receptor (GPER) and a putative receptor (ER-X)(Heldring *et al.,* 2007). These receptors are found in the prostate, breast, vagina, urethra, skin, ovary, lungs, mammary gland, bone, uterus, epididymis, kidney, bladder, intestine, nervous system, endometrium, liver, adipose tissue, cardiovascular system, testis and brain (Dahlman-Wright *et al.,* 2006).

2.2.2 Progesterone

Progesterone is a C21 steroid which is synthesized from both tissue and circulating cholesterol. Cholesterol is transformed to pregnenolone which is then converted via a combined dehydrogenase and isomerase to progesterone. Progesterone is produced in the corpus luteum of the ovary after ovulation, in the placenta during pregnancy, in the adrenal glands and also in the central and peripheral nervous systems. The majority of this steroid is metabolized in the liver to pregnanediol and conjugated as a glucuronide prior to excretion by the kidneys. Progesterone prepares and maintains the uterus for pregnancy (Schmacher *et al.,* 2007; Abcam, 2011).

2.2.3 Prolactin

Prolactin is a polypeptide hormone. Prolactin is synthesized not only by the lactotrophs of the anterior pituitary but also in the hypothalamus, placenta, uterus, decidua, mammary gland and lymphocytes. Prolactin receptors are found in the

mammary gland, ovaries, CNS, heart, lung, thymus, spleen, liver, pancreas, kidney, adrenal gland, uterus, skeletal muscle and skin. Prolactin has a role in mammogenesis, lactogenesis, galactopoiesis, luteolytic/luteotrophic roles, angiogenesis, immunity and osmoregulation (Freeman *et al*., 2000).

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 ETHICAL CONSIDERATION

Ethical approval for the study was obtained from the Ahmadu Bello University Teaching Hospital Human Research Ethics Committee to carry out the research. The details of the experiment were explained to the participants and written consent was obtained.(Appendix 1)

3.2 STUDY POPULATION

The population for the study comprised 67 apparently healthy, literate females in Ahmadu Bello University, Samaru, Zaria aged 18-40.The convenience sampling technique was be used in the research. The study was conducted among women in their reproductive years attending ante-natal clinics at The University Health Service, ABU, Zaria and also women within the University Campus. The details of the study was explained to the women. Women who indicated interest to participate in the study were enlisted as participants. They were screened by physical examination and a questionnaire. The Exclusion criteria were: epilepsy, meningitis, retroviral disease, use of psychoactive substances and ill-health (Tende*et al.*, 2012).

3.3 MATERIALS

Questionnaire, bio-data forms, pens, sphygmomanometer, stethoscope, clinical thermometer, cotton wool, alcohol, weighing scale, syringes, needles, vacutainers, tourniquet, Mini Mental State Examination(MMSE), computerized software of N-back task, laptop, estradiol, progesterone and prolactin assay kits were the materials used for the study.

3.4 RESEARCH DESIGN

The participants filled the questionnaires. The weight of the participants was measured with a weighing scale, after which the MMSE and the N-back task were administered. After the neuropsychological tests, 5ml of blood was taken from the ante-cubital vein and subjected to hormonal assay.

3.5 NEUROPSYCHOLOGICAL TESTS

3.5.1 Mini-Mental State Examination (MMSE)

The MMSE is a widely used clinical instrument for global assessment of cognitive functions, detection, assessment and monitoring of cognitive impairment over time. The MMSE consisted of a variety of questions designed to elicit information about orientation, registration, attention, calculation ability, recall language and praxis. MMSE was administered in 5-10 minutes. There were 31 questions. The maximum number of right answers was 31. A score of 24-31 was classified as no cognitive impairment, 18-23 as mild cognitive impairment and 0-17 as severe cognitive impairment(Folstein*et al.*, 1975).

