EVALUATION OF THE MANAGEMENT OF ANXIETY DISORDERS AT AHMADU BELLO UNIVERSITY TEACHING HOSPITAL, KADUNA, NIGERIA

BY

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DEPARTMENT OF PHARMACOLOGY AND CLINICAL PHARMACY

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DECLARATION

I declare that the work in the thesis entitled 'evaluation of the management of anxiety disorders at Ahmadu Bello University Teaching Hospital, Kaduna, Nigeria' has been performed by me in the Department of Pharmacology and Clinical Pharmacy under the supervision of Dr (Mrs.) H.O. Kwanashie, Professor I. Abdu-Aguye and Dr. T.L. Sheikh.

The information derived from the 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 any university.

Aimola, Edward Kehinde	_____	22nd May, 2006
Name of student	Signature	Date

CERTIFICATION

This thesis entitled "EVALUATION OF THE MANAGEMENT OF ANXIETY DISORDERS AT AHMADU BELLO UNIVERSITY TEACHING HOSPITAL, KADUNA, NIGERIA" by AIMOLA, Edward Kehinde meets the regulations governing the award of the degree of Master of Science of Ahmadu Bello University, Zaria, and is approved for its contribution to knowledge and literary presentation.

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DEDICATION

….To him who is able to do

immeasurable more than all we ask or imagine,

according to his power that is at work within us,

be glory and honor forever amen.

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I wish to express sincere appreciation to my supervisors Dr. (Mrs.) H.O. Kwanashie, Professor I. Abdu-Aguye and Dr T.L. Sheikh for their guidance through this work. I also wish to express my heartfelt appreciation to the members of Record Department of the Psychiatry Unit of Ahmadu Bello University Teaching Hospital, Kaduna for their support.

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ABSTRACT

Anxiety disorders are mental disorders that share extreme or pathological anxiety as the principal disturbance of mood or emotional tone. This study involved a retrospective analysis of data obtained from hospital records of patients attending clinic at the psychiatry unit of Ahmadu Bello University Teaching Hospital, Kaduna, Nigeria for a two year period spanning January 1st, 2003 to December 31st, 2004. The study population of 875 patients consisted of only patients who attended clinic six times or more within the period under study. This study was carried out to describe prevalence, comorbidity, management and burden of anxiety disorders among patients.

Average clinic attendance in 2004 (72.5) increased as against 2003 (64.6). With respect to relative occurrence, anxiety disorders (8.0%), ranked lower than schizophrenia (46.6%), depression (13.7%) and seizure disorders (12.1%). Majority of anxiety disorders patients were male (62.3%), married (70.5%), Hausa (34.4%) from Kaduna state (41.0%) and of the Muslim faith (57.4%). Most were in their twenties (26.2%) and thirties (32.8%) and had been attending clinics for five years or less. The mean age of patients (36.3 years) diagnosed as having anxiety disorders (n=61) was higher than that for the study population (29.2 years) of mental disorders (n=875). Half of anxiety disorders patients were employed (50.8%) and very few had tertiary education (1.6%). Generalised anxiety disorder (80.3%) was the most prevalent subtype of anxiety disorder. Anxiety depressive disorder (16.4%), obsessive compulsive disorder (1.6%) and panic disorder

(1.6%) were other subtypes of anxiety disorders identified. Only 11.5% of patients had records showing family history of mental disorders.

Majority of anxiety disorder patients (62.8%) had another comorbid diagnosis. Non psychiatric comorbid diagnoses (50.8%) were more prevalent while psychiatric comorbid diagnoses were present in 14.7% of anxiety disorder patients. Hypertension (36.1%) was the most prevalent non psychiatric comorbid diagnosis, while somatization disorder (6.6%) and depressive disorders (4.9%) were the most prevalent psychiatric comorbid diagnosis. The mean age for patients with comorbid disorders was significantly higher than for patient who had no comorbid disorders ($P<0.01$). Comorbid disorders were found to have no association with sex or marital status; however, average frequency of clinic visits increased significantly in the presence of non psychiatric comorbid disorders ($P<0.05$).

Signs and symptoms varied and they included somatoform complaints (which were the most prevalent), insomnia and sleep disorders, cardiovascular complaints, anxious mood, gastrointestinal symptoms and tension. Hematological investigations (31.1% of patients), serum / urea / electrolyte / creatinine (26.2%), and stool microscopy (13.1%) were the most frequently requested laboratory investigations. Management of anxiety disorders involved the use of pharmacotherapy (67.2%) or a combination of psychotherapy and pharmacotherapy. Drugs employed include; amitriptyline (used in 83.6% of patients), imipramine (16.4%), nitrazepam (13.0%), bromazepam (11.5%) and diazepam (6.6%). Antipsychotics employed included; trifluperazine (77.0%), chlorpromazine (9.8%) and

thioridazine (8.2%). Antihypertensives employed included; propranalol (23.0%), nifedepine (14.8%), bendrofluazide (11.5%) and amiloride-hydrochlorothiazide (9.8%). Other drugs encountered include vitamin B complex (70.5%), benzhexol (57.4%), and carbamazepine (4.9%). Non pharmacological approaches included; psychotherapy (54.1% of times), counseling (insight counseling and counseling with family members) (41.7%), and relaxation therapy (4.2%). Mean frequency of clinic visit did not differ significantly in patients that received either pharmacotherapy only or a combination of psychotherapy and pharmacotherapy. However, one-way analysis of variance show that with increase in years since registration there was significant decrease in cost of treatment ($P<0.05$). Neither accessibility nor employment status was found to affect adherence with clinic visits. Drug use was accompanied by side effects in significant number of patients (82.0%). Predominant side effects included; insomnia (in 7.4% of patients), weakness (4.5%), headaches (4.1%), dizziness (2.5%) and excessive sleep (2.0%). Use of other drugs (38.0% of times), reduction of drug dose (23.0%), taking of drugs at a different time of the day (11.5%), counseling (11.5%), drug discontinuation (7.7%) and increase drug dose (e.g. increase dose of amitriptyline when insomnia was the complain) (7.7%) were methods employed in management of side effects.

Calculated annual drug cost (₦276,750:84) far outweighed cost of laboratory investigations (₦32,530:00) and cost of hospitalization (₦14,500:00). The average cost of treatment per patient per month was ₦1,200:00 while the average cost of laboratory investigations per patient per month was ₦ 403:91. Average of percentage number of

times patients were accompanied to clinic was 17.76%. Travel time and waiting were sources of loss in productive time identified.

In conclusion, anxiety disorders are common and their course can be complicated by the presence of comorbid disorders, however, early diagnosis and proper management can help improve health care outcomes.

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ABBREVIATIONS, DEFINITIONS, GLOSSARIES AND SYMBOLS

α	Alpha
ABUTH	Ahmadu Bello University Teaching Hospital
APA	American psychiatric association
CBT	Cognitive behavioral therapy
CNS	Central nervous system
CRF	Corticotrophin releasing factor
DSM-IV	Diagnostic and statistical manual of mental disorders-Forth edition
GABA	Gamma amino butyric acid
GAD	Generalised anxiety disorder
HPA	Hypothalmo-pitutary-adrenal axis
ICD-10	International classification of diseases and related health disorders-Tenth edition
MAO	Monoamine oxidase
MAOI	Monoamine oxidase inhibitor
OCD	Obsessive compulsive disorder
PTSD	Post Traumatic stress disorder
SSRI	Selective serotonin reuptake inhibitors
TCAD	Tricyclic antidepressants
WHO	World Health Organization
WHR	World Health report
β	Beta
γ	Gamma

CHAPTER ONE

INTRODUCTION

1.1 INTRODUCTION

Inseparable and crucial to the proper functioning and well being of individuals, families, societies, countries and economies is mental health. Disorders characterized by abnormalities in cognition, emotion or mood, or the highest integrative aspect of behavior such as social interactions or planning of future activities are described as mental disorders (Mental health: A Report of Surgeon General). The World Health Report (WHR, 2001), is dedicated to mental health, and describes mental and behavioral disorders as clinically significant conditions characterized by alterations in thinking, mood (emotions) or behaviour associated with personal distress and / or impaired functioning. From the above definitions it is generally agreed that mental disorders share the following features in common: alterations in thinking, mood or behaviours (or some combination thereof) associated with distress and / or impaired functioning.

Historically public attitudes and perceptions towards mental illness shows poor understanding and were manifested as bias, distrust, fear, embarrassment, avoidance, stigma, shame and exclusion. This attitudes and perceptions have combined over the years to build real and perceived barriers to care and cure of mental illness. The theme of World Health Day 2001 “Stop Exclusion – Dare to Care” is a confirmation of this, and this call is being joined by nations all over the world. Advances and integration of research findings in several fields of science including neuroscience, genetics, psychology, sociology, behavioural medicine, neuroimaging, neurophysiology and

molecular biology among others, have led to greater understanding of the basis of normal and abnormal mental functioning and how the complex relationships between genetic, biological, social and environmental factors combines to cause mental and brain illnesses. The new understanding is bringing hope for management and cure of mental illnesses.

There are large disparities in prevalence of mental disorders between and within countries (Araya, 2000). Cross national comparative studies carried out by International Consortium in Psychiatric Epidemiologists (ICPE) showed variations in prevalence estimates from greater than 40% life time prevalence of any mental disorder in Netherlands and U.S.A., to Levels of 12% in Turkey and 20% in Mexico (WHR, 2000). Review of studies carried out in Europe (Alonzo *et al.*, 2004), Australia (Henderson, 2002), Moscow (Gavrilor *et al.*, 1983), Canada (Dewa *et al.*, 2004), Zambia (Mayeya *et al.*, 2004), Japan (Matsumura, 2004) and America (NIHIM, 2004) have shown that prevalence vary from study to study and by implication from country to country. Recent analysis carried out by the World Health Organization (WHO) shows life time prevalence for mental and behavioural disorders of more than 25% (WHR, 2001); while the Global Burden of Disease study show that neuropsychiatry conditions are present at any point in time in 10% of adult population (Mathers *et al.*, 2002).

Mental disorders are chronic, have early age of onset and are related, to socioeconomic measures and conditions (WHR, 2001 and Bijl *et al.*, 2001). Worldwide, unchecked massive productivity losses and immense human suffering are resulting from the invasive

impact of mental disorders in every work of life and society. One in four families is likely to have at least one member with a mental or behavioral disorder. These families not only provide physical and emotional support, but also bear negative impact of stigma and discrimination (WHR, 2001). Increase dependence of work places on mental capacities and faculties of skilled workers; leaves disability and not mortality the most significant health-related cost and performance issue facing workplaces. Clinical depression is by far the leading cause of disability in the world today, accounting for 12% of all disability (Marten & Bill, 2000 and Mathers *et al*., 2002). About 20% of patients seen by primary health care professional have one or more mental disorders (WHR, 2001). Mental disorders if left unchecked therefore, will account for significant productivity loses, increased health and social services needs, lost employment, impact on families and care givers, increased levels of crime, decreased levels of public safety, as well as premature mortality, and hence an unarguably, source of global economic retardation (Marten & Bill, 2000).

Fear and anxiety are essential, natural healthy coping reactions that help us adapt to threatening or dangerous situations. Apprehension, uncertainty, worry and fear characterize these states. The brain triggers the release of hormones which trigger the activation of the sympathetic nervous system and what is commonly referred to as the fight or flight response hence, anxiety and fear can be viewed as part of a problem solving process. In certain instances anxiety loses its adaptational character, causes distress and impairs function in such individuals, at which point it is referred to as anxiety disorder. Anxiety disorders are the most common and frequently occurring mental

disorders (Swinson, 1997; Costa e Silva, 1998; Pelissolo *et al*., 2002 and Alonso *et al*., 2004). Anxiety disorders occur more frequently in women, and also frequently coexist with other illnesses such as heart diseases, irritable bowel syndrome, thyroid conditions and migraine headaches. Because these disorders may also need to be treated, it is important to have a through medical examination before initiating any treatment.

Several outcome measures have been used to describe the impact of anxiety disorders on families, communities, economies, and quality of life. Patients diagnosed as having anxiety disorders in mid / late life are more likely to have an additional diagnosis, consult a specialist more frequently, use health care services more frequently, require hospitalization and visit emergency rooms more frequently. They also have significantly increased medical cost, show impaired productivity, have elevated risk of suicide, have impaired functioning and quality of life (Goisman *et al*., 1995; Goldenberg *et al*., 1996; Costa e Silva, 1998; Marshall *et al*., 2000; Wittuchen, 2002; Pelissolo *et al*., 2002; McLaughlin *et al*., 2003; Alonso *et al*., 2004 and Marciniak *et al*., 2004). This ugly situation is made even less pleasant by research findings which show, that patients with anxiety disorders are less likely to seek medical advice, are more likely to be misdiagnosed, are under diagnosed, undergo unnecessary medical procedures, and are under treated (Swinson, 1997 and Costa e Silva, 1998 and Afana *et al*., 2002).

CHAPTER TWO

LITERATURE REVIEW

The immediate presence of an obviously harmful stimulus elicits fear, while the perceived possibility of the occurrence of negative consequences producers' anxiety (Cannistraro & Rauch, 2003). Anxiety is distinguished from fear by the presence of subjective uncertainty with respect to the distress inducing stimulus or situation. Anxiety sometimes loses its adaptational character, and becomes greater than would be expected for a given situation and thus causes distress and impairs function, at which point it is referred to as a disorder.

2.1 CLASSIFICATION OF ANXIETY DISORDERS

There are several diagnostic and classification systems worldwide. The two best known are; Diagnostic and Statistical Manual of Mental Disorder–Forth Edition (DSM-IV) which is developed and published by American Psychiatric Association (APA), and International Classification of Diseases and Related Health Problems–Tenth Edition (ICD-10) developed by WHO. There was close collaboration between APA and WHO during the development of the two systems. This has helped to reduce unnecessary differences between both systems and enable fully compatible diagnosis.

The ICD-10 classification of mental and behavioural disorders brings together neurotic, stress related and somatoform disorders because of their historical association with the concept of neurosis and the association of a substantial (though uncertain) proportion of

this disorders with psychological causation. An overview of anxiety disorders in this class is given below;

2.1.1 Neurotic Stress Related and Somatoform Disorders

Phobic anxiety disorders

- Agoraphobia
  - Without panic disorder
  - With panic disorder
- Social phobias
- Specific (isolated) phobias
- Other phobic anxiety disorders
- Phobic anxiety disorders unspecified

Other anxiety disorders

- Panic disorder (episodic paroxysmal anxiety)
- Generalised anxiety disorder
- Mixed anxiety depressive disorders
- Other mixed anxiety disorders
- Other specified anxiety disorders
- Anxiety disorder, unspecified

Obsessive-compulsive disorder

- Predominantly obsessional thoughts or ruminations
- Predominantly compulsive acts (obsessional rituals)
- Mixed obsessional thoughts and acts

Other obsessive-compulsive disorders

Obsessive-compulsive disorder, unspecified

Reaction to severe stress, and adjustment disorders

Acute stress reaction

Post-traumatic stress disorder

Adjustment disorders

Brief depressive reaction

Prolonged depressive reaction

Mixed anxiety and depressive reaction

With predominant disturbance of other emotions

With predominant disturbance of conduct

With mixed disturbance of emotions and conduct

With other specified predominant symptoms

Other reactions to severe stress

Reaction to severe stress, unspecified

2.2 EPIDERMIOLOGY OF ANXIETY DISORDERS

Anxiety disorders are the most common of all mental disorders (Bland & Newman, 1988 and Swinson, 1997), with life time and point prevalence higher in the women than men (Kessler *et al*., 1994; Hacker, 1997; Bijl *et al*., 2002; Fullerton *et al*., 2001; Wittuchen & Hoyer, 2001; Pigott, 2003 and Jerliyn, 2004).

Majority of cases of anxiety disorder develops relatively early in life (Tanja *et al*., 2004 and Kessler *et al*., 2001). However, studies have also shown that these disorders can develop in late life (Lenze *et al*, 2005 and Le Roux *et al*., 2005). Significant differences have been observed with regards to age of onset, of the various subtypes of anxiety disorders (Tanja & Jűrgen, 2004). Twelve months prevalence rates are somewhat lower than life time prevalence rates, indicating that the aetiopathology is in most cases, but not all cases, chronic (Tanja & Jűrgen, 2004 and Kessler, 2001).

The relative occurrence of subtypes of anxiety disorder varies depending on the study characteristics (Wacker, 1997 and Diala & Muntaner, 2003). Coexistence of anxiety disorders with other psychiatric conditions (Sanderson *et al*., 1994; Goisman *et al*., 1995; Cosoff *et al*., 1998; Taman *et al*., 2002 and Rodriguez *et al*., 2004), as well as non-psychiatric conditions (Stark *et al*., 2002) have been studied extensively. The implications of such co-occurrences have also been studied (Shankman *et al*., 2002 and Henry *et al*., 2003).

Anxiety disorders are associated with significant economic and societal burdens owing to lost productivity and health service utilization (Marshal *et al*., 2000; Lim *et al*., 2001; Ninan, 2001 and Wittuchen, 2002). In another study posttraumatic stress disorders (PTSD) was shown to be a predictor of higher medical cost (Marshal *et al*., 2000). Diala and Muntaner (2003) have studied mood and anxiety disorders among rural, urban and metropolitan residents living in the United States. They reported that, mood and anxiety disorders were more prevalent among. They suggested that male mood and anxiety

disorders may be a function of diminishing resources or increasing financial strain (Diala & Muntaner, 2003). The following socio-demographic variables have been found to be consistently linked with higher prevalence of anxiety disorders: divorce, widowhood, unmarried status, unemployment, low levels of education and low income (Tanja & Jűrgen, 2004).

High prevalence of non-consulting and low detection rates in general practice are some important public health problems observed in patients with mental disorders (Andrew *et al*., 2001 and Afana *et al*., 2002).

2.3 ETIOLOGY OF ANXIETY DISORDERS

The etiology of anxiety disorders is not fully understood. However the likelihood of developing anxiety involves a combination of life experiences, psychological traits, and / or genetic factors. The etiology of anxiety disorders may be viewed from an anatomical, biochemical or psychological basis (see 2.2.1-2.2.3 below).

2.3.1 Neural Circuitry of Anxiety

Anxiety engages a wide range of neurocircuits. Fear inducing stimulus is channeled by sensory fibers from visual, auditory, olfactory, nociceptive and visceral pathways through the anterior thalamus to the lateral nucleus of the amygdala and is then transferred to the central nucleus of the amygdala.

The central nucleus of the amygdala serves as a hub both for integration of information and for execution of autonomic and behavioral fear responses. Efferent from the central nucleus of the amygdala extend to para brachial nucleus (causing tachypnea), lateral hypothalamus (which initiates sympathetic responses), locus coerulus (causing increased blood pressure and heart rate as well as initiating behavioral response to fear) and to the para ventricular nucleus of the hypothalamus (resulting in activation of hypothalamic-pituitary-adrenal axis (HPA), which stimulates increase in adrenocorticoids).

Normally this system is tuned by information processed by sensory thalamus, prefrontal cortex, insular and somatosensory cortex. Rapid fear responses are less finely-tuned and are needed for response to immediate threats. They are activated through direct input from sensory thalamus. Slower fear responses which are more finely-tuned have the benefits of thalamo-cortico-amgadalo inputs which allow for valuable cortical assessment of threat-related information.

Two other potential sites of pathology in anxiety disorder are:

1. The hippocampus which is implicated in processing contextual information regarding safe versus potentially dangerous contexts and have influence on fear response. Overgeneralization, a consequence of hippocampus dysfunction, leads to deficient appreciation for contextual specificity of potentially threatening stimuli.
2. Impaired extinction leads to inability to efficiently modify previously experienced associations between innocuous cues and genuinely threatening stimuli. This may be the result of lesions in the medial prefrontal cortex.

From the above perspective anxiety disorder might be viewed as predominant amygdala involvement (social phobia), predominant cortical involvement (specific phobia), or a combination of cortical and amygdala involvement (PTSD). Cortical-striatal systems are involved in pathophysiology of obsessive–compulsive disorders. Data suggest that panic disorder should fall in the second or third category, and there is insufficient evidence to categorize generalized anxiety disorder by this scheme (Cannistraro & Rauch, 2003).

2.3.2 Role of Neurotransmitters in Etiology of Anxiety Disorders

Many neurotransmitter alterations occur in anxiety disorders. Those neurotransmitters most implicated in the etiology of anxiety disorders include; noradrenaline, serotonin, gamma-amino butyric acid and the opoids. However, corticotrophin-releasing hormone (CRH) has also been implicated.

Serotonergic System

Serotonin (5-HT) modulates numerous processes in the central nervous system (CNS) and dysregulation of the 5-HT system appears to be relevant to numerous psychiatric disorders including anxiety (Naughton *et al*., 2000 and Jay *et al*., 2003).

Knock out technologies are genetic strategies employed to ablate specific components of 5-HT system. Mice possessing mutations in serotonergic system have been used to study the possible role of this system in the production of specific behavioral changes related to neuropsychiatric disorders, and how alterations in 5-HT metabolism during development may increase vulnerability to anxiety disorders.

The presence of a behavioural phenotype of elevated anxiety in knockout mice from divergent genetic backgrounds, suggest that, this receptor is an important mediator of anxiety. Furthermore, the presence of anxiety phenotype during early life and not in adulthood of mice lacking 5-HT-$_{1A}$ receptors lends evidence to the fact that 5-HT-$_{1A}$ receptors are important modulators of brain development in establishing anxiety related behaviors (Gingrich *et al*., 2003).

Gamma-Amino Butyric Acid System (GABA)

Clinical experience shows success of benzodiazepines in the management of anxiety disorders and this lends evidence supporting the role of GABA system in pathophysiology of anxiety disorders.

Findings from studies employing genetic engineering techniques (e.g. knockout and knockin technologies) reveal that GABA receptor dysfunction may predispose individuals to symptoms of generalised anxiety disorder and panic disorder. Furthermore anxiolytic effects of benzodiazepines are mediated by α_2 sub-units of GABA receptors.

These results have been substantiated by evidence from neuroimaging studies in humans with anxiety disorders. Reduction in GABA levels and $GABA_A$-benzodiazepine receptor binding have been reported in different regions of brains of patients with various types of anxiety disorders (Malizia *et al*., 1998; Abadie *et al*., 1999 and Bermner, *et al*., 2000).

Noradrenergic System

Investigating the role of α_{2A}-adrenorecptor in mice with genetic deletion of this receptor revealed, disturbed noradrenergic neurotransmission was associated with an anxiety prone phenotype in elevated plus maze and exploratory activity test (Janne, 2004). Results from a study evaluating noradrenergic functions in different groups of anxious, depressed, comorbid anxious depressed patients and healthy controls, demonstrate central nervous system (CNS) noradrenergic dysfunction in patients with anxiety disorders (Cameron *et al*., 2004).

Increased anxiety like behaviour and increased sensitivity of noradrenergic neuronal receptors suggest that α_{2A}-adrenoreceptor-knock out mice (α_{2A}-AR KO) might be useful as models for anxiety disorders. Drugs targeted at α_{2A}-AR may have potential therapeutic utility in treatment of anxiety disorders, and potential for understanding the role of α_{2A}-AR in pathophysiology of anxiety disorders (Janne, 2004).

Opoid System

The observation that naloxone is able to reverse stress induced analgesia in patients with PTSD is suggestive of centrally mediated opoid response in psychobiology of PTSD (Vander kolk *et al*., 1989).

Sher (1998), suggested that anxiety disorders are related to a deficiency in 'adaptational reserve' in endogenous opoid system and that therapeutic maneuvers decrease anxiety because they are able to activate endogenous opoid system. This suggestion is supported

by findings that patients with PTSD have reduced concentrations of resting plasma beta-endorphins and lower pain threshold (Friedman & Soutewick, 1995).

Neuroendocrine system

Several studies have implicated dysfunctional hypothalamic–pituitary–adrenal (HPA) axis in the etiology of anxiety disorders (Condren *et al*., 2002; Kehne & Lambert, 2002 and Marshall *et al*., 2002). Anxiolytic effects of corticotrophin releasing factor receptor antagonist CRF(1) further provides evidence for the role of dysregulation or dysfunctional HPA axis in the pathophysiology of anxiety disorders (Kehne & De lombaert, 2002 and Mc Elory *et al*., 2002).

Makiono *et al*., (2002) proposed multiple feed back mechanisms activating CRH system in the brain during stress. Anxiolytic effects produced by CRF(1) may be mediated by noradrenergic and serotonergic systems (Kagamiishi *et al*., 2003 and Jedema & Grace, 2004).

2.3.3 Psychological Views of Anxiety

Psychological theories of anxiety include psychoanalytic and psychodynamic theories, as well as behavioural and cognitive theories (Brenner, 1978; Kadzin, 1996; 1997; Feldman, 1997 and Thorn *et al*., 1999). Psychodynamic theories focus on symptoms as an expression of underlying unresolved conflicts in intimate relationships or expression of anger, for example, ritualistic composite behavior can be viewed as a specific defense mechanism that serves to channel psychic energy away from conflict or forbidden

impulses. Psychodynamic theories though not empirical are amendable to scientific study (Kandel, 1999).

Classical conditioning and vicarious or observational learning are more recent behavioral theories. In classical conditioning, a neutral stimulus acquires the ability to elicit a fear response after repeated pairings with a frightening (unconditioned) stimulus. In vicarious learning, fearful behavior is acquired by observing the reaction of others to fear-inducing stimuli (Thorn *et al*., 1999).

Cognitive factors play a critical role in the etiology of anxiety (Barlow *et al*., 1996), with negative cognitions frequently occurring in individuals with anxiety (Ingram *et al*., 1998). One of the most salient negative cognitions in anxiety is the sense of uncontrollability. It is typified by a state of helplessness due to perceived inability to predict, control or obtain desired results (Barlow *et al*., 1996).

2.3.4 CAUSES AND RISK FACTORS

Genetics

Evidence for genetic contribution and / or influences in the development of anxiety disorders has been extensively studied (Scherrer *et al*., 2000; Hettema *et al*., 2001; Van Beek & Griez, 2003 and Arnold *et al*., 2004). Results indicate that genes play a role in the etiology of panic disorder, generalized anxiety disorder and phobias.

Exposure to Traumatic Events

Reviews of literature suggest relationships between exposure to traumatic life experiences and increased prevalence rates of certain anxiety disorders among populations exposed to traumatic events (Fierman *et al*., 1993; Hiott & Labbate, 2002; Safren, *et al*,, 2002; Van der Kolk, 2003 and Black, *et al*., 2004).

The following have also been identified as causes / risk factors for anxiety disorders: family upbringing (being raised by parents with mental illness), childhood variables (emotional insecurity during childhood), life stressors (socioeconomic status) and associated medical conditions (e.g. cancer) (Messer & Beidel, 1994; Rogers *et al*., 1994; Kendler *et al*., 1995; Hirshfeld *et al*., 1997; Stein & Matsunaga, 2001; Rapee, 2002 and Stark *et al*., 2002).

2.4 FEAUTURES OF ANXIETY DISORDERS

2.4.1 Generalized Anxiety Disorders (GAD)

Features of generalized anxiety disorders include persistent (more days than not for the last six months), excessive, hard to control worry about every day events and problems. Associated symptoms include tension, fatigue, insomnia and impaired concentration. Patients may complain of significant distress or impairment of social, occupational and important areas of functioning.

2.4.2 Panic Disorder

When an individual suffers recurrent, unexpected panic attacks that are not consistently associated with a specific situation or object they may be diagnosed as having this anxiety disorder. The attacks are usually accompanied by concerns for further attacks, and avoidance of perceived environmental triggers.

Panic attacks are characterized by abrupt onset of intense fear or discomfort with associated somatic and / or cognitive symptoms. Somatic symptoms include stimulation of respiratory, cardiac and gastrointestinal systems, whereas cognitive symptoms include fears of dying, losing one's mind or fainting.

2.4.3 Agoraphobia

Agoraphobia is derived from the Greek word "agora", meaning "out door market place". In its severest form, agoraphobia is characterized by a paralyzing terror of being in places or situations from which the patient feels there is neither escape nor accessible help in case of an attack. Consequently there is avoidance or anxiety related to open places which are unrelated to, and are unaccompanied by panic disorders.

2.4.4 Panic Disorder with Agoraphobia

Patients with panic disorder may also suffer from agoraphobia, or marked distress arising from being in places or situations which might trigger a panic attack, or in which assistance or escape might be difficult.

2.4.5 Specific Phobia

Claustrophobia (small spaces), acrophobia (height) and arachnophobia (spiders) all belong to this class. This is unreasonable fear or anxiety associated with exposure to specific objects or situations. Phobic situations are avoided, or else endured with intense anxiety or distress, significantly affecting individual daily routine or social and occupational functioning.

2.4.6 Social Phobia

Social phobia describes, acute anxiety response during social situations, which is marked by fear of being the focus of attention or related to concerns that one will be scrutinized or humiliated by others or fear of behaving in a way that will be embarrassing or humiliating. Although patients realize their fears are unreasonable, there is marked avoidance of phobic situations.

2.4.7 Obsessive Compulsive Disorders (OCD)

Either obsessions (thoughts, impulses of images) or compulsions (ritualized behaviours or mental acts) or both are experienced by such individual. Though they are aware that they are inappropriate and unreasonable, compulsions are performed in an attempt to reduce anxiety associated with obsessions.

Obsessive compulsive disorders are usually time consuming and cause distress or interfere with the subjects' social or individual functioning.

2.4.8 Post Traumatic Stress Disorder (PTSD)

This is severe, persistent emotional reaction which occurs when an individual is exposed to a traumatic / stressful event or situation of exceptionally threatening or catastrophic nature in which the individuals' response was intense fear, helplessness or horror.

Associated symptoms include re-experiencing (re-experiencing traumatic events in recurrent images, thoughts, flashback, dreams, or feeling distressed at reminders of traumatic events), avoidance (avoids thoughts, people or factors that trigger recollection of traumatic events), increased arousal or physiological sensitivity (insomnia, irritability, hypervigilance, easily startles) and inability to recall either partially or completely some important aspects of exposure to stressor. Symptoms are chronic lasting more than four weeks.

2.4.9 Anxiety Disorder Due to General Medical Condition

When there is evidence that anxiety symptoms e.g. obsessions, compulsions or panic attacks, are the direct physiological consequences of a general medical condition, a diagnosis of anxiety disorders due to general medical condition is made.

2.4.10 Substance Induced Anxiety Disorder

Anxiety symptoms arising from prescribed or "recreational" drug use or withdrawal from them, characterize this anxiety disorder. Medication use should be etiologically related to disturbances and symptoms should develop during or within one month of substance intoxication or withdrawal.

2.4.11 Mixed Anxiety Depressive Disorders

There are so many possible combinations of comparatively mild symptoms for these disorders that specific criteria are not given, other than those already in the diagnostic guidelines.

2.4.12 Separation Anxiety Disorder

Separation anxiety disorder occurs predominately in children, usually as a result of separation from important family members or home. It is associated with distress (from either anticipating or actually being away from home or loved ones) and extreme or intense worry (about possible harm befalling a loved one or getting lost or being kidnapped).

2.4.13 Acute Stress Disorder

Acute stress disorder is a syndrome, in which symptoms of PTSD occur within two days to four weeks of the traumatic event. Immediate symptoms include, numbing, reduction in awareness of surroundings, derealization, depersonalization and dissociative amnesia.

2.5 DIAGNOSIS OF ANXIETY DISORDERS

Diagnosis of anxiety disorders is reached after careful physical examination and proper medical and personal history is taken. Care should be taken to rule out conditions that accompany, resemble or may mask anxiety disorders e.g. depression, heart problems (in which chest pain resemble panic attack), asthma, hyperthyroidism, epilepsy etc.

Family history of anxiety or depressive disorders, associated risk factors (stressful events), basic lifestyle information (e.g. drug use, excessive alcohol intake), are also very important as they may contribute or result from anxiety disorders.

2.6 TREATMENT OF ANXIETY DISORDERS

2.6.1 Pharmacotherapy

Tricyclic Anti Depressants (TCAD)

Referred to as tricyclics due to their structure, (three cycles) drugs in this class include; amitriptylline, impramine, clomipramine, doxepin etc.

These drugs are inhibitors of neuronal reuptake of both serotonin and noradrenaline. Clomipramine shows selectivity against serotonin. These with secondary amine side chains or N-demethylated metabolites (nor) of agents with tertiary amine moieties, are relatively selective inhibitors of noradrenaline examples include amoxapine, maproptilline, and nortriptylline. The observation that the TCAD, impramine had a different anxiolytic profile from diazepam helped to differentiate panic disorder from GAD and subsequently social phobia.

Studies have shown TCAD to be effective in the treatment of GAD, Panic disorders and OCD (Casacalenda & Boulenger, 1998). Better safety and tolerability profiles are reasons why current practice guidelines recommend Selective Serotonin Reuptake Inhibitors (SSRl) as first line drugs for the management of anxiety disorders. (March, *et al*., 1997; APA, 1998).

Pharmacology

In addition to their effects on amine uptake, most TCAD affect one or more neurotransmitter receptor, including muscarinic Acetylcholine (ACh) receptors, histamine receptors and serotonin receptors. In non-depressed human subjects, TCAD cause sedation, confusion and motor in-coordination. These effects occur also in depressed patients in the first few days of treatment, but tend to wear off in 1-2 weeks as antidepressant effects develop.

Pharmacokinetic aspects

TCAD are all rapidly absorbed when given orally and bind strongly to plasma albumin, most being 90-95% bound at therapeutic plasma concentrations. They bind to extra vascular tissue, which account for their generally large distribution volumes (usually 10-50 L/Kg) and low rates of elimination. This extra vascular sequestration means that extracorporeal dialysis is rather ineffective in acute over dosage. TCAD are metabolized in the liver by two main routes namely N-demethylation, whereby tertiary amines are converted to secondary amines (e.g. Imipramine → desmethylimipramine; amitriptyline → nortriptyline) and ring hydroxylation. Both the desmethyl and the hydroxylated metabolites commonly retain biological activity. During prolonged treatment with TCA, the plasma concentration of these metabolites is usually comparable to that of parent drug, though there is wide variation between individuals. Inactivation of the drug occurs by glucoronide conjugation of the hydroxylated metabolites, the glucoronides being excreted in the urine.

The overall half-times for elimination of TCA are generally long, ranging from 10-20 hours for imipramine and desipramine to about 80 hours for protriptyline. They are even longer in older patients. Thus, gradual accumulation is possible, leading to slowly-developing side effects.

Side effects

Include atropine like effects, postural hypotension, and sedation. Arrhythmias, heart block, convulsions, hepatic and hematological reactions are some of the side effects experienced with TCAD use. Others are drowsiness, dry mouth, blurred vision, constipation, urinary retention (all of which are associated with its antimuscarinic activity) sweating. Syncope has also been reported in elderly patients.

Selective Serotonin Reuptake Inhibitors (SSRI)

This class includes drugs like paroxetine, citaprolam, fluoxetine, fluvoxamine, sertraline and venlafaxine. They inhibit active reuptake of 5-HT into nerve terminals. Others including bupropion, nefazodone and mirtazapine have less well defined neuropsychopharmacology and can be considered “atypical”.

Relative safety and tolerability have led to their rapid acceptance. A substantial body of data exist showing that SSRI are effective in the management of several anxiety disorders in both adults and children as well as comorbid anxiety depressive disorders (Birmaher *et al*., 1994; Pallock, 1996; Van-Ameringen *et al*., 1999; Hacket, 2000; Figgit & McClellan,

2000; Cheer & Figgitt, 2002; Ryan *et al.*, 2001; Marshall *et al.*, 2001 and Williams & Miller, 2003).

Full therapeutic effects are reached slower than with Benzodiazepines (Kesely, 2000). On initiation, nausea, worsening of anxiety, jitteriness, and insomnia frequently occur. Clinical implications of this are that they are initiated at much lower doses than in depression and slowly triturated upwards. An alternative strategy is to co-administer benzodiazepines to prevent dropout from therapy due to either worsening anxiety or side effects.

Pharmacology

The SSRIs selectively and powerfully inhibit serotonin reuptake and result in a potentiation of serotonergic neurotransmission. The property of potent serotonin reuptake appears to give a broad spectrum of therapeutic activity in depression, anxiety, obsessional and impulse control disorders. However, despite the sharing of the same principal mechanism of action, SSRIs are structurally diverse with clear variations in their pharmacodynamic and pharmacokinetic profiles. The potency for serotonin reuptake inhibition varies amongst this group, as does the selectivity for serotonin relative to noradrenaline and dopamine reuptake inhibition. Citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline, are potent 5-HT reuptake inhibitors, and the demethyl metabolites, norfluoxetine, demethylsertraline, and demethylcitalopram, also show selectivity. Paroxetine and sertraline are the most potent inhibitors of 5-HT reuptake, whereas citalopram is the most selective. Fluoxetine is the least selective and the

metabolite of fluoxetine, norfluoxetine, is a more selective and more potent 5-HT reuptake inhibitor than the parent compound. The relative potency of sertraline for dopamine reuptake inhibition differentiates it pharmacologically from other SSRIs. Affinity for neuroreceptors, such as sigma1, muscarinic and 5-HT2c, also differs widely. Furthermore, the inhibition of nitric oxide synthetase by paroxetine, and possibly other SSRIs, may have significant pharmacodynamic effects. Citalopram and fluoxetine are racemic mixtures of different chiral forms that possess varying pharmacokinetic and pharmacological profiles.

Pharmacokinetic aspects

They are well absorbed after oral administration with mean peak plasma concentration occurring between 6 to 8 hours post-dose. Food appears to affect systemic availability variably. There are important clinical differences among the SSRIs in their pharmacokinetic characteristics. These include differences in their half-lives, linear versus non-linear pharmacokinetics, effect of age on their clearance and their potential to inhibit drug metabolising cytochrome P450 (CYP) isoenzymes. These pharmacological and pharmacokinetic differences underly the increasingly apparent important clinical differences amongst the SSRIs. The metabolite of fluoxetine, norfluoxetine, is a more selective and more potent 5-HT reuptake inhibitor than the parent compound and has an extremely long half-life (7-15 compared to 1-3 days). Thus the metabolite plays an important role for the therapeutic effect of fluoxetine. Fluoxetine is also a 5-HT2C receptor antagonist. Demethylsertraline is a weaker and less selective 5-HT reuptake inhibitor in vitro than sertraline, but demethylsertraline has a very long half-life (62-104

hr) compared to the parent compound (24 hr) and it might play a role in the therapeutic effects of sertraline. Demethylcitalopram has about a 10 times lower 5-HT reuptake inhibitory potency in vitro than citalopram, and the elimination half-lives are approximately 1.5 and 2 days, respectively.