3.5.2 N-back Task

The N-back task is the gold standard for assessing working memory. It is a computerized test adopted from Tende*et al.*, (2012). The participantswere required to keep in memory, a series of letters that are constantly updated every 2 seconds and appear in the middle of a computer screen. The participantswere instructed to make a sign when there was a repetition of a letter with exactly one intervening character and remain silent when any other character appears. The test lasted two minutes, comprising 80 trials (performance scores (PS) = 1-80) with varied numbers of target and non- target letters. Accuracy score was the critical variable assessed. Errors consisted of either errors of commission (making a sign for a non-target letter) or

errors of omission (not making a sign for a target letter)(Kane *et al.*, 2007;Tende*et al*., 2012).

3.6 HORMONAL ASSAY

3.6.1 Estradiol Assay

Estrogen levels were assessed with the ELISA estradiol(E2) assay kit.The Estradiol ELISA test kit is based on the principle of competitive binding between E2 in the test specimen and E2-HRP conjugate for a constant amount of rabbit anti-Estradiol reagent at room temperature(18-25oC) for 90 minutes. During the incubation, a fixed amount of HRP-labeledE2 competes with the endogenous E2 in the sample or quality control serum for a fixed number of binding sites of the specific E2 antibody. Thus, the amount of E2 peroxidase conjugate immunologically bound to the well progressively decreased as the concentration of E2 in the specimen increased. Unbound E2 peroxidase was then removed and the wells washed. Next, a solution of TMB Reagent was added and incubated at room temperature for 20 minutes, resulting in the development of blue colour. The color development was stopped with the addition of 1N HCl and the absorbance was measured spectrophotometrically at 450nm. The intensity of the colur formed was proportional to the amount of enzyme present and inversely related to the amount of unlabelled E2 in the sample. A standard curve was obtained by plotting the concentration of the standard versus the absorbance. The E2 concentration of the specimens and controls run concurrently with the standards were calculated from the standard curve. (Diagnostic automation, 2013).

3.6.2 Progesterone Assay

The progesterone levels were obtained using progesterone ELISA Kit by Diagnostic automation. The Diagnostic Automation Inc. progesterone EIA is based on the principle of competitive binding between progesterone in the test specimen and progesterone-HRP conjugate for a constant amount of Rabbit anti- progesterone. In the incubation, goat anti-Rabbit IgG-coated wells are incubated with 25ul progesterone standards, controls, volunteer samples, 100ul progesterone-HRP conjugate Reagent and 50ul rabbit anti-progesterone reagent at room temperature(18-25 ^{o}C) for 90 minutes. During the incubation, a fixed amount of HRP-labeled progesterone competes with the endogenous progesterone in the standard,sample or quality control serum for a fixed number of binding sites of the specific progesterone antibody. Thus, the amount of progesterone peroxidase conjugate immunologically bound to the well progressively decreases as the concentration of progesterone in the specimen increases. Unbound progesterone peroxidase conjugate was then removed and the wells washed. Next, a solution of TMB Reagent was then added and incubated at room temperature for 20 minutes, resulting in the development of blue color. The color development was stopped with the addition of stop solution and the absorbance was measured spectrophotometrically at 450nm. The intensity of the color formed was proportional to the amount of enzyme present and was inversely related to the amount of unlabeled progesterone in the sample. A standard curve was obtained by plotting the concentration of the standard versus the absorbance. The progesterone concentration of the specimens and controls run concurrently with the standards were calculated from the standard curve.(Diagnostic Automation, 2013).

3.6.3 Prolactin Assay

The prolactin Quantitative Test Kit is based on a solid phase enzyme-linked immunosorbent assay. The assay system utilizes one anti-prolactin antibody for solid phase(microtiter wells) immobilization and another mouse monoclonal anti-prolactin antibody in the antibody-enzyme(horseradish peroxidase) conjugate solution. The test sample was allowed to react simultaneously with the antibodies, resulting in the prolactin molecules being sandwiched between the solid phase and enzyme linked antibodies. After a 60 minute incubation at room temperature, the wells were washed with water to remove unbound labeled antibodies. A solution of TMB was added and incubated for 20 minutes, resulting in the development of a blue color. The color development is stopped with the addition of 2N HCL, and the color is changed to yellow and measured spectrophotometrically at 450nnm. The concentration of prolactin is directly proportional to the color intensity of the test sample.