The primary route of elimination appears to be hepatic metabolism to inactive metabolites excreted by the kidney. Approximately 98% of sertraline and 94% of fluoxetine is plasma protein bound.

Side effects

Side effects of SSRIs include headaches, restlessness, insomnia, palpitations, tremor, confusion, hypotension and hypomania or mania. Others are drowsiness, dizziness, gastrointestinal side effects (e.g. nausea, vomiting, dyspepsia, diarrhea, and constipation), convulsions, fever, sexual dysfunction, sweating, movement disorders, dyskinesia, etc.

Benzodiazepines

Benzodiazepines exert their therapeutic effects by interacting with inhibitory neurotransmitter receptors directly activated by GABA. Benzodiazepines act at $GABA_A$ but not $GABA_B$ receptors, by binding directly to specific sites that are distinct from those of GABA binding on receptor / ion channel complex. Benzodiazepines do not directly activate $GABA_A$ receptor but require GABA to express their effects: i.e. they only modulate the effect of GABA (enhance inhibitory neurotransmitter systems).

Benzodiazepines represent a relatively safe group of medications with rapid, profound anti anxiety and sedative hypnotic effect (Lemonie *et al*., 1996). Alprazolam and larozepam have shorter elimination half lives, while diazepam and clonazepam have longer period of action.

Benzodiazepines have been found to effectively reduce anxiety in patients with GAD, panic disorder and social anxiety disorder (Cutler, *et al*., 1993; Klein *et al*., 1994 and Davidson, 2004). However benzodiazepine use is limited due to risks associated with their use and these include: tolerance, dependency and withdrawal symptoms, intense rebound anxiety, drowsiness, confusion, muscle weakness, and psychomotor impairment (Bradwejn, 1993; Klein, *et al*., 1994 and Mandos *et al.*, 1995).

Rickels *et al*. (2000), suggest benzodiazepine discontinuation could be facilitated significantly by co-prescribing impramine before and during the benzodiazepine taper in patients with GAD.

Pharmacology

The most important effects are on the central nervous system and consist of:

1. Reduction of anxiety and aggression
2. Sedation and induction of sleep
3. Reduction of muscle tone and coordination.
4. Anticonvulsant effect.

Pharmacokinetic aspects

Benzodiazepines are all completely absorbed when given orally, usually given a peak plasma concentration in about 1 hour. Some (e.g. Oxazepam, Lorazepam) are absorbed more slowly. They bind strongly to plasma proteins, but their high lipid solubility causes many of them to accumulate gradually in body fat. These two factors result in distribution volumes not far from 1 liter/ Kg body weight for most drugs. They are normally given by mouth, but can be given intravenously (e.g. diazepam in status epilepticus). Intramuscular injection often results slow absorption.

Benzodiazepines are all inactivated by metabolic processes, and are eventually excreted as glucoronide conjugates in the urine. They vary greatly in duration of action, and can be roughly divided into short and long-acting compounds. The distinction between these two categories depends on weather or not the drug forms a long-lasting pharmacologically active metabolite, such as N-desmethyldiazepam (nordiazepam). The half-life of this compound, which lies in the metabolic pathway of many of the benzodiazepines, is about 60 hours, and this accounts for the tendency of many benzodiazepines to produce cumulative effects and long hangovers when they are given at regular intervals. The short-acting compounds are those that are metabolized directly by conjugation with glucoronide. Advancing age affects the rate of oxidative reactions more than that of conjugation reactions. Thus the effect of long-acting benzodiazepines, which may be used regularly as hypnotics or anxiolytic agents for many years, tends to increase with age, and it is common for drowsiness and confusion to develop insidiously for this reason.

Adverse effects

1. Toxic effects resulting from acute over dosage, which is to cause prolonged sleep without serious depression of respiratory or cardiovascular system.
2. Unwanted effects occurring during normal therapeutic use which include drowsiness, confusion and impaired motor cordination.
3. Tolerance and dependence.

Azapirones (Buspirone)

This class of agents has shown beneficial effects in disorders marked by anxiety or dysphoria of moderate intensity. Their action is probably mediated through their selective affinity for serotonin receptors of the 5-HT_{1A} type, for which they appear to be partial agonists. Buspirone and ipsapirone are examples of drugs in this class.

Azapirones have proven anxiolytic properties, without concurrent hypnotic, anticonvulsant and muscle relaxant properties (Schneirer *et al*., 1993 and Cutler *et al*., 1994). They are less likely to impair psychomotor and cognitive performance. They also do not cause dependence, abuse or rebound anxiety (Faludi, 1994 and Delle-Chiaie *et al*., 1995).

Pharmacology

Buspirone is a psychotropic drug with anxiolytic properties which belongs chemically to the class of compounds known as the azaspirodecanediones. Buspirone shares some of the properties of the benzodiazepines and the neuroleptics, as well as demonstrating other pharmacological action. It attenuates punishment suppressed behavior in animals and

exerts a taming effect, but is devoid of anticonvulsant and muscle relaxant properties and does not bind to the benzodiazepine/GABA receptor complex. Buspirone affects a variety of dopamine mediated biochemical and behavioral events, but is free of cataleptic activity. Buspirone has an affinity for brain D(2)-dopamine receptors, where it acts as an antagonist and agonist, and for the 5-HT(1A) receptors, where it acts as an agonist. Buspirone does not block the neuronal reuptake of monoamines and, on chronic administration, it does not lead to changes in receptor density in the models investigated. However, the mechanism of action of buspirone remains to be fully elucidated.

Pharmacokinetic aspects

Buspirone is rapidly absorbed in man and undergoes extensive first pass metabolism. Following oral administration, low peak plasma levels of unchanged drug, of 1 to 6 ng/mL were observed 40 to 90 minutes after a single 20 mg dose. In a number of studies performed in healthy volunteers, the mean half-life of buspirone ranged from 2 to 3 hours up to approximately 11 hours with considerable variation in individual values. Multiple dose studies suggest that steady state plasma levels were usually achieved within a few days. Buspirone is metabolized primarily by oxidation, producing several hydroxylated derivatives and a pharmacologically active metabolite, 1-pyrimidinylpiperazine (1-PP). Peak plasma levels of 1-PP have been found to be higher than those of its parent drug and its half-life to be approximately double that of unchanged buspirone. In a single dose study using (14)C labeled buspirone, 29 to 63% of the dose was excreted in the urine within 24 hours, primarily as metabolites, while fecal excretion accounted for 18 to 38% of the dose. In man, approximately 95% of buspirone is plasma protein bound, but other

highly bound drugs, e.g. phenytoin, propranolol and warfarin, are not displaced by buspirone from plasma protein in vitro. However, in vitro binding studies show that buspirone does displace digoxin. The effect of food upon the bioavailability of buspirone was studied in 8 subjects. The area under the plasma concentration curve (AUC) and peak plasma concentration (C(max)) of unchanged buspirone increased by 84% and 116% respectively when the drug was administered with food, but the total amount of buspirone immunoreactive material did not change. The significance of this finding is not known, but it could indicate that food may decrease the presystemic clearance of buspirone. Buspirone had no effect on hepatic microsomal enzyme activity when administered to rats for 5 days. In man, the effect of buspirone on drug metabolism or concomitant drug disposition has not been studied.

After single or multiple doses in adults, no significant differences in buspirone pharmacokinetics (AUC and Cmax) were observed between elderly and younger subjects or between men and women. After multiple-dose administration of buspirone to patients with hepatic impairment, steady-state AUC of buspirone increased 13-fold compared with healthy subjects. Four fold increase in steady-state AUC was also observed in subjects with renal impairments. The effects of race on the pharmacokinetics of buspirone have not been studied.

Side effects

Side effects experienced with drug use include; nausea, dizziness, headaches, nervousness, lightheadedness, excitement, rarely tachycardia, palpitations, chest pain, confusion, dryness of mouth, fatigue and sweating.

Monoamine Oxidase Inhibitors (MAOI)

Monoamine Oxidase (MAO), a flavin containing enzyme, regulates metabolic degradation of catecholamine and serotonin in the CNS and peripheral tissues. There are two molecular species of MAO; types A and B. Type A prefers serotonin as substrate and is selectively inhibited by clogyline. Type B prefers phenylethylamine as substrate and is inhibited by selegilline. Both types are found in the liver and brain of most species. Except for selegilline (in low doses), clinically employed MAOI inhibit both MAO-A and B. Drugs in this class include meclobemide and phenelzine.

They are seldom used unless simpler medications strategies have failed, although significant anti-obsession, anti-panic and anti-social anxiety disorder activities have been demonstrated (Sheehan *et al*., 1980; APA, 1998 and Stein *et al*., 2002). Significant drug and dietary interactions are also reasons why they are not prescribed frequently.

Pharmacology

MAOI causes a rapid and sustained increase in the serotonin, noradrenaline and dopamine content of the brain, serotonin being affected most and dopamine least. Similar

changes occur in peripheral tissues such as heart, liver and intestine, and increases in the plasma concentrations of these amines are also detectable. Although these increases in tissue amine content are largely due to accumulation within neurons, transmitter release in response to nerve activity is not increased. In contrast to the effect to TCA, MAOI do not increase the response of peripheral organs, such as heart and blood vessels, to sympathetic nerve simulation. The main effect of MAOI is to increase cytoplasmic concentrations of monoamines in nerve terminals, without greatly affecting the vesicular stores which form the pool that is releasable by nerve stimulation.

In normal human subjects, MAOI causes an immediate increase in motor activity, and euphoria and excitement develop over the course of a few days. This is in contrast to TCAD which cause only sedation and confusion when given to non-depressed subjects. The effects of MAOI on amine metabolism develop rapidly, and the effect of a single dose last for several days.

Adverse effects

Many of the unwanted effects of MAOI result directly from MAO inhibition, but some are produced by other mechanisms. These effects include hypotension, these occurring from excessive central stimulation (tremors, excitement, insomnia) weight gain, atropine like side effects (dry mouth, blurred vision, urinary retention) etc.

2.6.2 Other drugs used in the treatment of anxiety disorders:

Alpidem

Alpidem an imidazole pyridine has been shown to possess, useful anxiolytic properties, but hepatic toxicity has prompted its discontinuation (Frattola *et al*., 1994).

Abecarnil

Abecarnil (β-carboline), a partial agonist, is selective for particular benzodiazepine receptor. It has early onset of action (l week) (Aufdembrinke, 1998), it is safe, effective and it is useful for short term treatment of GAD without significant rebound effect (Pollack *et al*., 1997).

Beta-blockers

Drugs in this class include propranalol and atenolol. They reduce autonomic symptoms (physiological symptoms only) associated with specific situational or social phobias (performance anxiety), but do not appear to be effective in GAD or panic disorders (Gleiter and Deckert, 1996).

Anti-adrenergic Agents

Clonidine is a member of this class, and they modify autonomic expression of anxiety disorders e.g. relaxation of blood vessels. They have been used to treat children with PTSD. Experts believe they should only be used when other therapies have failed.

Atypical Antipsychotic Agents

Agents in this class include; risperidone, olnazepine, quetiapine and ziprasidone etc. They may be useful in certain severe cases of OCD and GAD when patients do not respond to conventional therapies. Side effects experienced with drug use include sleepiness, dizziness, extra pyramidal symptoms, weight gain etc.

Kava-Kava

Alternative medicines research show *kava kava* extract may reduce anxiety in patients, however, caution should be taken as such medicines are not regulated and quality is not publicly controlled (Boerner, 2001).

2.6.3 Psychotherapy

The influence of anxiety on a persons emotional response is mediated by psychological– factors, (prior leaning in an individual's past is implicated in current distress, behavior or attitudes, and beliefs that a persons hold about themselves and the world), as well as genetic and biological factors. Cognitive behavioral therapy (CBT) is one intervention for which there is evidence of efficacy in management of anxiety disorder such as OCD, GAD, PTSD, phobias and panic disorder (Hunsley, 2002).

Cognitive Behavioral Therapy (CBT)

CBT teaches patients to react differently to situations and bodily sensations that trigger attacks and other anxiety symptoms. Cognitive techniques focus on identifying and changing irrational, faulty thinking and assumptions which lead to emotional distress and

replacing these thought patterns with ones which are more realistic and adaptive. Patients learn to understand how their thinking patterns contribute to their symptoms and how to change their thoughts so that symptoms are less likely to occur. This awareness of thinking patterns is combined with exposure and other behavioral techniques to help people confront their feared situations. Behavioral interventions focus on changing emotional distress and disturbed behavior, by directly altering behavior, for example use of reinforcement and exposure. For example, some one who becomes lightheaded during a panic attack and fears he is going to die can be helped with the following approach used in CBT. The therapist asks him to spin in a circle until he becomes dizzy. When he becomes alarmed and starts thinking, "I'm going to die," he learns to replace that thought with a more appropriate one, such as "It's just a little dizziness, I can handle it." CBT is employed either as individual or group oriented therapy.

Behavioural Therapy

Behavioural therapy focuses on changing specific actions and uses several techniques to decrease or stop unwanted behaviour. An example is diaphragmatic breathing, a special breathing exercise involving slow, deep breathe to reduce anxiety. This is necessary because people who are anxious often hyperventilate; taking rapid shallow breaths that can trigger rapid heartbeat, light headedness, and other symptoms. Another technique, exposure therapy, gradually exposes patients to what frightens them and helps them cope with their fears.

2.6.4 Combining Pharmacotherapy and Psychotherapy

Multimodal therapy may not exactly be cost effective and the benefits of multimodal therapy are not yet clear and further studies are required. CBT has the advantage of lesser risk of relapse at cessation of therapy (Mental Health: A Report of Surgeon General, 2001)

2.6.5 Treatment of Anxiety Disorders in Pregnancy

Managing anxiety disorders in pregnancy is challenging. The implication and or effects of medication on fetus and implication and or effects of untreated anxiety on mother have to be carefully balanced. McGrath *et al*. (1999) suggest that non pharmacological treatment such as CBT be employed, and if the use of medication is unavoidable, the highest dose for the minimum amount of time be prescribed.

2.6.6 Contraindications

Symptoms consistent with serotonin-syndrome have been observed when buspirone and fluoxetine are administered concurrently (Manos, 2000). Fatal reactions may also occur when SSRI and MAOI are administered concurrently. There should be at least 2–5 weeks break when switching from one drug to the other.

2.7 COMORBIDITY

Comorbidities includes co-occurrence (in the same individual) of two or more physical diseases (e.g. heart disease and diabetes) which are defined in terms of their underlying cause (e.g. pathophysiological process or a micro organism) or which are defined in terms of their characteristic symptoms, rather than underlying cause (e.g. depression and alcohol dependence).

Simultaneous interaction of two or more comorbid conditions is particularly challenging for the following reasons; detection, exploring, understanding and treatment of such comorbid disorders (Siegfried, 1998 and Kavanagh, 2000).

Comorbid disorders may be heterotypic; i.e. between different classes of mental disorders (Anglod *et al*., 1999), or homotypic; i.e. between different members of a general class of mental disorders (e.g. between phobia and generalized anxiety disorders). They may also be 'concurrent' in which two or more disorders are present at the same time (e.g. schizophrenia and alcohol dependence) or 'successive' in which disorders may occur at different times in a person's life, in ways that may or may not be casually related to each other. A number of possible explanations for co-occurrence of disorders have been suggested:

- Caron and Rutter (1999) suggested that comorbidity may be artefactual. This is because supposedly separate mental disorders may not be as separate as they seem. This explanation is most plausible for homotypic comorbid disorders.

Kessler suggested these hypotheses to explain non artefactual comorbid disorders (Kessler, 1995):

- Mental disorders may directly produce other mental disorders e.g. drug induced psychosis.
- The presence of one disorder may indirectly increase the risk of developing another e.g. persons with anxiety and affective disorders may begin to use alcohol and other drugs in an effort to medicate their distress.
- Comorbidities may arise from common causes e.g. the syndrome of delinquency, alcohol and drug abuse, precocious sexual activity and poor school performance may, for example be manifestations of common genetic predisposition and family circumstances all of which increase the chance of developing alcohol and drug dependence disorders as well as antisocial personality disorder (Jessor and Jessor, 1997).

For the purpose of this study Comorbidities are conditions that exist at the same time as the primary condition in the same patient. This definition was adopted from National Centre for Health Statistics. A number of reasons why studying comorbid disorders is important include:

Firstly, comorbidity is the rule rather than the exception with mental disorders, as is clear from studies in number of countries including Australia (Merikangas *et al.*, 1998 and Andrews *et al.*, 1990).

Secondly, if comorbidity is not taken into account when studying individual mental disorders, characteristic of the disorder under study may be mistaken for those that are due to an ignored comorbid condition (Kessler, 1995).

Thirdly, understanding why different disorders co-occur may provide important opportunities for prevention. For example, if we can identify people with symptoms of anxiety and affective disorders we could intervene to reduce self-medicating with alcohol and other drugs.

Fourthly, persons with comorbid mental disorder often have a poor treatment response and a worse course of illness over time (Kessler, 1995). They are more impaired, suffer greater social disability and generate larger social cost. This is probably in part, because comorbid disorders are not diagnosed and treated, and in part because, persons with more than one mental disorder have poorer outcomes than those who have a single disorder. This has been well demonstrated in schizophrenia (Drake *et al*., 1996) and is also the case in depression and anxiety (Kranzler e*t al.,* 1996). For example, the treatments of comorbid alcohol dependence and depression tend to be less effective when conducted in the presence of the other disorder, than when the comorbidity is absent.

Fifthly, comorbidity has important implications for treatment, for example, in persons for whom alcohol dependence is a cause of depression; treatment of alcohol dependence may alleviate or eliminate depressive symptoms (Schuckit *et al.,* 1997a; 1997b). Conversely, if alcohol dependence arises from self-medication of depression, the treatment of

depression may reduce symptoms of alcohol dependence whereas the treatment of alcohol problems may not affect symptoms of depression.

Sixthly, even when there is no casual relationship between alcohol dependence and an affective disorder, having one disorder may worsen the symptoms and course of the other. For example, depressive symptoms may increase alcohol consumption and alcohol-related harm in persons who are vulnerable to developing alcohol disorders. It may also impair compliance with treatment of alcohol dependence.

2.8 PHARMACOECONOMICS

Though a relatively new field a comprehensive review of pharmacoeconomic literature has been provided by Smith (1998), department of vaccines and biologicals (2001), National Medicines Information Centre (2002) and Wally (2004), and is summarized below.

Pharmacoeconomics is a social science concerned with impact of pharmaceutical products and services on individuals, health systems and societies, as well as description and analysis of cost. The goals of pharmacoeconomics analysis include;

- Providing information on which health care alternative provides the best health care outcome per unit currency spent.
- Improving allocation of resources for pharmaceutical products and services.