3.7 STATISTICAL ANALYSIS

Data obtained were expressed as mean± SEM. Students t-test was used to analysethe significance of difference between serum levels of Estrogen, Progesterone, Prolactin, MMSE and N-back task between pregnant and non-pregnant women. Pearson's correlation analysis was used to determine the relationship between the serum hormonal concentration (Estrogen, Progesterone and Prolactin) and global cognition(MMSE) and also between the serum hormonal concentration (Estrogen, Progesterone and Prolactin) and WM(N-back task).Graphpad Prism Version 4.0 for windows (Graphpad Software,San Diego, U.S.A.) was used for the analyses. Values with $P< 0.05$ were considered significant.

CHAPTER FOUR

4.0 RESULTS

4.1 SOCIO-DEMOGRAPHIC DISTRIBUTION OF STUDY POPULATION

The socio-demographic characteristics of the study population are presented in figure1. 68.4% of the pregnant women had tertiary education as against 100% of the non-pregnant women. All the non-pregnant women were students while only10.5% of pregnant women were students.81.6% and 70% of pregnant and non-pregnant women respectively were of northern Nigerian extract.3.3% of the non-pregnant group were married while 97.3% of their counterparts were married.

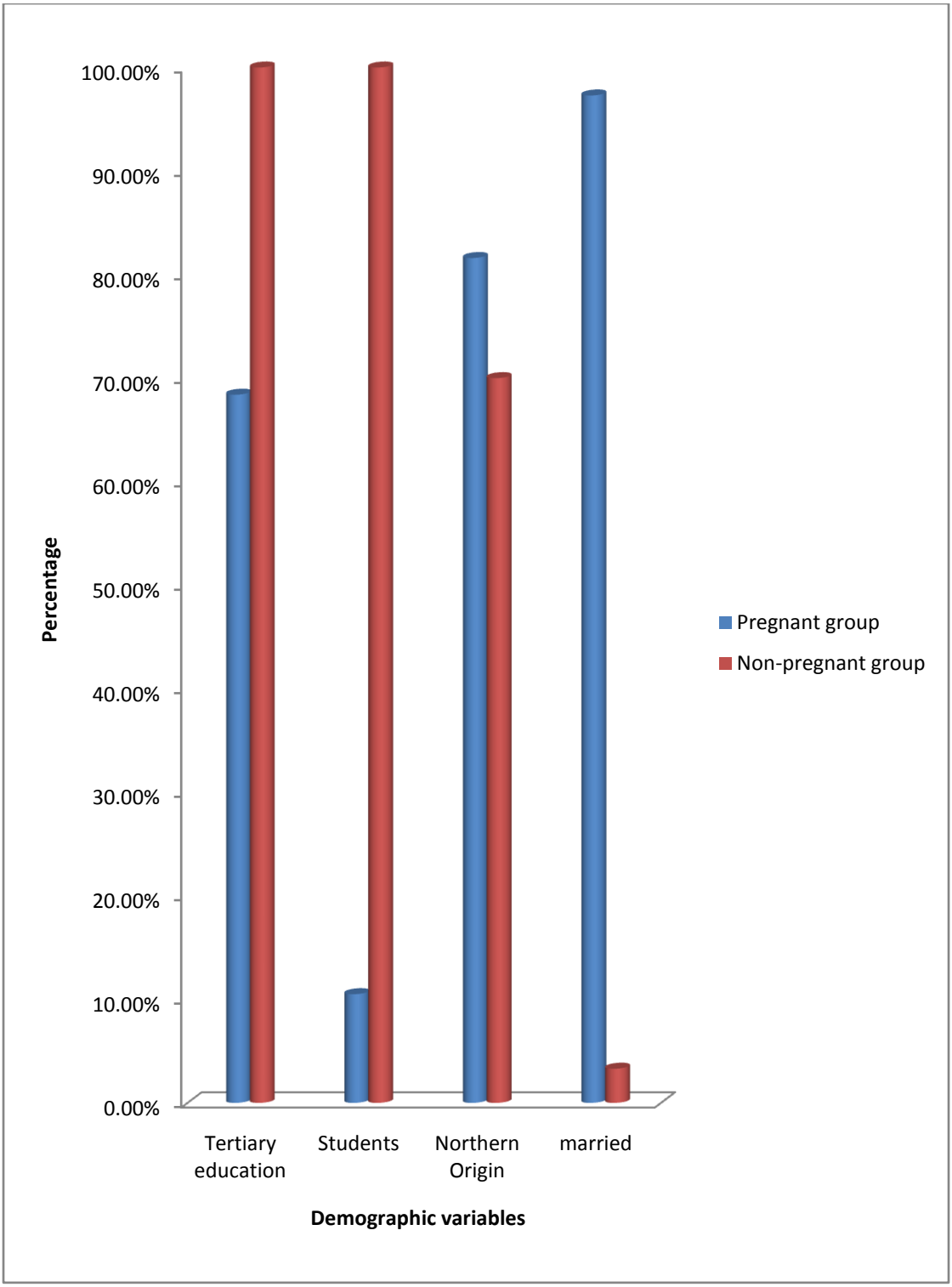


Figure1: Sociodemographic distribution of volunteers

4.2 AGE AND WEIGHT OF STUDY POPULATION

Table 4.1 presents the mean age and weight of the study population. The mean age of the pregnant women was 28.4 ± 0.99 years which was higher than the group of non-pregnant women(26.54 ± 0.54 years). The mean weight of the non-pregnant group(57.79 ±2.22Kg) was lower than the pregnant group(67.49 ±2.53Kg).

Table 4.1: Age and Weight of Pregnant and Non-pregnant Women

	Pregnant	Non-pregnant
Age(years)	28.4 ± 0.99	26.54 ±0.54
Weight(Kg)	67.49± 2.53	57.79 ± 2.22

4.3 NEUROPSYCHOLOGICAL ASSESSMENT OF PREGNANT AND NON-PREGNANT WOMEN

The results of the Neuropsychological assessment of the volunteers isshown in Table 4.2. In the MMSE, the pregnant group had a mean of 27.45 ± 0.57 while the non-pregnant group had 29.55 ± 0.13. In the N-back task, the mean values for the pregnant group was 70.32± 0.73, while that of the non-pregnant group was 74.41 ± 0.45. The pregnant group significantly outperformed the non-pregnant group in both the MMSE and the N-back task.

Table 4.2: Neuropsychological assessment of Pregnant and Non-pregnant Women

	Pregnant(n=38)	Non-pregnant (n=29)
MMSE	27.45 ±0.57[a]	29.55 ±0.13[b]
N-Back Task	70.32 ± 0.73[a]	74.41±0.45[b]

Data expressed as Mean ± SEM. [a, b]=means with different superscript letters between columns are significantly different (P<0.05).

4.4 SERUM HORMONAL CONCENTRATIONS OF VOLUNTEERS

Serum concentrations of Estradiol, Progesterone and Prolactin are shown in table 4.3. Concentrations of estrogen, progesterone and prolactin were 1125 ±75 pg/ml, 67.70 ± 7.9 ng/ml, 134.3 ± 12.04 ng/ml respectively for pregnant women and 20.90 ± 1.9 pg/ml, 3.0 ± 0.6 ng/ml and 11.6 ± 1.8 ng/ml for non-pregnant women. The pregnant women had significantly higher concentrations of all these hormones compared to the non-pregnant women.

Table 4.3: Serum Hormonal Levels in Pregnant and Non-pregnant Women

	Estradiol (pg/ml)	Progesterone (ng/ml)	Prolactin (ng/ml)
Pregnant (n=38)	1125 ±75[a]	67.70± 7.9[a]	134.3± 12.04[a]
Non-pregnant (n=29)	20.90 ±1.9[b]	3.0± 0.6[b]	11.6 ±1.8[b]

Data expressed as Mean ± SEM. [a, b]=means with different superscript letters between rows are significantly different($P<0.05$)

4.5 CORRELATION OF NEUROPSYCHOLOGICAL TESTS AND HORMONAL CONCENTRATIONS OF PREGNANT WOMEN

Table 4.4 presents the coefficient of correlation for each of the hormones against each Neuropsychological test. Estradiol was negatively correlated to the two neuropsychological tests while Progesterone was positively correlated to the Neuropsychological tests.Prolactin had a positive correlation with the MMSE but the relationship between Prolactin and the N-back task was negative. All the relationships were insignificant.