The control of health expenditure is a very important aspect of health policy. pharmacoeconomic studies (which are concerned with identification and estimation of overall cost of a particular disease on a defined population as well as provide economic estimates that can be used by policy makers and administrators to guide their resource allocation decisions) are indispensable tools for determining the economic impact of disease, and for assigning resources (material and human), required for prevention, diagnosis, and treatment of patients with different diseases. This involves computation of direct and indirect costs attributable to a specific disease.

Pharmacoeconomics considers all cost that stems from an illness or condition, in other words the value of resources used and value of resources lost, in general terms this requires consideration of both direct cost and indirect cost. Pharmacoeconomics employs either cost of illness or a number of cost outcome analyses as detailed below:

2.8.1 Cost Analysis

Cost analysis considers cost of providing health care products and services; an example is the cost of illness study. It does not take into consideration outcomes experienced by patients or providers.

2.8.2 Cost Outcome Analysis

Cost and outcomes are considered. The most commonly used are;

I) **Cost effectiveness studies**; For a specific disease condition, this analysis compares two or more treatment options. Outcomes which are valued in non

monetary terms (e.g. number of life years saved, glucose lowering) are compared to treatment cost.

II) **Cost minimization studies**: Here outcomes have been determined or are considered to be the same; hence treatment option which minimizes cost can be determined.

III) **Cost benefit analysis**: Compares cost and outcomes of treatment options (outcomes are expressed in monetary terms). This has advantage as it can be used to compare across a wide range of options.

III) **Cost utility analysis**: This method has the advantage of being able to compare therapies from different disease states because the outcome measure is quality adjusted life years saved i.e. it integrates both cost and consequences of therapy into its comparison.

2.8.3 Direct cost

These are resources spent as a result of treatment of disease and they include; pharmaceutical drugs, medical devices, physicians visit, emergency room visits, diagnostic testing services, education, and research. In some other cases, direct cost may also include elements such as: transport cost in other to receive treatment, lost productivity cost due treatment, time cost associated with waiting for treatment etc.

Direct cost can also be viewed as;

I) Medical Direct Cost (within the health care sector); work time of medical personnel, cost of drugs, cost of hospitalization, administrative cost etc.

ii) Non Medical Direct Cost (outside the health care sector); transport cost / cost to receive treatment, special diet cost etc.

2.8.4 Indirect cost

These are resources lost as a result of treating the disease and they include; lost school days, lost work days, lost productivity, travel time, waiting time, etc. Underemployment or unemployment which results from disease condition itself, and from possible early disability and death due to condition is also considered here.

Indirect cost can also be viewed as:

i) Medical Indirect Cost (within the health care sector); medical cost which arise during life years that have been saved.

ii) Non Medical Indirect Cost (outside the health care sector); loss productivity (lost work, unemployment etc).

2.8.5 Intangible Cost

Examples include pain, suffering, etc. which understandably are difficult to measure.

2.9 PROBLEMS ASSOCIATED WITH MANAGEMENT

Recognizing and managing mental illnesses may be difficult during brief consultations in busy primary health care clinics. Other elements identified to affect detection and management include: practitioner characteristics (skills, attitudes, knowledge, interviewing style etc), and patient characteristics (limited disclosure of distress, preferences for describing physical symptoms, negative attitudes towards acknowledging

emotional distress, denial of problems especially in relation to substance use, rates of recognition are lower when disorder is more chronic or less obvious) (Bushnell *et al.*, 1998).

2.10 PROJECT AIM AND OBJECTIVES

The aim of the current study was to evaluate the management of anxiety disorders at psychiatric unit of Ahmadu Bello University Teaching Hospital Kaduna, Nigeria, with the following specific objectives:

i. To ascertain relative occurrence of anxiety disorders vis-à-vis other psychiatric disorders, as well as relative occurrence of its subtypes in the patient population of this hospital.

ii. To document features of anxiety disorders and existing comorbid disorders as seen in the teaching hospital.

iii. To evaluate the pharmacological management of anxiety disorders, rationale for drug used, handling of side effects, drug interactions and treatment outcomes.

iv. To assess the role of non pharmacological strategies in management of anxiety disorders and attempt to evaluate cost associated with treatment.

CHAPTER THREE

METHODS

3.1 METHODOLOGY

The study was a retrospective one. It involved analysis of data obtained from patient folders who attended clinic regularly at the psychiatry unit of Ahmadu Bello University Teaching Hospital (ABUTH) located at Kaduna for the period spanning 1st January, 2003 to 31st December, 2004.

The first stage of data collection involved use of attendance registers from the records department of the psychiatric unit. A total of 13,417 attendances were recorded by 2,780 patients in 196 clinics held within the two year period. Folder selection criteria entailed that the patient attended clinic regularly (from discussions with psychiatrist involved in patient care this was set at three times a year, this is because stable patients were given clinic appointments every 12 weeks). Only folders of patients who met the entry criteria (n=875) were selected for the next stage of study i.e. minimum of six times within the two year under study.

Socio demographic data, which included; sex, marital status, date of first contact with orthodox facility, age at first contact with orthodox facility, geopolitical zone, state of origin, ethnicity, place of origin, occupation, next of kin, place of residence, and specific diagnosis were then collected from folders. Based on specific diagnosis, patients were further grouped into categories, and only folders of patients diagnosed as having anxiety disorders (n=61) were selected for the next stage of the study.

A researcher designed data form was then used to guide the collection of data on medical history, drug and non drug management, side effects and their management, laboratory investigations carried out etc.

Cost of treatment was calculated using drug records, lab investigations and data on hospitalizations as well as hospital and community pharmacy cost.

Data's obtained were subjected to analysis using statistical package for social scientists (SPSS version 11) and appropriate statistical tools such as student's t-Test, chi square test, one way analysis of variance, and regression analysis.

CHAPTER FOUR

RESULTS

4.1 Introduction

This chapter presents the findings of this study. The study population (875) consisted of all mental disorder patients who used this facility regularly (i.e. visited the psychiatry clinic six times or more) within the period under study (i.e. January 1st, 2003 to December 31st, 2004). A total of 61 data forms were used to collect relevant data from folders of patients suffering from various anxiety disorders and this represented the study population for anxiety disorder patients.

4.2 Summary of Data on Clinic Attendances for patients Visiting ABUTH Psychiatry Clinic from 1st January, 2003 to 31st December, 2004

Analysis of attendances show that with increased number of attendance, there was a decrease in number of patient folders e.g. patients who had attended clinic once within the study period were 1,096, twice were 290 etc. Only folders of patients who had attended clinic six times or more (875) were considered for this study.

Table 4.1 **Summary of Clinic Attendances for Patients Visiting ABUTH Psychiatry Clinic from 1st January, 2003 to 31st December, 2003**

Month	Number of Clinics	Clinic Attendance	Average Attendance Per Clinic
January	9	495	55
February	8	450	56
March	9	508	56
April	7	385	55
May	8	457	57
June	9	507	56
July	9	568	63
August	8	551	69
September	9	710	79
October	9	682	76
November	7	579	83
December	8	568	71
Totals	100	6460	65

Table 4.2 **Summary of Clinic Attendances for Patients Visiting ABUTH Psychiatry Clinic from 1st January, 2004 to 31st December, 2004**

Month	Number of Clinics	Clinic Attendance	Average Attendance Per Clinic
January	8	559	70
February	7	567	81
March	9	702	78
April	8	666	83
May	9	667	74
June	8	543	68
July	9	679	75
August	9	635	71
September	9	768	85
October	6	410	68
November	8	552	69
December	6	209	35
Totals	96	6957	73

From tables 4.1 and 4.2 a total of 13,417 attendances were recorded by 2,780 patients during the 196 clinics held between 1st January, 2003 and 31st December, 2004. Therefore average number of clinics attended by each patient was 4.8 clinics and average attendance per clinic was 69.

Table 4.3 **Relative Prevalence of Mental and Neurological Disorders at ABUTH Kaduna in 2003 and 2004**

Category of Disorder	Number of Patients	Percent
Schizophrenia	355	46.6
Depression	104	13.7
Seizure disorders	92	12.1
Anxiety disorders	61	8.0
Bipolar affective disorder	57	7.5
Mania	27	3.5
Organic brain disorders	26	3.4
Substance use disorders	16	2.1
Somatization disorders	16	2.1
Dementia	2	0.3
Personality disorders	1	0.1
Mental retardation	1	0.1
Autistic disorder	1	0.1
Developmental disorders	1	0.1
Insomnia	1	0.1
Total	761	100.0

Some patients folders could not be located at the time of study (60) or patients diagnosis was not specified (54).

Schizophrenia, depression, and seizure disorders were more prevalent than anxiety disorders which occurred in 7.0% (using entire study population) or 8.0% (using those patients whose folders carried specific diagnosis).

4.3 FEATURES OF ANXIETY DISORDERS

Table 4.4 **Sex, Religion and Marital Status of Patients Suffering from Anxiety Disorders Visiting Psychiatry Unit of ABUTH in 2003 and 2004**

SEX	MARITAL STATUS	RELIGION			
		Christian	Islam	Not Recorded	Total
Male	Single	7	7		14
	Married	9	13		22
	Widowed	1			1
	Not Recorded			1	1
Total		17	20	1	38
Female	Single	1			1
	Married	6	15		21
	Separated	1			1
Total		8	15		23

There were more male anxiety disorder patients than female. The majority of the patients were Muslims and most were married.

Table 4.5 **Age Distribution at First Contact with Orthodox Facility for Patients Suffering from Anxiety Disorders Visiting Psychiatry Unit of ABUTH in 2003 and 2004**

	Number of Patients	Percent	Cumulative percent
10 – 19 Years	3	4.9	4.9
20 – 29 Years	16	26.2	31.1
30 – 39 Years	20	32.8	63.9
40 – 49 Years	13	21.3	85.2
50 – 59 Years	6	9.8	95.1
60 – 69 years	3	4.9	100.0
Total	61	100.0	

Note worthy is the absence of records for children under the age of ten. The predominant class was 30 to 39 years. Minimum and maximum ages were 14 and 66 years receptively. Calculated average age and standard deviation were 36.33 years and 11.65 years.

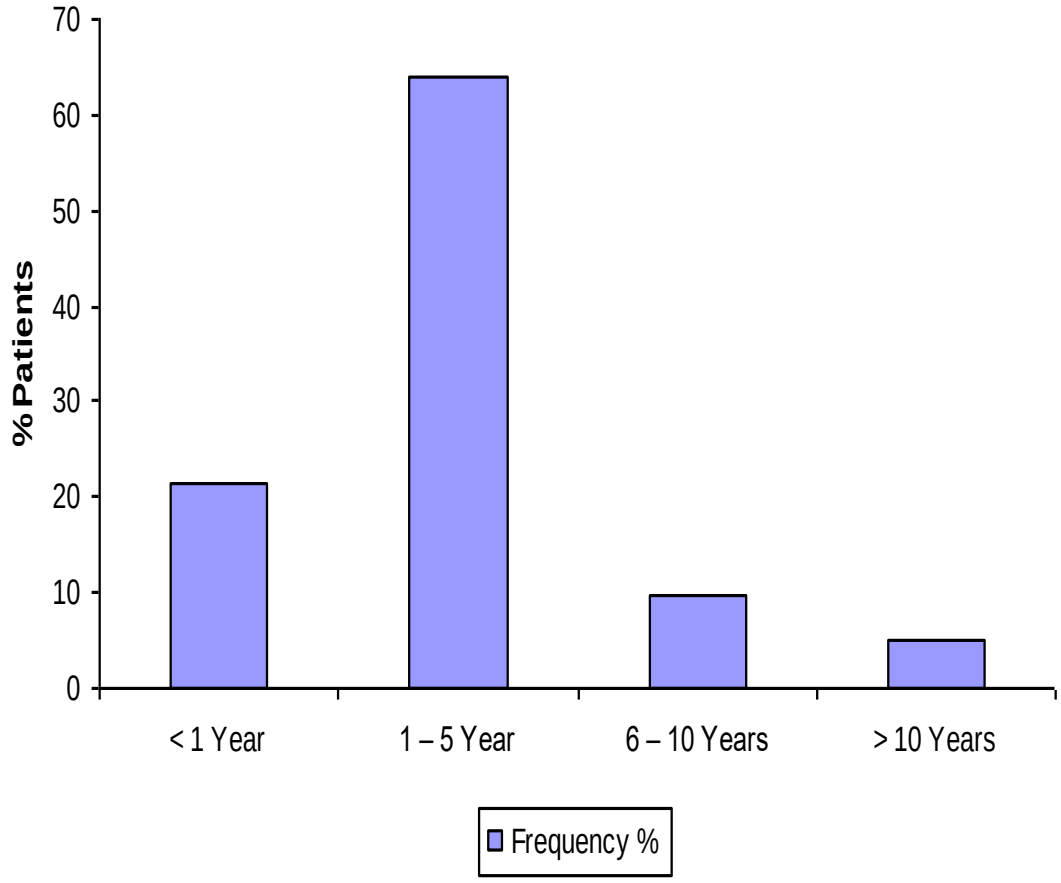

Fig. 4.1 **Years since First Contact with Orthodox Facility for Patients Suffering from Anxiety Disorders Visiting Psychiatry Unit of ABUTH in 2003 and 2004**

At first clinic visit most of the patients were in their twenties (26.2%) and thirties (32.8%). Majority (85.2%) had been attending clinic for 5 years or less (average 2.99 years).

4.31 Prevalence of Anxiety Disorders at ABUTH by Ethnicity / Tribe, State of Origin and Geopolitical Zones in 2003 and 2004

Data obtained from folders of patients suffering from anxiety disorders reveal that the prevalence of anxiety disorders cut across all geopolitical zones, 18 states of the country and several ethnic groups / tribes. Noteworthy ethnic groups / tribes include Hausa (34.4%), Fulani (9.8%), Yoruba (6.6%), Igbo (6.6%), and Jaba (4.9%). Other ethnic groups / tribes represented by this population include; Igala, Adara, Baju, Baomono, Bariza, Ebira, Gbagaji, Gbayi, Gwari, Idoma, Ishan, Kagoma, Kanuri, Kukuruku, Kuturmi, Magaro, Nupe, Tarok and Tiv.

Record for ethnicity / tribe was not available for six folders and one patient was a foreigner.

Further analysis show that significant proportion of patient population come from Kaduna (41.0%), Kogi (8.2%), Edo (4.9%), Kano (4.9%) and Niger states. Other states recorded include; Enugu, Katsina, Plateau, Anambra, Bauchi, Benue, Borno, Cross Rivers, Imo, Lagos, Nasarawa and Zamfara.

The North west (50.8%) and North central (19.7) geopolitical zones by implication were regions where sizeable proportion of this population came from.

Table 4.6 **Occupation of Patients Suffering from Anxiety Disorders Visiting ABUTH in 2003 and 2004**

Occupation	Number of Patients	**Percent**
House wife	9	**14.8**
Civil servant	8	**13.1**
Student	7	**11.5**
Unemployed	7	**11.5**
Petty Trader	6	**9.8**
Driver/Mechanic/Carpenter	6	**9.8**
Teacher/Lecturer	5	**8.2**
Business man	4	**6.6**
Farmer	3	**4.9**
Police/Soldier/Navy	2	**3.3**
Retiree	2	**3.3**
Lawyer	1	**1.6**
Engineer	1	**1.6**
Total	**61**	**100.0**

Half (50.8%) of patients were gainfully employed, majority being self employed (34.3%) while 16.5% were civil servants. In the self employed category petty traders (9.8%), drivers/ mechanics/ and carpenters (9.8%) were in the majority. Others include business men, farmers, lawyers and engineers. In the unemployed category, unemployed housewives (14.8%) were in the majority. Others include 'the unemployed', students, and retirees.

Table 4.7 **Level of Education of Patients Suffering from Anxiety Disorders Visiting ABUTH in 2003 and 2004**

	Number of Patients	**Percent**
Junior secondary school completed	9	**14.8**
Junior secondary school uncompleted	6	**9.8**
Senior secondary school completed	4	**6.6**
Koranic school	2	**3.3**
Primary school uncompleted	2	**3.3**
Pre primary school	1	**1.6**
Tertiary education completed	1	**1.6**
Adult literacy	1	**1.6**
Not recorded	35	**57.4**
Total	**61**	**100.0**

Majority (29.5%) had not completed secondary school while only 6.6% had completed secondary school education, 3.3% Koranic school, 1.6% adult literacy and only 1.6% had completed tertiary education.

Table 4.8 **Prevalence of Subtypes of Anxiety Disorders among Patients Visiting Psychiatric Unit of ABUTH in 2003 and 2004**

Subtype of anxiety disorder	Number of patients	Percent
Generalized Anxiety Disorder	49	80.3
Anxiety Depressive Disorder	10	16.4
Obsessive Compulsive Disorder	1	1.6
Panic Disorder	1	1.6
Total	61	100

Generalised anxiety disorder was the most frequently occurring subtypes of anxiety disorder reported being present in 80.3% of patients. Anxiety depressive disorder (16.4%), Obsessive compulsive disorder (1.6%) and panic disorder (1.6%) were also reported.

4.32 History of Mental Disorders among Families of Patients suffering form Anxiety Disorders Visiting ABUTH in 2003 and 2004

Thirty one (50.8%) patient folders were not documented for family history of mental disorders. Patient / patient representatives who did not consent to any family history of mental disorders made up 34.4% of the study population. On the contrary only 11.5% of patients / patient representatives consented to any family history of mental disorders. Another 3.3% say they do not know if any history of mental disorders existed in their families.

For patients who consented to existence of mental disorders among family members, their relationship to such family members included mother (3.3%), cousins (3.3%), father (1.6%) and siblings (1.6%).

Table 4.9 **Prevalence of Non Psychiatric Comorbid Disorders among Patients Diagnosed with Anxiety Disorders Visiting ABUTH in 2003 and 2004**

Non psychiatric Comorbid Disorder	Number of Patients	**Percent**
Hypertension	14	**23.0**
Malaria	8	**13.1**
Typhoid	8	**13.1**
Diarrhea	3	**4.9**
Urinary Tract Infections	3	**4.9**
Diabetes	2	**3.3**
Ear infection	2	**3.3**
Asthma	1	**1.6**
None	20	**32.8**
Total	**61**	**100.0**

Table 4.10 **Prevalence of Psychiatric Comorbid Disorders among Patients Diagnosed with Anxiety Disorders Visiting ABUTH in 2003 and 2004**

Psychiatric Comorbid Disorder	Number of Patients	**Percent**
Somatoform disorder	4	**6.6**
Depression	3	**4.9**
Parkinsonism	1	**1.6**
Schizophrenia	1	**1.6**
None	51	**85.3**
Total	**61**	**100.0**

Comorbid disorders were present in 62.3% of patients. While 42.6% of patients had more than one comorbid diagnosis only 19.7% of patients had only one comorbid diagnosis. Majority (50.8%) of patients presented with signs and symptoms of non psychiatric comorbid disorders and only 14.7% of patients presented with signs and symptoms of psychiatric comorbid disorders.

Table 4.11 **Health Behaviors among Patients Diagnosed with Anxiety Disorders Visiting ABUTH in 2003 and 2004**

	Number of Patients	**Percent**
Alcohol consumption	3	**4.9**
Physical exercise	2	**3.3**
Tobacco use	1	**1.6**
Coffee consumption	1	**1.6**
Not recorded	54	**88.6**
Total	**61**	**100.0**

Table 4.12 **Signs and Symptoms Presented by Patients Diagnosed with Anxiety Disorders Visiting ABUTH Psychiatry Clinic in 2003 and 2004**

Signs/Symptom	Number of Patients	Percent
Insomnia	34	13.9
Palpitations	31	12.7
Fear (non specific)	18	7.4
Headaches	15	6.2
Weakness	10	4.1
Crawling (pulsating) sensation in the body	9	3.7
Dizziness	8	3.3
Excessive worries	8	3.3
Anorexia	7	2.9
Feel sad (depression)	5	2.1
Anxious mood	4	1.6
Restlessness	4	1.6
Tremor (trembling)	4	1.6
Abdominal discomfort (fullness, tenderness etc)	3	1.2
Blurred vision	3	1.2
Internal heat	3	1.2
Nightmares	3	1.2
Sweating	3	1.2
Choking sensation	2	0.8
Easily startled	2	0.8
Epigastric pain	2	0.8
Fears (specific)	2	0.8
Lack of personal care	2	0.8
Loss of sexual desire	2	0.8
Low energy	2	0.8
Nausea and Vomiting	2	0.8
Noise in the left ear	2	0.8
Obsessional thoughts	2	0.8
Pulsating vortex of head	2	0.8
Suicidal tendencies	2	0.8
Tension easily cries	2	0.8
Chest pain, Cold sensation in feet, Constipation, Difficulty in interacting with people, Difficulty in sitting up, Dry mouth, Easily upset, Eats excessively, Excessive sleep, Excessive anger, Faintness, Feel like defecating, Feels light, Fever episodes, Forgetful, Giddiness, Hopelessness, Hunger, Increased ventilation, Intrusive thoughts, Low mood, Muscle spasm, Negative thoughts, Nervousness, Obsessions with thoughts of failure, Olfactory hallucinations, Panic, Poor vision, Pounding sounds in the head, Shallow breathing, Shortness of breathe, Somatic complains, Sore in the mouth, Suspiciousness, Talkativeness, Unable to concentrate, Aches and pains and Weight loss.	1(each)	0.4

Table 4.13 **Drug Use Pattern and One Year Drug Cost at Psychiatric Unit of ABUTH for Patients Diagnosed With Anxiety Disorders in 2003 and 2004**

Drug Class	Drug Name	(%) Patients Drug Was Prescribed for	Drug cost (in Naira)
Anxiolytic Drugs	Amitriptyline	85.246	87,057.50
	Clomipramine	6.557	8,820.00
	Imipramine	16.393	5,508.50
	Nitrzepam	14.754	2,170.00
	Bromazepam	11.475	1,880.00
	Diazepam	6.557	392.00
	Total Cost		***105,828.00***
Antipsychotic Drugs	Trifluperazine	78.689	35,032.50
	Thioridazine	8.197	16,287.50
	Chlorpromazine	9.836	3,332.00
	Halopridol (Inj.)	1.639	100.00
	Total Cost		***54,752.00***
Antihypertensive Drugs	Nifedepine	16.393	30,866.00
	Moduretic	9.836	5,555.00
	Atenolol	8.197	4,006.06
	Propranalol	22.951	2,558.50
	Bendrofluazide	11.475	2,472.00
	Amlodepine	1.639	1,960.00
	Total Cost		***47,417.56***
Antimalarial Drugs	Dihydroartemisinin	1.639	371.88
	Fansidar	3.279	140.00
	Chloroquine	3.279	80.00
	Total Cost		***591.88***
Antibiotic Drugs	Ciprofloxacin	6.557	1,785.00
	Ampicillin / Cloxacillin	3.279	140.00
	Metronidazole	3.279	140.00
	Genticin Ear Drops	1.639	70.00
	Cotrimoxazole	4.918	40.00
	Total Cost		***2,175.00***
Multivitamin/ Nutritional Supplement	Vitamin B Complex	70.492	6,263.50
	Encephabol	1.639	1,937.50
	Neurobion	1.639	672.00
	Ascorbic Acid	3.279	63.00
	Vitamin K (Inj.)	1.639	55.00
	Total Cost		**8,991.00**
Others	Carbamazepine (CR)	4.918	32,130.00
	Benzhexol	57.377	10,559.40
	Albendazole	6.557	4,350.00
	Diclofenac Potasium	1.639	1,512.00
	Ibuprofen	4.918	165.00
	Polycrol Forte Gel	1.639	110.00
	Levamisole	1.639	75.00
	Prednisolone	1.639	56.00
	Chlopheniramine	1.639	41.00
	Paracetamol	4.918	32.00
	Total Cost		***49,030.40***

Table 4.14 **Laboratory Investigations carried out by Patients Diagnosed with Anxiety Disorders Visiting ABUTH Psychiatry Clinic in 2003 and 2004**

Laboratory Investigation	Number of Patients	Percent
General hematological/investigations (Hb, PVC etc)	19	31.1
Serum urea /electrolyte /creatinine	16	26.2
Stool microscopy	8	13.1
Serum glucose	7	11.5
FBC and Differentials	7	11.5
Urinalysis	6	9.8
Urine microscopy	5	8.2
FBS	5	8.2
Culture and sensitivity	4	6.6
Malaria parasite	4	6.6
Widal test	4	6.6
Abdominal ultrasound	3	4.9
HIV screening	2	3.3
Others Include; Liver function test, Mantoux, VDRL, X-ray and Occult blood.	1(each)	1.6 (each)

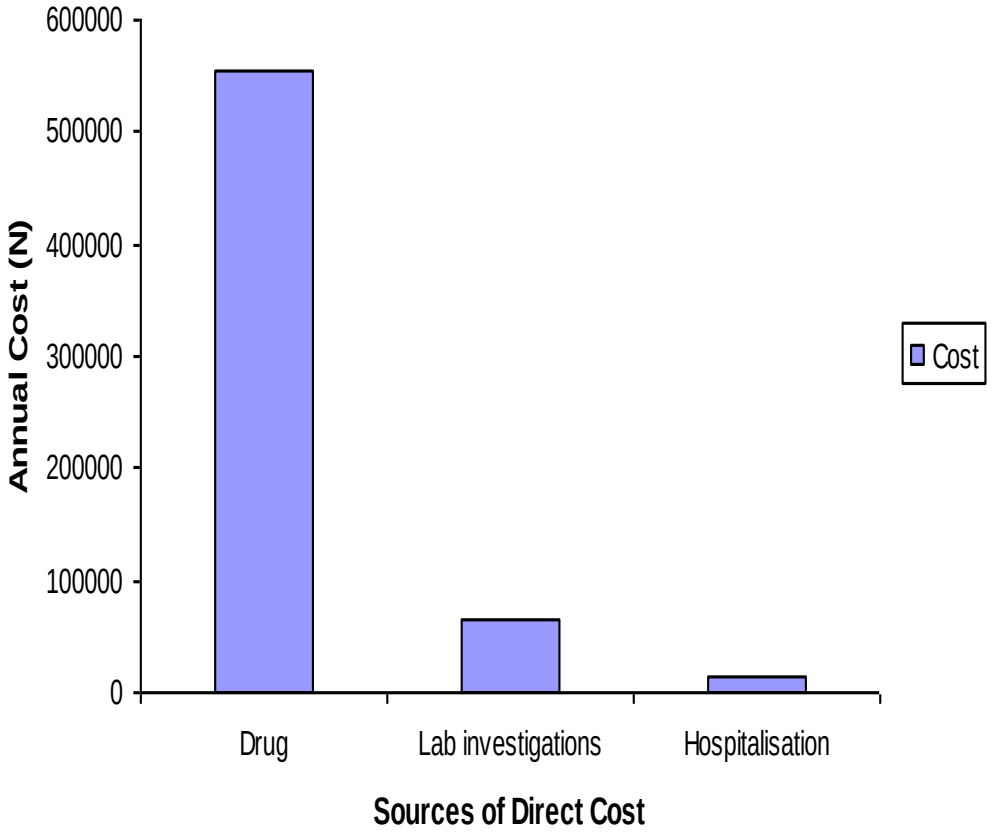

Fig. 4.2 **Comparison of Some Direct Cost Sources for Patients Diagnosed With Anxiety Disorders at ABUTH in 2003 and 2004**

Table 4.15 **Non Pharmacological Methods of Management Employed in Patient Care for Patients Diagnosed as Having Anxiety Disorders Visiting ABUTH Psychiatry Clinic in 2003 and 2004**

	Number of Patients	**Percent**
Psychotherapy	13	**54.1**
Insight counseling	9	**37.5**
Relaxation therapy	1	**4.2**
Counseling with family	1	**4.2**
Total	**24**	**100.0**

Table 4.16 **Summary of Clinic Default by Patients Suffering from Anxiety Disorders Visiting ABUTH Psychiatry Clinic in 2003 and 2004**

	Number of Patients	**Percent**
Did not default Clinic Appointment	46	**75.5**
Defaulted once	11	**18.0**
Defaulted twice	3	**4.9**
Defaulted three times	1	**1.6**
Total	**61**	**100.0**

- N.B Three patients defaulted once before the period under study, but were not included in this results.

Table 4.17 **Adverse Events Experienced by Patients Diagnosed as Having Anxiety Disorders Managed with Pharmacotherapy Visiting Psychiatry Unit of ABUTH in 2003 and 2004**

	Number of Patients	Percent
Insomnia	18	7.4
Weakness	11	4.5
Headache	10	4.1
Palpitation	7	2.9
Dizziness	6	2.5
Excessive sleep	5	2.0
Crawling sensation in the body	4	1.6
depressed feelings (sadness)	4	1.6
Dryness of mouth	4	1.6
Internal heat	4	1.6
Prurities	4	1.6
Chest pain	3	1.2
Emotional upset	3	1.2
Somatic complains	3	1.2
Abdominal pain	2	0.8
Amenorrhea	2	0.8
Anorexia	2	0.8
Constipation	2	0.8
Dry cough	2	0.8
Dyspepsia	2	0.8
Epigastric pain	2	0.8
Feeling afraid	2	0.8
Offensive odour from nose	2	0.8
Sensation in the ear	2	0.8
Tremors	2	0.8
Abdominal discomfort, Blurred vision, Canesthetic hallucination, Drug allergy, Dysphoria, Epitaxis, Excessive salivation, Feels like something is in his head, Forget fullness, Furnicle, Joint pains, Neck and back pain, Nervousness, Poor erection, Prickly sensation, Suicidal thoughts, Vertigo, Weight gain , Irritation of throat, Difficulty in concentrating and Restlessness.	1 (each)	0.4 (Each)
Experienced no side effects	11	4.5

Table 4.18 **Management of Adverse Events Experienced by Patients Diagnosed as Having Anxiety Disorders Managed with Pharmacotherapy Visiting Psychiatry Unit of ABUTH in 2003 and 2004**

	Number of Patients	**Percent**
Use of other drugs	10	**38.5**
Reduction in drug dosage	5	**19.3**
Take drug at a different time	3	**11.5**
Counseling	3	**11.5**
Drug Discontinuation	2	**7.7**
Increase drug dose	2	**7.7**
Reduction in frequency of dosing	1	**3.8**
Total	**26**	**100.0**

CHAPTER FIVE

DISCUSSION

5.1 Clinic Attendance and Frequency of Occurrence of Mental Disorders

This study conducted at the psychiatry unit of Ahmadu Bello University Teaching Hospital (ABUTH) Kaduna, was designed to access characteristics, management and burden of anxiety disorders among patients who attended psychiatry clinics between the periods of January, 2003 and December, 2004.

Clinics were regularly held at ABUTH as and when due (Tables 4.1 and 4.2). At two clinics per week (Mondays and Thursdays) the 100 clinic attendances for 2003 was as expected. The short fall in 2004 (96 clinics only) can be accounted for by resident doctors' strike in December of that year. Regular clinics even on public holidays would contribute positively towards patient's prognosis and this practice at ABUTH is commendable.

It was observed that clinic attendances increased in 2004 relative to 2003 despite fewer clinics held in 2004. This was evident from increase average clinic attendance, increasing from 65 patients per clinic in 2003 to 73 patients per clinic in 2004. The non corresponding increase in clinicians and other staff within these years would no doubt have impacted on quality of services rendered to these patients. The 13,417 attendances were made by 2,780 patients who attended clinics from 1-29 times. Patients who are clinically stable are usually given appointments at intervals not less than 4 months (i.e. 3 times per year), Thus it was the "unstable" patients who attended a minimum of 6 clinics

in 2003 and 2004, totaling 875, that were purposively taken as the study population (Fig. 4.1). It should be noted that frequency of clinic attendance is an indicator of healthcare facility usage (Kennedy and Schwab, 1997).

The relative frequencies of occurrence for the various categories of mental disorders were: schizophrenia 355(46.6%), depression 104(13.7%), seizure disorders 92(12.1%), anxiety disorders 61(8.0%), bipolar affective disorders 57(7.5%), mania 27(3.5%), organic brain disorders 26(3.4%), substance use disorders 16(2.1%) and somatization disorders 16 (2.1%) (Table 4.3). This relative proportion is dissimilar with previously reported works in literature including reports from Africa; which show that anxiety disorders are second only to mood disorders (Mathers et al., 2002 and Alanso *et al.*, 2004). A study in Chile also showed that the most common life time diagnosis was agoraphobia (11%) (Vicente *et al.*, 2002).

5.2 **Features of Anxiety Disorders**

Contrary to most published literature (Lindal and Stelansson, 1993; Kessler *et al.*, 1994; Hacker, 1997; Fullerton *et al.*, 2001; Wittuchen and Hoyer, 2001; Bijl *et al.*, 2002; Piggot, 2003; Anonymous, 2004 and Jerliyn, 2004), majority of patients presenting at ABUTH psychiatry clinic with anxiety disorders were male (62.3%) (Table 4.4). Martin *et al.* (1998), reporting in a study conducted in southwest France (Aquitaine), found no sex difference among general practice patients. It is noteworthy that the reverse was observed here although this could not be compared locally as there are no reports from Nigeria. Although no obvious reasons could be ascribed to explain this situation, cultural

/ religious barriers which limit female participation and male preponderance with regards societal and family responsibilities are suggested. Fluctuations in reproductive hormone levels during the female life cycle are also thought to be responsible for modulating anxiety. Additional work is required to understand the biological and psychosocial causes of these differences (anonymous, 2004).

Over 70% of these patients were married while 24.6% were single and 1.6% each were separated or divorced at first presentation (Table 4.4). This is not surprising since 59% were in their twenties and thirties (Table 4.5). That 57.4% of patients suffering form anxiety disorders in ABUTH were of the Muslim faith (Table 4.4), may be explained by the fact that ABUTH in located in northern Nigeria where Islam is the prevalent religion. The mean age for patients diagnosed with anxiety disorders (36.3 years) was higher than that observed for the general population (29.2 years). The mean age for men (37.1 years) did not differ significantly from that of women (35.0 years). As previously indicated 59.0% of patients suffering from anxiety disorders are in their twenties (26.2%) and thirties (32.8%) (Table 4.5). This data shows that anxiety disorders are predominant among the productive class of the society. Records for children under the age of 14 years were absent, even though there is an abundance of literature for anxiety disorders in children (particularly separation anxiety disorder). These results are in agreement with published works (Bijl et al., 1998; Andrews et al., 2001; Kringlen et al., 2001 and Wittchen & Jacobi, 2001). Based on data calculated from date of first registration until December 31, 2004, majority of anxiety disorder patients (82.5%) have been attending clinics for 5 years or less, 9.8% have been attending clinics for between 6 and 10 years

and only 4.95% have been patients for more than 10 years. The average duration of attendance for all anxiety disorder patients was 2.99 years (see fig 4.2). This data is similar to what had been observed for seizure disorders where unstable patients tended to be less than five years since registration (Omoniwa, 2006).

Findings from analysis of data on prevalence of anxiety disorders at ABUTH by tribe / ethnicity shows anxiety disorders were ubiquitous, with a Hausa majority (34.4%). Other tribes / ethnic groups include Fulani (9.8%), Yoruba (6.6%), Igbo (6.6%) and Jaba (4.9%) (4.31). Kaduna (41.0%), Kogi (8.2%), Kano (4.9%), Niger (4.9%) and Edo (4.9%) were states that the patients principally came from. Thus substantial proportions were from the north western (50.8%) and north central (19.7%) zones of the country, which was not unexpected as ABUTH is located in the north western zone of the country.

Analysis of data on occupational status of patients with anxiety disorders show 50.8% were employed (Table 4.6), this represents a deviation from findings of Araya (2001) and Butterworth (2003). Araya found higher prevalence among the unemployed, while Butterworth found higher prevalence as well as physical and mental disability among income support recipients in Australia. In view of the fact that anxiety disorders were also found to be prevalent among the productive class, anxiety disorders would no doubt impact on productivity of these individuals. Kennedy *et al*. (2002), Dewa *et al*. (2003) and Cuijpere (2005), suggest early diagnosis, rational management and possible prevention could help reduce the enormous burden of this disorders.

Even though majority of patients were in their twenties and thirties (Table 4.5), data for level of education of patients diagnosed as having anxiety disorder show that only a very small percentage had any tertiary education (1.6%) (Table 4.7). Although the study did not further attempt to find out why this was so, Van Ameringen *et al*. (2003) in a study to determine "impact of anxiety disorders on educational achievements" found that anxiety disorders are associated with premature withdrawal from school, which resulted from significant disability in social and occupational functioning. This result is also similar to the findings of Araya *et al*. (2001)

Generalised anxiety disorder (80.3%) was the most common subtype of anxiety disorder reported and this finding is consistent with several published literature (Martin *et al*., 1998; Pelissolo *et al*., 2002 and McLaughlin *et al*., 2003). Anxiety depressive disorders (16.4%), obsessive compulsive disorders (1.6%), and panic disorders (1.6%) were also reported (Table 4.8).

Only 11.5% of patients had records indicating family history of mental disorders (4.32). Records were not available for 50.8% of patients, while 34.4% said there were no histories of such occurrences in their families. Only 3.3% reported that they did not know if such family histories of mental disorders were present in their families. This is not in agreement with available literatures which show familial aggregation among mental disorders (Hetema *et al.*, 2001 and Niemi *et al*., 2004).