Table 4.4: Correlation of Neuropsychological tests and Hormonal Levels in Pregnant Women

	Estradiol	Progesterone	Prolactin
N-back	-0.0232^{NS}	0.0902^{NS}	-0.029^{NS}
MMSE	-0.171^{NS}	0.0998^{NS}	0.717^{NS}

Correlation coefficients are notsignificant

4.6 CORRELATION OF NEUROPSYCHOLOGICAL TESTS AND HORMONAL CONCENTRATIONS IN NON-PREGNANT WOMEN

The correlation of the Neuropsychological tests and hormonal concentrations of the pregnant women is presented in Table 4.6.Progesterone was positively correlated to the two Neuropsychological tests while Prolactin was negatively correlated to the two Neuropsychological tests. Estradiol positively correlated to MMSE but negatively correlated to the N-back task. None of the relationships had statistical significance.

Table 4.5: Correlation of Neuropsychological tests and Hormonal Levels in Non-pregnant Women

	Estradiol	Progesterone	Prolactin
N-back	-0.2536 ^{NS}	0.03494 ^{NS}	-0.0864 ^{NS}
MMSE	0.1756 ^{NS}	0.251 ^{NS}	-0.0277 ^{NS}

Correlation coefficients are insignificant

CHAPTER FIVE

5.0 DISCUSSION

In this study, concentrations of endogenous serum levels of estrogen, progesterone and prolactin were evaluated in both pregnant and non-pregnant women. Global cognition was assessed with the MMSE while WM was assessed with the N-back task. Each of the Hormones was correlated with WM and also with global cognition. Non-pregnant women had lower hormonal levels but performed significantly better in both global cognitive and WM assessments. Some studies have associated pregnancy with cognitive deficits while others have counter claims. This study showed poorer global cognition and working memory during pregnancy.

The results show that the pregnant group had lower educational attainment as only 68% of the group compared to 100% of the non-pregnant group had tertiary education. Also, only 10.5% of the pregnant group were students as at the time of the study compared to 100% of the pregnant group who were students. Pregnancy is associated with a myriad of physiological and biochemical changes which are often associated with hormonal changes. Although the pregnant women had higher levels of Estrogen, Progesterone and Prolactin, they had poorer performance in the Neuropsychological tests. In pregnant women, estrogen was negatively correlated to global cognition and WM, Progesterone had a positive correlation with both WM and cognition while prolactin had a negative correlation with WM but a positive correlation with cognition. In non-pregnant women, estrogen was negatively correlated with WM but positively correlated with global cognition; prolactin had a negative correlation with working memory and global cognition while progesterone

positively correlated with WM and global cognition. The correlation of the hormones with WM and global cognition were insignificant.

The results of the current study are contrary to Maki *et al.*,(2002) that estrogen facilitates WM, and Castanho*et al*.,(2014), who showed that lower Estradiol is associated with poorercognition. The results of the study are similar to the finding of Gasbarri*et al*., (2008) and Hampson and Morley, (2013) who showed that high levels of Estradiol may impair performance of WM. The study is in line with the findings of Castanho*et al*., (2014) which showed that higher prolactin levels are associated with worse cognitive performance.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The study has shown that:

1. Pregnant women have significantly higher concentrations of endogenous serum estrogen, progesterone and prolactin compared to non-pregnant women.
2. Compared to non-pregnant women, pregnant women showed significantly deficit in WM and Global cognition.
3. No significant correlation exists between any of the three hormones and either WM or global cognition. Thus, the hormones may not have a direct effect on either WM or global cognition.

6.2.Recommendations

Further studies should critically examine:

1. the causes and the mechanism of WM deficit in pregnancy
2. possible differences in WM along occupational lines
3. genetic variations and interventions in WM deficits
4. Working memory Levels with consideration for the health status of the patient (through full blood count), anxiety, stress, depression and other factors that affect cognition and working memory in particular.

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Appendix 1: SUBJECT INFORMATION SHEET

ASSESSMENT OF THE RELATIONSHIP BETWEEN WORKING MEMORY AND SOME REPRODUCTIVE HORMONES IN SELECTED PATIENTS OF AHMADU BELLO UNIVERSITY MEDICAL CENTRE.

Working memory is a central construct in cognitive neuroscience that is responsible for orchestration of daily activities and is important in learning. The part of the brain that subserves working memory has many estrogen receptors. Estrogen levels differ across the different phases of a womans life.

This study seeks to assess working memory, serum estrogen,progesterone and prolactin levels of pregnant and Non-pregnant women. The procedures include filling questionnaires, measurement of height,weight,pulse, blood pressure,working memory and collection of blood samples. All these risk free beneficial assessments would be done at no cost .You are also assured that all information provided will be treated with utmost confidentiality and your identity would be guaranteed anonymity. There is no conflict of interest.

The study may give empirical evidence and explanation for hormone influenced cognitive patterns that have ramifications for cyclic proficiency at tasks, general lifestyle, occupational, social and academic leanings and as such has implications for women, educationists, policy makers and scientific research.

To this end, I solicit your unequivocal support and request that you participate in the study. If you agree to participate, kindly endorse the space provided below.

Thank you.

Ake Bisola

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Ahmadu Bello University, Zaria

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08036423480

_____ _____

SIGNATURE OF RESEARCH RESPONDENT DATE

Appendix 2: QUESTIONNAIRE

Age

Marital status: single married

Geo-political origin: NE NW NC SS SE SW

Family type of parents: polygamy monogamy

Family type of volunteer: polygamy monogamy

Birth order

Parity: Age of children:

Height(m)

Weight(Kg)

Systolic blood pressure(mmHg)

Diastolic Blood Pressure(mmHg)

Body temperature(^{o}C)

Pulse rate(beats / minute)

Level of education: primary secondary Tertiary

Occupation:

Date of last Menstrual period

Are you pregnant? If yes, which trimester? 1st 2nd 3rd

Are you lactating? If yes, for how long?

Are you sick? Are you on medication?

Are you epileptic?

Have you had Meningitis?

Is there a history of mental disease in your family?

Do you have a history of trauma?

Do you use Tobacco, alcohol or any psychoactive substance?

HEALTH RESEARCH ETHICS COMMITTEE

AHMADU BELLO UNIVERSITY TEACHING HOSPITAL

SHIKA - ZARIA, NIGERIA.

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Our Ref: ABUTH/HREC/TRG /36

Your Ref: _____

Date: 13th Oct, 2014

ABUTH HREC FULL ETHICAL CLEARANCE CERTIFICATE

RE: APPLICATION FOR ETHICAL CLEARANCE CERTIFICATE

Evaluation of Working Memory, Serum Estrogen, Progesterone and Prolactin Levels of Women in Zaria, Northern Nigeria.

ABUTH Ethics Committee assigned number:	-	ABUTHZ/HREC/G14/2013
Name of the principal Investigator:	-	Bisola Ake
Address of the Principal Investigator:	-	Dept. of Human Physiology A.B.U, Zaria.
Date of receipt of valid application:	-	3/7/2013
Date of meeting when final determination on ethical approval was made:	-	3rd & 4th Sept, 2014

This is to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed and *given full approval by the Health Research Ethics Committee.*

Please note: this approval dates from 14th October, 2014– 14th October, 2015

No participant recruitment into this research may be conducted outside these dates.

All informed consent forms in this study must carry the ABUTH HREC number assigned to this research and the duration of ABUTH HREC approval of the study.

This HREC expects that you submit your application as well as an annual report for ethical clearance renewal 3 months prior to expiration of study dates. This is to enable you obtain renewal of your approval and avoid interruption of your research.

If there is delay in starting the research, please inform the ABUTH HREC so that starting dates can be adjusted accordingly.

No changes are permitted in the research without prior approval by ABUTH HREC, except in circumstances outlined in national code for Health Research Ethics: http://www.nhrec.net.

ABUTH HREC reserves the right to conduct compliance assessment visits to your research site without prior notification.

Prof. A. I. Mamman
Chairman, ABUTH HREC