5.3 **Comorbidity**

Comorbid disorders were present in 62.3% of patients. This result is consistent with the findings of Goldenberg *et al*. (1996) in which they described the infrequent occurrence of "pure culture" anxiety disorders. The prevalence of non psychiatric comorbid disorders (50.8%) was observed to be higher than that for psychiatric comorbid disorders (14.7%). Hypertension was the most frequently occurring non psychiatric comorbid disorder (36.1%) (Table 4.9) and this observation is similar to results published by McLaughlin *et al*. (2003). Others are malaria (13.1%), typhoid fever (13.1%), urinary tract infections (4.1%), diarrhoea (4.1%), ear infection (3.3%), diabetes (3.3%) and asthma (1.6%). The high prevalence of malaria and typhoid fever are not surprising as these infections occur very frequently in this part of the world. The most frequently reported psychiatric comorbid disorder was somatization disorder (6.6% of patients) (Table 4.10). This result is consistent with the findings of Rogers *et al*. (1996) who observed similar frequent coexistence between somatoform disorders and anxiety disorders. Depression (4.9%) was second only to somatization disorders. This is similar to the findings of McLaughlin *et al*. (2003). They found depression to be the most frequently occurring psychiatric comorbid disorder. Other psychiatric comorbid disorders reported were schizophrenia and parkinsonism both of which occurred each in 1.6% of patients. Understanding comorbidity patterns is essential for accurate differential diagnosis, for understanding how comorbidity influences illness course and severity as well as for developing rational plan for treatment (Goisman *et al*., 1995).

The mean age of patients with comorbid diagnosis was found to be significantly higher (t=2.6, df=59, sig.=0.01) and this result is dissimilar to the published work of Goldenberg *et al*. (1996) who observed that absence of comorbid disorder was associated with later onset of illness. Further analysis of age distribution reveals that while the above observation is true in the presence of non psychiatric comorbid disorders (t=3.1, df=59, sig.=0.003), the same is not true in the presence of psychiatric comorbid disorders (t=0.1, df=59, sig=0.9).

Neither non psychiatric comorbid disorders nor psychiatric comorbid disorders was found to have any association with sex or marital status (Appendices I, II, III, IV, V and VI). Average frequency of clinic visits also did not increase significantly in the presence of comorbid disorders (t=1.3, df=59, sig.=0.19). This finding is not is not similar to the results of the works of Lecrubier (1998) and Andrews *et al*. (2001) who found comorbid disorders to be associated with increased service utilization and disability. Further analysis of the influence of comorbid disorder on average frequency of clinic visits show that while average frequency of clinic visits increased significantly in the presence of non psychiatric comorbid disorders (t=1.9, df=59, sig.=0.058), the presence of psychiatric comorbid disorders did not significantly increase average frequency of clinic visits (t=1.0, df= 59, sig.=0.3).

The average cost of treatment per patient per month was not significantly increased in the presence of comorbid disorders (t=0.67, df=59, sig.=0.51). Further more neither the presence of non psychiatric comorbid disorders nor the presence of psychiatric comorbid

disorders influenced average cost of treatment per patient per month significantly (see appendices XV, XVI and XVII). These results are not in agreement with findings of the works of McLaughlin *et al*. (2003) who found that treatment cost are significantly higher when patients are diagnosed with anxiety disorders, highlighting the impact of these charges on patients.

Data regarding health behaviors such as physical exercise and tobacco consumption were very scanty (records were unavailable for 88.6% of patients). Available records show that alcohol (4.9%) consumption predominated (Table 4.11). The extent to which these behaviors influenced the course and management of anxiety disorders could not be determined because of deficiency of records and the retrospective design of this study. Association between anxiety disorders (such as GAD and social phobia) and alcohol or tobacco dependence is well established. The presence of anxiety disorders may increase self mediation with alcohol or tobacco and this has been implicated with treatment failure as well as relapse (Cox *et al.*, 1994; Schade *et al.*, 1998 and Lagrue *et al*., 2002).

5.4 **Management of Anxiety Disorders at ABUTH**

Signs and Symptoms

Signs and symptoms of anxiety disorders frequently reported by physicians were somatoform complaints (headaches, aches, pains, crawling / pulsating sensation in head or body, tinnitus etc), insomnia and other sleep disorders (difficulty in falling or staying asleep, nightmares etc), cardiovascular complaints (palpitations, feeling faint, etc), anxious mood (worries, anticipates the worst, etc), gastrointestinal symptoms (abdominal

discomfort, anorexia, etc) and tension (restlessness, easily startled, cries easily, trembling, etc) (Table 4.12).

Laboratory Investigations

Frequently requested laboratory investigations include, general hematological investigations (31.1% of patients), serum / urea / electrolyte / creatinine (26.2%), stool microscopy (13.1%), serum glucose (11.5%) and full blood count and differentials (11.5%) (Table 4.14). These laboratory investigations were usually required for purposes other than diagnosis or treatment of anxiety disorders and similar findings have also been observed by Coste e Silva (1998). The frequent request for general hematological investigations may have been necessitated by the significant number of cardiovascular complaints and the high prevalence of comorbid hypertension among anxiety disorder patients. Psychiatrists involved in the patients care explained that frequent requests of laboratory investigations thus; that diagnosis of anxiety disorders involves a process of exclusion. Laboratory investigations are required to exclude disorders that are similar or mimic anxiety disorders.

Pharmacotherapy and Psychotherapy

Patients were managed either with Pharmacotherapy (67.2%) or Pharmacotherapy plus psychotherapy (32.8%).

Anxiolytics used in pharmacotherapy include TCAD: amitriptylline (in 83.6% of patients), imipramine (16.4%), and benzodiazepines: nitrzepam (13.0%), bromazepam

(11.5%), and diazepam (6.6%) (See table 4.19). Newer SSRIs which have been proven to be more effective and are better tolerated were rarely prescribed probably due to their prohibitive cost. TCAD achieve their effects by inhibiting reuptake of 5-HT and nor adrenaline (some e.g. desipramine inhibit just nor adrenaline). Their sedative side effects is due to blockade of histamine receptors (this makes them useful in treatment of insomnia, a presenting symptom in a large number of anxiety disorders patients presenting at the clinic). In addition, their effectiveness in management of comorbid depression is a major benefit in the use of these drugs for management of anxiety disorders. They are also known to be effective in the management of a wide range of anxiety disorders except social phobia. Antidepressants are known to worsen anxiety at the start of therapy. Nausea, jitteriness, and insomnia also frequently occur. The clinical implication is that they are initiated at very low doses and slowly titrated upwards. Poor tolerability and high toxicity profile especially in overdose are some of the reasons why SSRIs such as fluoxetine are now preferred to TCADS in management of anxiety disorders.

Reports of abnormalities in GABA receptor system of patients with anxiety disorders such as panic disorder, GAD, and PTSD favor the use of benzodiazepines in the management of anxiety disorders as they are viewed as offsetting an underlying abnormality. Benzodiazepines act at γ-amino butyric acid type A ($GABA_A$) receptor, where they increase neurotransmission produced by endogenous neurotransmitter, γ-amino butyric acid (GABA), the major inhibitory neurotransmitter in the brain. Advantages of the use of benzodiazepines include; rapid onset of action, they do not

produce worsening of anxiety as do antidepressants, and they improve sleep onset and its subjective quality, a factor which is often disrupted in anxiety disorder. They are effective in the management of most anxiety disorders, though their efficacy in treatment of OCD and PTSD are much less profound. Drawbacks in their use include; their poor efficacy in the management of comorbid depression, and the risk of developing tolerance, dependence and or withdrawal symptoms. However they may be co administered with antidepressants at initiation of therapy to prevent drop out from therapy due to worsening anxiety.

Non anxiolytic agents used in pharmacotherapy include antipsychotic: trifluperazine (77.0%), chlorpromazine (9.8%), and thioridazine (8.2%), antihypertensive: propranalol (23.0%), nifedepine (14.8%), bendrofluazide (11.5%), and moduretic (9.8%). Though there is little support for the use of antipsychotic in the management of anxiety disorders, both classical and atypical antipsychotic agents have been used in clinical trials as well as in combination with antidepressants in management of certain anxiety disorders e.g. OCD disorders and PTSD (El-Khayat *et al.*, 1998 and Bjerrum *et al.*, 1992). For example Bjerrum *et al.* (1992) attempted to evaluate effectiveness of benzodiazepines, flupenthixol and placebo in management of GAD and reported that only flupenthixol showed statistically significant improvement in patients.

Deficiency in evidence of efficacy from literature, unfavorable side effect profile, toxicity in overdose, and contraindication in certain patient's e.g. asthmatics, limits the use of propranalol and atenolol in treatment of anxiety disorder. However, they do find

usefulness where autonomic symptoms are a significant issue (Gleiter and Deckert, 1996). Use of antihypertensive can be explained by the fact that significant number of patients presented with cardiovascular symptoms as well as the fact that hypertension was the most prevalent non psychiatric comorbid disorder.

Other drugs used include vitamin B complex (in 70.5% of patients), probably due to its neurological effects (as deficiency leads to development of neuropathies e.g. neuritis, convulsions and neuromuscular degeneration), benzhexol (57.4%), explained by the high rate of antipsychotic use (which predisposes patients to peripheral neuropathy, for which benzhexol is effective in treating), and Carbamazepine (4.9%), probably due to its effect on mood (mood stabilizing effect).

Non pharmacological therapy was usually undertaken in conjunction with drug therapy. The forms of non pharmacological therapy (in 32.8% of patients) prescribed were psychotherapy (54.1%), counseling (insight or with family) (41.7%), and relaxation therapy (4.2%) were the forms of psychotherapy reported (Table 4.15). Mean frequency of clinic visits did not differ significantly in groups of patients that received pharmacotherapy or psychotherapy plus pharmacotherapy (t=0.7, df=59, sig.=0.5) Multimodal therapy may not exactly be cost effective. Benefits of multimodal therapy are not yet clear and further studies are required (Mental Health: A Report of Surgeon General, 2001). Benefits of psychological interventions are numerous. Hunsley (2002) showed compelling evidences that psychological interventions can effectively treat a wide range of childhood and adult health problems. They also showed psychological

treatments can be more cost-effective than common pharmacological interventions. Beyond this, psychological interventions also appear to have the potential to reduce health care cost, as successfully treated patients reduce their utilization of health care services. This facility has only one psychotherapist. In other to explore the full benefits of such interventions the facility would need to be adequately staffed.

While the presence of comorbid disorders did not significantly increase drug cost, duration for which patient had been on treatment was found to have a negative relationship with average cost of treatment per patient per month (regression of average cost to treat per month and years since registration = -0.08) and longer duration of treatment was found to significantly reduce cost of drug treatment (One way ANOVA of category of duration on treatment and average cost to treat per month shows, F =3.751, df =59, sig.=0.029).

A closer look at data on clinic default (Table 4.16) show that 24.5% of patients suffering from anxiety disorders defaulted clinic appointments one or more times during the period under study. This study attempted to investigate if any association existed between place of residence of patients , employment status of patients and clinic default. Despite the fact that about one third of anxiety disorder patients live outside Kaduna metropolis (27.9%), and 49.2% are not gainfully employed, neither place of residence nor employment status was found to have any significant relationship with clinic defaulting, and hence do not contribute significantly to poor adherence with clinic appointments (Appendices VII and

VIII). The consequences of poor adherence to long-term therapies for chronic illnesses are poor health outcomes and increased health care costs.

Adverse Events and Their Management

Over four fifth (82.0%) of patient's receiving drug therapy experienced one or more adverse event. Frequent Complains included; insomnia (7.4%), weakness (4.5%), headaches (4.1%), dizziness (2.5%), and excessive sleep (2.0%) (Table 4.17). Weakness, dizziness, excessive sleep and palpitations can be explained by frequent use of amitriptylline and trifluperazine. However, insomnia and headaches could not be related to drug use. Polypharmacy and frequent changes in drugs therapy make it difficult to tie adverse events to any particular drug used.

Use of other drugs to suppress adverse events (38.0%), reduction in drug dose / frequency (23%), taking drug at a different time of the day (11.5%), counseling (11.5%), drug discontinuation (7.7%) and increased dose of drug (7.7%) were methods identified for management of adverse events (Table 4.18).

5.5 Cost of Treatment

The retrospective design used in this study limited measurement of cost items to; cost of drugs, cost of laboratory investigations and cost of hospitalization; which are all sources of direct cost. Annually, calculated drug cost (₦276,750: 84) far outweighed cost of laboratory investigations (₦32,530: 00) and cost of hospitalization (₦14,500: 00) (Fig. 4.2). The average cost of treatment per patient per month was ₦1,200: 00

(SD = ₦1, 448: 91). Maximum and minimum calculated costs of treatment per patient per month were ₦9,056: 25 and ₦114: 27 respectively. The average cost of laboratory investigations per patient per month was ₦403: 91(SD = ₦524: 99), with maximum cost being ₦4,700: 00.

Analysis of annual drug cost shows, amitriptyline (₦87, 057: 50), trifluperazine (₦35, 032: 50) and carbamazepine (₦32, 130: 00) were responsible for large proportions of drug cost (Table 4.13). Expenditure on anxiolytics (₦105, 828: 00) far outweighed expenditure on any other drug class. Antipsychotics (₦54,752: 00) and antihypertensives (₦47, 417: 56) were also responsible for significant drug expenditure. More money was spent buying multivitamins / nutritional supplement (₦8,991: 00) than was spent on antibiotics (₦2, 175: 00) or antimalarial (₦591: 88). Drug cost reflected frequency of prescriptions, and the influence of unit cost of drugs was minimal. General hematological investigations (₦16,150: 00), serum urea/electrolyte/creatinine (₦5,600: 00) and blood culture and sensitivity (₦1,800: 00) were principal cost components of laboratory investigations.

With 27.9% of patients living outside Kaduna metropolis, travel time and waiting time will account for significant loss in productive time. This situation is made even less pleasant when the fact that on the average, patents are accompanied 17.76% (SD=25.42%) of times they visit clinic, is taken into consideration.

CONCLUSION

Few data are currently available on anxiety disorder, its prevalence, and associated characteristics in this part of the country, yet this represents one of the principal systems of care for such patients. The burden of anxiety disorders will continue to increase as incidence increases with progressive years. Anxiety disorders are frequently occurring mental disorders with prevalence rates behind only these of schizophrenia, Depression, and seizure disorders.

Even though evidence abounds from published literature, anxiety disorders were found to be more prevalent among male patients, married patients, and the employed. Anxiety disorders did not show any familial aggregation. Anxiety disorders were also found to be prevalent among the productive class of the society and patients of the Muslim faith. Anxiety disorders also impacted on educational achievement and showed no geopolitical, ethnic or tribal barriers. The average age of anxiety disorder patients was higher than for the study population of mental disorders and most off these patients had been attending clinics for five years or less. Generalised anxiety disorder were the most prevalent subtype of anxiety disorder encountered.

Comorbid disorders were the rule rather than the exception. More than half the patients diagnosed as having anxiety disorders presented with signs and symptoms of another diagnosis. Non psychiatric comorbid disorders were more prevalent and the likelihood of a comorbid diagnosis increased with increase in age. Comorbid diagnosis showed no association with sex or marital status. The presence of comorbid diagnosis did not

increase average cost of treatment per patient per month significantly however; comorbid diagnosis significantly increased average frequency of clinic visits. Alcohol consumption was the most dominant associated health behavior.

Signs and symptoms presented by patients varied and somatoform complaints were the most dominant. Hematological investigations were the most requested laboratory investigations. Differences were observed between literature and findings from data on management of anxiety disorders at ABUTH. Patients were managed either with pharmacotherapy or psychotherapy plus pharmacotherapy. Drug preferences were for amitriptylline and trifluperazine. Other drugs used include imipramine, nitrazepam, bromazepam and diazepam. Antipsychotic drugs prescribed include chlorpromazine and thioridazine. Other drugs encountered include antihypertensive (e.g. propranalol, nifedepine, bendrofluazide and moduretic), vitamin B complex, benzhexol, and carbamazepine. Drug use was associated with side effects in significant number of patients and side effects were principally managed by either the use of other drugs which cancel out such effects, or discontinuation of drug used. Non pharmacological approaches used include psychotherapy, counseling, and relaxation therapy. No evidence for the efficacy of multimodal therapy over single therapy was observed, however, longer duration on therapy was observed to reduce cost of treatment.

With regards to patient expenses, drug cost far outweighed cost of laboratory investigations and cost of hospitalization. Travel time and waiting were sources of lost productive time identified.

In conclusion early diagnosis and management would improve health outcomes and burden of these disorders.

RECOMMENDATIONS FOR FUTHER STUDY

In the course of this research certain areas where data was either scanty or unavailable were identified. Availability of such records would not only aid in-depth analysis of research problems but would also encourage further research into this area of study. This would in turn help improve services rendered by members of the health care team. Areas identified include:

1) Records on differential diagnosis, which are of utmost importance for planning patient management, should always be available in folders and on patient prescriptions where they would always be easily accessible to all members of the health care team.

2) The unavailability of comprehensive pharmacy records which should contain patient drug history as well as information on allergies, and hypersensitivities, would no doubt impact on physicians choices of drug and non drug management.

3) The following records are necessary to institute proper pharmacoeconomic management and as such physicians or pharmacists should obtain such records form patients to ensure that therapy is tailored to suit patient, and ensure compliance with therapy. They include: records on patient income / occupation, educational status, and basic life style / health behaviors.

Prospective research in this area should be encouraged to provide information not made available due to limitations of the retrospective design this study. For example further evaluation of treatment responsiveness and drug or type of therapy administered will help identify which subtypes benefit from which for of treatment suing randomized controlled trials. Prospective research would reveal level of awareness and knowledge as well as the role and extent to which stigma hampers people from acknowledging their mental problems. Research would also refine services provided by psychiatrists, and better understanding of cultural influences on curse and response to treatment. Most importantly, the psychiatric unit should encourage innovative strategies that help implement findings from such research.

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APPENDICES

Appendix I

Cross Tabulation of Gender and Presence of Comorbid Disorders; X^2 Statistic

			Comorbid Disorder		**Total**
			Present	Absent	
Sex	Male	Count	23	15	**38**
		Expected Count	21.8	16.2	**38.0**
		% within Q_4	60.5%	39.5%	**100.0%**
		% within Q_31V	65.7%	57.7%	**62.3%**
		% of Total	37.7%	24.6%	**62.3%**
	Female	Count	12	11	**23**
		Expected Count	13.2	9.8	**23.0**
		% within Q_4	52.2%	47.8%	**100.0%**
		% within Q_31V	34.3%	42.3%	**37.7%**
		% of Total	19.7%	18.0%	**37.7%**
Total		Count	35	26	**61**
		Expected Count	35.0	26.0	**61.0**
		% within Q_4	57.4%	42.6%	**100.0%**
		% within Q_31V	100.0%	100.0%	**100.0%**
		% of Total	57.4%	42.6%	**100.0%**

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	**0.409**	**1**	0.523
Number of Valid	61		

Cases			

Appendix II

Cross Tabulation of Gender and Presence of Psychiatric Comorbid Disorders; X^2 Statistic

			Psychiatric Comorbidity		**Total**
			Present	Present	
Sex	Male	Count	5	33	**38**
		Expected Count	5.0	33.0	**38.0**
		% within Q_4	13.2%	86.8%	**100.0%**
		% within Q_30IV	62.5%	62.3%	**62.3%**
		% of Total	8.2%	54.1%	**62.3%**
	Female	Count	3	20	**23**
		Expected Count	3.0	20.0	**23.0**
		% within Q_4	13.0%	87.0%	**100.0%**
		% within Q_30IV	37.5%	37.7%	**37.7%**
		% of Total	4.9%	32.8%	**37.7%**
Total		Count	8	53	**61**
		Expected Count	8.0	53.0	**61.0**
		% within Q_4	13.1%	86.9%	**100.0%**
		% within Q_30IV	100.0%	100.0%	**100.0%**
		% of Total	**13.1%**	**86.9%**	**100.0%**

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	**0.000**	**1**	0.990

N of Valid Cases	61		

Appendix III

Cross Tabulation of Gender and Presence of Non-Psychiatric Comorbid Disorders; X^2 Statistic

			Comorbid Disorder		Total
			Present	**Absent**	
Sex	**Male**	**Count**	**21**	**17**	38
		Expected Count	**19.3**	**18.7**	38.0
		% within Q_4	**55.3%**	**44.7%**	100.0%
		% within Q_31IV	**67.7%**	**56.7%**	62.3%
		% of Total	**34.4%**	**27.9%**	62.3%
	Female	**Count**	**10**	**13**	23
		Expected Count	**11.7**	**11.3**	23.0
		% within Q_4	**43.5%**	**56.5%**	100.0%
		% within Q_31IV	**32.3%**	**43.3%**	37.7%
		% of Total	**16.4%**	**21.3%**	37.7%
Total		**Count**	**31**	**30**	61
		Expected Count	**31.0**	**30.0**	61.0
		% within Q_4	**50.8%**	**49.2%**	100.0%
		% within Q_31IV	**100.0%**	**100.0%**	100.0%
		% of Total	50.8%	49.2%	100.0%

Chi-Square Tests

	Value	Df	Asymp. Sig. (2-sided)

Pearson Chi-Square	**0.796**	**1**	0.372
N of Valid Cases	61		

Appendix IV

Cross Tabulation of Marital Status and Presence of Comorbid Disorders; X^2 Statistic

			Comorbid Disorder		**Total**
			Present	**Absent**	
Marital Syatus	**Not Married**	**Count**	**10**	**8**	**18**
		Expected Count	**10.3**	**7.7**	**18.0**
		% within Q_15M	**55.6%**	**44.4%**	**100.0%**
		% within Q_31V	**28.6%**	**30.8%**	**29.5%**
		% of Total	**16.4%**	**13.1%**	**29.5%**
	Married	**Count**	**25**	**18**	**43**
		Expected Count	**24.7**	**18.3**	**43.0**
		% within Q_15M	**58.1%**	**41.9%**	**100.0%**
		% within Q_31V	**71.4%**	**69.2%**	**70.5%**
		% of Total	**41.0%**	**29.5%**	**70.5%**
Total		**Count**	**35**	**26**	**61**
		Expected Count	**35.0**	**26.0**	**61.0**
		% within Q_15M	**57.4%**	**42.6%**	**100.0%**
		% within Q_31V	**100.0%**	**100.0%**	**100.0%**
		% of Total	**57.4%**	**42.6%**	**100.0%**

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	**0.035**	**1**	**0.852**
N of Valid Cases	**61**		

Appendix V

Cross Tabulation of Marital Status and Presence of Psychiatric Comorbid Disorder; X^2 Statistic

			Comorbid Disorder		Total
			Present	Absent	
Marital Status	Not Married	Count	4	14	18
		Expected Count	2.4	15.6	18.0
		% within Q_15M	22.2%	77.8%	100.0%
		% within Q_30IV	50.0%	26.4%	29.5%
		% of Total	6.6%	23.0%	29.5%
	Marred	Count	4	39	43
		Expected Count	5.6	37.4	43.0
		% within Q_15M	9.3%	90.7%	100.0%
		% within Q_30IV	50.0%	73.6%	70.5%
		% of Total	6.6%	63.9%	70.5%
Total		Count	8	53	61
		Expected Count	8.0	53.0	61.0
		% within Q_15M	13.1%	86.9%	100.0%
		% within Q_30IV	100.0%	100.0%	100.0%
		% of	13.1%	86.9%	100.0%

		Total			

Chi-Square Tests

	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	**1.859**	**1**	**0.173**
N of Valid Cases	**61**		

Appendix VI

Cross Tabulation of Marital Status and Presence of Non Psychiatric Comorbid Disorders; X^2 Statistic

			Comorbid Disorder		**Total**
			Present	**Present**	
Marital Status	**Not Married**	**Count**	**9**	**9**	**18**
		Expected Count	**9.1**	**8.9**	**18.0**
		% within Q_15M	**50.0%**	**50.0%**	**100.0%**
		% within Q_31IV	**29.0%**	**30.0%**	**29.5%**
		% of Total	**14.8%**	**14.8%**	**29.5%**
	Married	**Count**	**22**	**21**	**43**
		Expected Count	**21.9**	**21.1**	**43.0**
		% within Q_15M	**51.2%**	**48.8%**	**100.0%**
		% within Q_31IV	**71.0%**	**70.0%**	**70.5%**
		% of Total	**36.1%**	**34.4%**	**70.5%**
Total		**Count**	**31**	**30**	**61**
		Expected Count	**31.0**	**30.0**	**61.0**
		% within Q_15M	**50.8%**	**49.2%**	**100.0%**

		% within Q_31IV	100.0%	100.0%	100.0%
		% of Total	50.8%	49.2%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	0.007	1	.934
N of Valid Cases	61		

Appendix VII

Cross Tabulation of Place of Residence and Abscondment from Treatment; X^2 Statistic

			Absconded From Treatment		Total
			Yes	No	
Place of Residence	Kaduna Metropolis	Count	14	30	44
		Expected Count	11.7	32.3	44.0
		% within Q_25II	31.8%	68.2%	100.0%
		% within Q_48II	87.5%	68.2%	73.3%
		% of Total	23.3%	50.0%	73.3%
	Outside Kaduna Metropolis	Count	2	14	16
		Expected Count	4.3	11.7	16.0
		% within Q_25II	12.5%	87.5%	100.0%
		% within Q_48II	12.5%	31.8%	26.7%
		% of Total	3.3%	23.3%	26.7%
Total		Count	16	44	60

		Expected Count	**16.0**	**44.0**	**60.0**
		% within Q_25II	**26.7%**	**73.3%**	**100.0%**
		% within Q_48II	**100.0%**	**100.0%**	**100.0%**
		% of Total	**26.7%**	**73.3%**	**100.0%**

Chi-Square Tests

	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	**2.239**	**1**	**0.135**
N of Valid Cases	**60**		

Appendix VIII

Cross Tabulation of Employment Status and Abscondment from Treatment; X^2 Statistic

			Abscondment from Treatment		**Total**
			Yes	**No**	
Employment Status	**Employed**	**Count**	**10**	**34**	**44**
		Expected Count	**11.7**	**32.3**	**44.0**
		% within Q_23II	**22.7%**	**77.3%**	**100.0%**
		% within Q_48II	**62.5%**	**77.3%**	**73.3%**
		% of Total	**16.7%**	**56.7%**	**73.3%**
	Unemployed	**Count**	**6**	**10**	**16**
		Expected Count	**4.3**	**11.7**	**16.0**
		% within Q_23II	**37.5%**	**62.5%**	**100.0%**
		% within Q_48II	**37.5%**	**22.7%**	**26.7%**
		% of	**10.0%**	**16.7%**	**26.7%**

		Total			
Total		**Count**	**16**	**44**	**60**
		Expected Count	**16.0**	**44.0**	**60.0**
		% within Q_23II	**26.7%**	**73.3%**	**100.0%**
		% within Q_48II	**100.0%**	**100.0%**	**100.0%**
		% of Total	**26.7%**	**73.3%**	**100.0%**

Chi-Square Tests

	Value	**df**	**Asymp. Sig. (2-sided)**
Pearson Chi-Square	**1.309**	**1**	**0.253**
N of Valid Cases	**60**		

Appendix IX

Distribution of Age at Registration and T-Test for Equality of Means for Age at Registration for Men and Women

		Sex		**Total**
		Male	**Female**	
Age Category	**< 20 Years**	**3**		**3**
	21 – 30 Years	**12**	**10**	**22**
	31 – 40 Years	**9**	**8**	**17**
	41 - 50 Years	**7**	**3**	**10**
	> 50 Years	**7**	**2**	**9**
Total		**38**	**23**	**61**

T-Test

Group Statistics

	Sex	N	Mean	Std. Deviation	Std. Error Mean
Age At Registration	**Male**	**38**	**37.13**	**12.499**	**2.028**
	Female	**23**	**35.00**	**10.211**	**2.129**

Independent Samples test

		t-Test for equality of means						
		t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Age At Registration	**Equal variances assumed**	**0.690**	**59**	**0.493**	**2.13**	**3.091**	**-4.053**	**8.316**
	Equal variances not assumed	**0.725**	**53.723**	**0.472**	**2.13**	**2.940**	**-3.764**	**8.027**

Appendix X

Regression and Correlation between Duration of Treatment and Frequency of Clinic Visits

Regression

Descriptive Statistics

	Mean	Std. Deviation	N
Average Frequency of Attendance '02 & '03	**6.254**	**2.3177**	**61**
Years Since Registration	**2.99**	**3.97**	**61**

		Average Frequency of Attendance '02 & '03	Years Since Registration
Pearson Correlation	**Average Frequency of Attendance '02 & '03**	**1.000**	**-0.037**
	Years Since Registration	**-0.037**	**1.000**
Sig. (1-tailed)	**Average Frequency of Attendance '02 & '03**	**.**	**0.388**
	Years Since Registration	**0.388**	**.**
N	**Average Frequency of Attendance '02 & '03**	**61**	**61**
	Years Since Registration	**61**	**61**

Correlations

			Average Frequency of Attendance '02 & '03	Years Since Registration
Kendall's tau_b	**Average Frequency of Attendance '02 & '03**	**Correlation Coefficient**	**1.000**	**-0.215**
		Sig. (2-tailed)	**.**	**.017**
		N	**61**	**61**
	Years Since Registration	**Correlation Coefficient**	**-0.215***	**1.000**
		Sig. (2-tailed)	**0.017**	**.**

		N	**61**	**61**
Spearman's rho	**Average Frequency of Attendance '02 & '03**	**Correlation Coefficient**	**1.000**	**-0.301***
		Sig. (2-tailed)	**.**	**.018**
		N	**61**	**61**
	Years Since Registration	**Correlation Coefficient**	**-0.301**	**1.000**
		Sig. (2-tailed)	**0.018**	**.**
		N	**61**	**61**

* Correlation is significant at the .05 level (2-tailed).

Appendix XI

Regression and Correlation between Duration of Treatment and Average Drug Cost Per Month

Regression

Descriptive Statistics

	Mean	**Std. Deviation**	**N**
Average Drug Cost Per Month	**1175.17**	**1462.36**	**61**

Years Since Registration	**2.99**	**3.97**	**61**

		Average Drug Cost per month	**Years since Registration**
Pearson Correlation	**Average Drug Cost per month**	**1.000**	**-0.080**
	Years since Registration	**-0.080**	**1.000**
Sig. (1-tailed)	**Average Drug Cost per month**	**.**	**0.271**
	Years since Registration	**0.271**	**.**
N	**Average Drug Cost per month**	**61**	**61**
	Years since Registration	**61**	**61**

Correlations

			Average Drug Cost per month	**Years Since Registration**
Kendall's tau_b	**Average Drug Cost per month**	**Correlation Coefficient**	**1.000**	**-0.252**
		Sig. (2-tailed)	**.**	**0.004**
		N	**61**	**61**
	Years Since Registration	**Correlation Coefficient**	**-0.252**	**1.000**

		Sig. (2-tailed)	**0.004**	**.**
		N	**61**	**61**
Spearman's rho	**Average Drug Cost per month**	**Correlation Coefficient**	**1.000**	**-0.361**
		Sig. (2-tailed)	**.**	**0.004**
		N	**61**	**61**
	Years Since Registration	**Correlation Coefficient**	**-0.361**	**1.000**
		Sig. (2-tailed)	**0.004**	**.**
		N	**61**	**61**

Appendix XII

T-Test for Equality of Means for Mean Frequency of Attendance in Patients with and Without Non-Psychiatric Comorbid Disorders

T-Test

Group Statistics

	Non Psychiatric Comorbid Disorder	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**

Average Frequency of Attendance	**Present**	**30**	**6.543**	**2.2122**	**.4039**
	Absent	**30**	**5.456**	**2.1364**	**.3900**

Independent Samples Test

		t-Test for equality of means						
		t	**Df**	**Sig. (2-tailed)**	**Mean Difference**	**Std. Error Difference**	**95% Confidence Interval of the Difference**	
							Lower	**Upper**
Average Frequency Of Clinic Visit	**Equal variances assumed**	**1.936**	**58**	**0.058**	**1.087**	**0.56**	**-0.037**	**2.21**
	Equal variances not assumed	**1.936**	**57.93**	**0.058**	**1.087**	**0.56**	**-0.037**	**2.21**

Appendix XIII

T-Test for Equality of Means for Mean Frequency of Attendance in Patients with and Without Psychiatric Comorbid Disorders

T-Test

Group Statistics

	Psychiatric Comorbid Disorder	N	Mean	Std. Deviation	Std. Error Mean
Average Frequency Of Attendance	Present	8	6.746	3.7103	1.3118
	Present	52	5.885	1.9327	.2680

Independent Samples Test

		t-Test for equality of means						
		T	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Avrg. Freq. Of Clinic Visit	Equal variances assumed	1.02	58	0.312	0.861	0.8446	-0.8296	2.5517
	Equal variances not assumed	0.64	7.595	0.539	0.861	1.3389	-2.2553	3.9774

Appendix XIV

T-Test for Equality of Means for Mean Frequency of Attendance in Patients with or Without Comorbid Disorders

T-Test

Group Statistics

	Presence Of Comorbid Disorder	N	Mean	Std. Deviation	Std. Error Mean
Average Frequency Of Clinic Visit	Present	30	6.543	2.2122	0.4039
	Absent	30	5.456	2.1364	0.3900

Independent Samples Test

		t-test for Equality of Means						
		t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Averg. Freq. of Clinic Visit	Equal variances assumed	1.33	58	0.189	0.77	0.57	-0.39	1.92
	Equal variances not assumed	1.34	55.922	0.185	0.77	0.57	-0.38	1.91

Appendix XV

T-Test for Equality of Means for Average Cost to Treat Per Month in Patients with or Without Psychiatric Comorbid Disorder

T-Test

Group Statistics

	Comorbid Psychiatric Disorder	N	Mean	Std. Deviation	Std. Error Mean
Average Drug Cost Per Month	**Present**	**8**	**1159.92**	**1429.50**	**505.40**
	Absent	**53**	**1177.47**	**1480.67**	**203.39**

Independent Samples Test

		t-Test for equality of means						
		t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Average Drug Cost Per Month	Equal variances assumed	-0.03	59	0.97	-17.6	559.4	-1136.8	1101.7
	Equal variances not assumed	-0.03	9.42	0.97	-17.6	544.8	-1241.7	1206.6

Appendix XVI

T-Test for Equality of Means for Average Cost to Treat Per Month in Patients with or Without Non Psychiatric Comorbid Disorder

T-Test

Group Statistics

	Non Psychiatric Comorbid Disorder	N	Mean	Std. Deviation	Std. Error Mean
Average Drug Cost Per Month	Present	31	1000.52	705.62	126.73
	Absent	30	1355.64	1960.39	357.92

Independent Samples Test

		t-Test for equality of means						
		t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Average Drug Cost Per Month	Equal variances assumed	-0.95	59	0.35	-355.1	374.8	-1105.18	394.9
	Equal variances not assumed	-0.93	36.18	0.36	-355.1	379.7	-1125.04	414.8

Appendix XVII

T-Test for Equality of Means for Average Cost to Treat Per Month in Patients With or Without Comorbid Disorders

T-Test
Group Statistics

	Comorbid Disorder	N	Mean	Std. Deviation	Std. Error Mean
Average Drug Cost Per Month	Present	35	1067.05	916.57	154.93
	Absent	26	1320.70	1987.83	389.85

Independent Samples Test

		t-Test for equality of means						
		t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Average Drug Cost Per Month	Equal variances assumed	-0.67	59	0.507	-253.7	380.4	-1014.79	507.49
	Equal variances not assumed	-0.60	32.92	0.550	-253.6	419.5	-1107.21	599.92

Appendix XVIII
T-Test for Equality of Means for Mean Age at Registration in Patients with or Without Comorbid Disorders

T-Test

Group Statistics

	Comorbid Disorder	N	Mean	Std. Deviation	Std. Error Mean
Age At Registration	Present	35	39.54	12.108	2.047
	Absent	26	32.00	9.604	1.884

Independent Samples Test

		t-Test for equality of means						
		t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
							Lower	Upper
Age At Reg.	Equal variances assumed	2.62	59	0.011	7.54	2.88	1.78	13.30
	Equal variances not assumed	2.71	58.71	0.009	7.54	2.78	1.98	13.11

Appendix XIX

ANXIETY DISORDERS DATA FORM

Q1. Unit Number

Q2. Number of clinic attendances within the last ten years

Q2i -2004	Q2vi-1999
Q2ii-2003	Q2vii-1998
Q2iii- 2002	Q2viii-1997
Q2iv-2001	Q2ix-1996
Qv-2000	Q2x-1995

Q3. Average frequency of clinic attendance:

Q3i- Using years in which clinic was attended only

Q3ii-Using all years patient attended clinic.

Q4. Sex:

01-Male

02-Female

03-Not recorded

Q5. Availability of initiated medical records (e.g. clerking):

01- Available

02- Not available.

Q6. Age at first registration:

Q7. Years since first registration:

Q8. Nationality:

01-Nigerian

02-Non Nigerian

03-Not recorded.

Q9. Geopolitical zone:

01-South West	05-North East
02-South East	06-North West
03-South South	07-Not applicable
04-North Central	08-Not recorded

Q10. State of Origin:

001-Abia	014-Enugu	027-Ogun
002-Adamawa	015-Gombe	028-Ondo
003-Akwa Ibom	016-Imo	029-Osun
004-Anambra	017-Jigawa	030-Oyo
005-Bauchi	018-Kaduna	031-Plateau
006-Bayelsa	019-Kano	032-Rivers
007-Benue	020-Katsina	033-Sokoto
008-Borno	021-Kebbi	034-Taraba
009-Cross River	022-Kogi	035-Yobe
010-Delta	023-Kwara	036-Zamfara
011-Ebonyi	024-Lagos	037-Abuja
012-Edo	025-Nasarawa	038-not recorded
013-Ekiti	026-Niger	039-Not applicable

Q11. Local Government area:

Q12. Place of origin:

Q13. Ethnicity:

01-Hausa

02-Yoruba

03-Igbo

09-Not applicable

Q14. Religion:

01-Christian

02-Islam

03-Traditional

07-Not recorded

Q14i. Denomination:

01-Protestants

02-Catholics

03- Not applicable.

Q15. Marital status:

01-Single

02-Married

03-Separated

04-Divorced

Q16. For married men only, Number of wives:

1-01

2-01

3-03

4-04

5- >4 Specify.-

06-Not recorded

07-Not applicable (i.e. Single, never married)

09- Not applicable (Female). .

Q17. For married women only: number of times married

1-01

2-02

3-03

4-04

5->4 specify

06-Not recorded

07-Not applicable (single women, never married)

09- Not applicable (male).

Q18. Number of children

01-1-2

02-3-4

03-5-6

04-7-8

05->8-specify

06-Unknown/not recorded

09- Not applicable (singles, never married).

Q19. Accompanying persons to clinic:

01-Father	06-Wife	11-Friend
02-Mother	07-Uncle	12-Niece
03-Brother	08-Aunty	13-Cousin
04-Sister	09-Aunt	99-Not recorded
04-Husband	10-Daughter	

Q20. Accompanying persons to clinic indicate number of times:

20i-Alone	20vi-Husband	20xi-Daughter
20ii-Father	20vii-Wife	20xii-Friend
20iii-Mother	20viii-UNcle	20xiv-Cousin
20iv-Brother	20ix-Aunt	20xv-Not recorded/mentioned
20v-Sister	20x-Son	

Q21. Calculate percentage times accompanied:

Q22. Highest Educational level attained:

01-None (i.e Never been to school)

02- Koranic school.

03-Preprimary School

04-Primary school uncompleted

05-Primary school completed

06-Junior secondary school uncompleted

07-Junior secondary school completed

08-Senior secondary school uncompleted

09-Senior secondary school completed

10-Tertiary education uncompleted

11-Tertiary education completed.

13-Post graduate

14-Adult literacy

99-not recorded

Q23. Occupation:

01-Farmer	10-Doctor
02-Petty trader	11-Lawyer
03- Businessman/Contractor.	12-Students
04-Driver/Mechanic/Carpenter	13-Unemployed
05- Civil/Servant.	14-Housewife
06-Teacher/Lecturer	15-Unemployed
08- Police/Soldier	16-Retiree
09-Health worker	17-Engineer

99-Not recorded/unknown

Q24. Estimated annual income:

Q25. Residence:

01-Kaduna Metropolis

02- Within Kaduna state

03-Outside Kaduna state

PART II

MEDICAL HISTORY

Q26. Specific diagnosis:

01-Anxiety disorder unspecified

02- Mixed anxiety disorder.

03-Mixed anxiety depressive

04- Generalized anxiety disorder

05- Panic anxiety disorder.

06-Anxiety/hypomania

07-Anxiety/hallucination

08-Anxiety/Neurosis

09- Anxiety/Somatic symptoms.

Q27. Family history of anxiety disorders:

01-Yes

02-No

03-Don't know

04-Not recorded.

Q27i. Specify disorder:

Q28. Family history of anxiety disorder, Relationship:

01-Father

02-Mother

03-Siblings

04-Paternal Grand parents

05-Maternal Grand parents

06-Cousin

07-Not recorded

09-Not applicable

Q29. Signs and symptoms which patient presented with:

1. Abdominal discomfort (fluffiness, tenderness, pains)

2. Abdominal felines in the head
3. Anorexia
4. Anxious mood
5. Blurred vision
6. Chest pain
7. choking sensation
8. cold sensation in feat
9. constipation
10. Crawling sensation in the body (moving pulsating Sensation)
11. Difficulty in interacting with people
12. Difficulty in sitting up
13. Dizziness
14. Dry mouth
15. easily startled
16. easily upset
17. eats excessively
18. Epigastria pain
19. excessive sleep
20. excessive worries
21. excessive anger
22. faintness
23. fears (specific)
24. fears (specific)

25. feel like defecating

26. feel sad (depression)

27. feel light

28. fever episodes

29. forgetfulness

30. giddiness

31. headache

32. hopelessness

33. hunger

34. increased ventilation

35. insomnia

36. internal heat

37. intrusive thoughts

38. lack of personal care

39. loss of sexual desire

40. low energy

41. low mood

42. muscle spasm

43. nausea and vomiting

44. negative thoughts

45. nervousness

46. nightmares

47. noise in the left ear (tinnitus)

48. obsessionnal thoughts

49. obsessions with though of failure

50. olfactory hallucination

51. palpitations

52. panic

53. pessimistic

54. poor vision

55. pounding sounds in the head

56. pulsating vortex of head

57. restlessness

58. shallow breathing

59. shortness of breath

60. somatic complains

61. sore in the mouth

62. suicidal tendencies

63. suspiciousness

64. sweating

65. talkativeness

66. tension easily cries

67. tremor (trembling)

68. unable to concentrate

69. weakness

70. weight loss

71. Aches and pains.

Q30. Co morbid Psychiatric disorder:

01- Dementia.

02-Depression

03-Drug/Substance use

04-Obsession

05-parkinsonism

06-Psychosomatic complains

07- Schizophrenia.

80-Somataization disorder

09- None.

Q31. Co morbid non psychiatric disorder

01-asthma	06-Entamoeabu histolitica	11-Tuberculosis
02-Diabetes	07-HIV/AIDS	12-Typoid fever
03-Diarrhoea	08-Hypertension	13-UTI
04-Dysurea	09-Malaria	99-None
05-Ear infection	10- Peptic ulcer disorder	

Q32 Basic life style information

01- Physical exercise.	06-Other drug/substance use
02- Other recreational activities	07- Multiple sex partners.
03-Alcohol consumption	08-Coffee
04-Tobacco use	09-Nore (i.e. of the above)
05-Marijuana	10-Not recorded (record not available).

Q33. Number of times hospitalized for psychiatric illness in the last ten years.

Q33i-2004	Q33vi-1999
Q33ii-2003	Q33vii-1998
Q33iii-2002	Q33viii-1997
Q33iv-2001	Q33ix-1996
Q33v-2000	Q33x-1995

NB.-O-Not hospitalised.

Q34. Average number of hospitalization per year:

Q35. Total duration of psychiatric hospitalization:

Q35i.-2003

Q35ii-2004

O-Not hospitalized

99-Not known

Q36. Hospital in which patient was hospitalized:

01-ABUTH

02-Psychiatric Hospital Barnawa

03-Barau Dikko specialist hospital

05-Not recorded

07- Not hospitalized

Q37. Laboratory Investigations carried out:

01-Culture and sensitivity

02- Electro encephalogram (EEG).

03-General hematological/investigations (Hb, PVC etc)

04-HIV screening

05-Liver function test

06-Malaria parasite

07-Serum glucose

08- Serum urea /electrolyte /creatinine.

09-Stool microscopy

10-Urinalysis

11-Urine microscopy

12-FBC and Differentials

13-Widal test

15-Abdominal ultrasound

16- Mantoux.

17- VDRL.

18-X-ray

19-FBS

20-Serum protein

21-Occult blood

99-None

PART III

DRUG TREATMENT HISTORY AND NON-DRUG ASPECTS OF MANAGEMENT

Q38. Psychiatric drug used:

Q39. Side effects experienced with drug use.

1. abdominal discomfort
2. abdominal pain
3. amenorrhea
4. anorexia
5. blurred vision
6. canesthetic hallucination
7. chest pain
8. constipation
9. crawling sensation in the body
10. depressed feelings (sadness)
11. drug allergy
12. dry cough
13. dryness of mouth
14. dyspepsia
15. dysphasia
16. dizziness
17. emotional upset
18. epigastric pain
19. epitasis

20. excessive sleep

21. excessive salivation

22. feeling afraid feels like something in his

23. head

24. forgetfulness

25. furuncle

26. headache

27. insomnia

28. internal heat

29. joint pains

30. neck and back pains

31. nervousness

32. offensive odor from nose

33. palpitation

34. poor erection

35. prickly sensation

36. purities

37. sensation in the ear (tinnitus)

38. somatic complains

39. suicidal thoughts

40. vertigo

41. weakness

42. weight gain

43. irritation of throat

44. tremors

45. difficulty in concentrating

46. restlessness.

99. none

Q40. Management of side effects:

01-discontinuation

02-Use of other drugs

03-Reduction in dosage

04-Increase in dosage of drug

05- Reduction in frequency of administration.

06-Take drug at a different time (at night)

07-Counseled

09-None

Q41. Reasons for drug discontinuation:

01-Side effects

02-Therapeutic failure

03-Non compliance/Adherence

04-Prohibitive cost

05-Not mentioned

09-Not applicable

Q42. Alternative drugs following discontinuation:

Q43. Individualized pharmacy records:

01-Available

02-Not available

Q44. Non pharmacological management :

Q44i-ECT

Q44ii-Insight Counseling

Q44iii- Counseling with family

Q44iv-Group Counseling

Q44v-Psycotherapy

Q44vi- Cognitive Behavioral therapy.

Q44vii-Relaxation therapy

NB-0- None

Q45. Number of Relapses:

Q45i-2003

Q45-2004

NB-0- No Relapse

Q46. Average number of relapses per year:

Q47. Reasons for relapses:

01-Abscondment

02-Therapeutic failure

03-Non-compliance

04-Prohibitive cost

05-Not applicable

06-Not recorded

Q48. Number of clinic defaults:

Q49. Assessment of drug compliance:

Appendix XX **Diagnosis, Direct and Indirect Cost Sources for Patients Suffering from Anxiety Disorders Visiting ABUTH in 2003 and 2004**

S/N	Specific Diagnosis	Comorbid Psychiatric Disorder	Comorbid Non-Psychiatric Disorder	Cost of Anxiolytic Drugs (in Naira)	Cost of Non-Anxiolytic Drugs (in Naira)	Duration of Drug Use	Total Cost of Drug (in Naira)	Average Cost of Drug Per Month (in Naira)	Cost of Laboratory Investigation (in Naira)	Place of Residence	Percentage Number of Times Accompanied to Clinic
1	GAD	None	Ear Infection	4095.00	2762.00	588	6857.00	349.85	0.00	Kaduna Metropolis	36.88
2	MADD	None	None	2184.00	3640.00	413	5824.00	423.05	0.00	Kaduna Metropolis	0.00
3	GAD	None	None	2488.50	829.50	553	3318.00	180.00	0.00	Kaduna Metropolis	5.26
4	GAD	None	Malaria, Typhoid Fever	12845.50	688.50	235	13534.00	1,727.74	0.00	Outside Kaduna Metropolis	60.00
5	GAD	None	None	2956.50	1027.50	377	3984.00	317.03	0.00	Outside Kaduna Metropolis	0.00
6	MADD	None	Hypertension	3567.00	12432.00	492	15999.00	975.55	0.00	Kaduna Metropolis	0.00
7	GAD	None	Asthma	4498.00	3255.00	325	7753.00	715.66	0.00	Outside Kaduna State	0.00
8	MADD	None	UTI	3573.00	16825.00	713	20398.00	858.26	3100.00	Kaduna Metropolis	75.00
9	GAD	None	Hypertension, Malaria	7624.00	1171.50	536	8795.50	492.29	0.00	Kaduna Metropolis	0.00
10	GAD	None	None	4704.00	336.00	336	5040.00	450.00	0.00	Outside Kaduna Metropolis	30.00
11	MADD	None	Hypertension	10332.00	21725.55	378	32057.55	2,544.25	0.00	Kaduna Metropolis	13.33
12	GAD	None	None	4210.50	672.00	336	4882.50	435.94	0.00	Kaduna Metropolis	0.00

S/N	Specific Diagnosis	Comorbid Psychiatric Disorder	Comorbid Non-Psychiatric Disorder	Cost of Anxiolytic Drugs	Cost of Non-Anxiolytic Drugs	Duration of Drug Use	Total Cost of Drug Used	Average Cost of Drug Per Month	Cost of Lab Inv	Place of Residence	Percentage Number of Times Accompanied to Clinic
13	MADD	None	None	4963.00	668.00	270	5631.00	625.67	0.00	Outside Kaduna State	58.33
14	GAD	None	Hypertension, UTI	11630.50	18819.50	371	30450.00	2,462.26	4700.00	Kaduna Metropolis	14.29
15	MADD	None	None	6437.00	747.00	245	7184.00	879.67	0.00	Kaduna Metropolis	0.00
16	MADD	None	Hypertension	8486.50	302.50	337	8789.00	782.40	2750.00	Kaduna Metropolis	0.00
17	GAD	None	None	3290.00	432.00	168	3722.00	664.64	2150.00	Kaduna Metropolis	28.57
18	GAD	None	None	966.00	18984.00	140	19950.00	4,275.00	0.00	Kaduna Metropolis	0.00
19	GAD	None	None	8204.00	1456.00	32	9660.00	9,056.25	4250.00	Kaduna Metropolis	77.78
20	GAD	None	None	4489.00	812.00	232	5301.00	685.47	2210.00	Kaduna Metropolis	0.00
21	GAD	None	Hypertension	3917.00	3813.04	161	7730.04	1,440.38	2100.00	Outside Kaduna Metropolis	0.00
22	GAD	None	None	4200.00	360.00	280	4560.00	488.57	3550.00	Kaduna Metropolis	31.03
23	GAD	Somatization Disorder	None	1330.00	5912.00	0	7242.00	0.00	0.00	Kaduna Metropolis	0.00
24	GAD	None	Malaria, Diarrhoea	840.00	4340.00	280	5180.00	555.00	3150.00	Kaduna Metropolis	0.00
25	GAD	None	Typhoid Fever	3108.00	518.00	517	3626.00	210.41	0.00	Kaduna Metropolis	0.00
26	GAD	None	None	2940.00	630.00	252	3570.00	425.00	0.00	Kaduna Metropolis	8.00

S/N	Specific Diagnosis	Comorbid Psychiatric Disorder	Comorbid Non-Psychiatric Disorder	Cost of Anxiolytic Drugs	Cost of Non-Anxiolytic Drugs	Duration of Drug Use	Total Cost of Drug Used	Average Cost of Drug Per Month	Cost of Lab Inv	Place of Residence	Percentage Number of Times Accompanied to Clinic
27	GAD	Somatization Disorder	Malaria	2818.00	546.00	336	3364.00	300.36	1800.00	Kaduna Metropolis	0.00
28	GAD	None	None	1578.50	231.00	203	1809.50	267.41	0.00	Kaduna Metropolis	12.50
29	GAD	None	None	4956.00	658.00	52	5614.00	3,238.85	0.00	Outside Kaduna Metropolis	0.00
30	GAD	None	None	4680.00	301.00	185	4981.00	807.73	0.00	Outside Kaduna Metropolis	10.00
31	GAD	None	Typhoid Fever, Hypertension	5827.50	1505.00	273	7332.50	805.77	0.00	Kaduna Metropolis	0.00
32	GAD	None	None	3570.00	8744.00	84	12314.00	4,397.86	0.00	Kaduna Metropolis	0.00
33	GAD	None	None	5334.00	644.00	549	5978.00	326.67	0.00	Kaduna Metropolis	0.00
34	GAD	None	None	2247.00	1428.00	266	3675.00	414.47	0.00	Outside Kaduna Metropolis	0.00
35	Panic disorder.	None	None	3220.00	2370.00	602	5590.00	278.57	0.00	Outside Kaduna Metropolis	61.11
36	GAD	None	Typhoid Fever	6083.00	5970.00	294	12053.00	1,229.90	3700.00	Outside Kaduna State	30.77
37	GAD	Schizophrenia	None	1008.00	7056.00	224	8064.00	1,080.00	2750.00	Kaduna Metropolis	20.00
38	GAD	Somatization Disorder	None	2681.00	538.00	140	3219.00	689.79	2050.00	Kaduna Metropolis	20.00

S/N	Specific Diagnosis	Comorbid Psychiatric Disorder	Comorbid Non-Psychiatric Disorder	Cost of Anxiolytic Drugs	Cost of Non-Anxiolytic Drugs	Duration of Drug Use	Total Cost of Drug Used	Average Cost of Drug Per Month	Cost of Lab Inv	Place of Residence	Percentage Number of Times Accompanied to Clinic
39	GAD	None	Malaria, Typhoid Fever	1421.00	168.00	98	1589.00	486.43	1900.00	Kaduna Metropolis	83.33
40	GAD	None	Diarrhoea	5453.00	574.00	574	6027.00	315.00	0.00	Outside Kaduna Metropolis	0.00
41	GAD	None	Hypertension	10563.00	1806.00	595	12369.00	623.65	0.00	Outside Kaduna Metropolis	100.00
42	GAD	None	Hypertension	2225.25	1603.00	315	3828.25	364.60	0.00	Outside Kaduna Metropolis	0.00
43	MADD	None	None	4816.00	1848.00	252	6664.00	793.33	2450.00	Outside Kaduna Metropolis	27.27
44	GAD	Somatization Disorder, Depression	Malaria	3986.50	3005.75	245	6992.25	856.19	0.00	Kaduna Metropolis	0.00
45	MADD	None	Diabetes, Hypertension	13076.00	0.00	252	13076.00	1,556.67	0.00	Kaduna Metropolis	28.57
46	GAD	None	Typhoid Fever	4221.00	443.50	238	4664.50	587.96	3050.00	Kaduna Metropolis	0.00
47	GAD	None	None	4788.00	723.80	325	5511.80	508.78	0.00	Kaduna Metropolis	36.36
48	MADD	None	Typhoid Fever	11094.50	1244.50	403	12339.00	918.54	1300.00	Kaduna Metropolis	0.00
49	GAD	Parkinsonism	Diabetes	4333.00	2224.00	336	6557.00	585.45	2700.00	Outside Kaduna Metropolis	26.67
50	GAD	None	None	363.00	56.00	110	419.00	114.27	350.00	Kaduna Metropolis	0.00

S/N	Specific Diagnosis	Comorbid Psychiatric Disorder	Comorbid Non-Psychiatric Disorder	Cost of Anxiolytic Drugs	Cost of Non-Anxiolytic Drugs	Duration of Drug Use	Total Cost of Drug Used	Average Cost of Drug Per Month	Cost of Lab Inv	Place of Residence	Percentage Number of Times Accompanied to Clinic
51	GAD	None	Hypertension	2571.75	4595.00	329	7166.75	653.50	0.00	Kaduna Metropolis	0.00
52	GAD	Depression	Hypertension	7154.00	6920.94	350	14074.94	1,206.42	2000.00	Kaduna Metropolis	0.00
53	GAD	None	None	6079.50	1973.66	315	8053.16	766.97	2400.00	Outside Kaduna Metropolis	11.11
54	GAD	None	Malaria	5631.50	432.00	287	6063.50	633.82	2300.00	Kaduna Metropolis	33.33
55	GAD	Depression	None	19337.50	31747.00	336	51084.50	4,561.12	700.00	Kaduna Metropolis	58.82
56	GAD	None	None	1505.00	16614.00	196	18119.00	2,773.32	3100.00	Kaduna Metropolis	14.29
57	GAD	None	UTI	7420.00	1218.00	308	8638.00	841.36	3000.00	Kaduna Metropolis	0.00
58	OCD	None	None	3633.00	36.00	148	3669.00	743.72	0.00	Kaduna Metropolis	0.00
59	GAD	None	Malaria, Typhoid Fever	3842.00	574.00	175	4416.00	757.03	300.00	Kaduna Metropolis	0.00
60	GAD	None	Hypertension	67.50	14168.00	154	14235.50	2,773.15	0.00	Outside Kaduna Metropolis	53.33
61	GAD	None	Hypertension	1827.00	11085.93	161	12912.93	2,406.14	1250.00	Kaduna Metropolis	100.00

Key
GAD: Generalised Anxiety Disorders
MADD: Mixed Anxiety Depressive Disorders
UTI: Urinary Tract Infections