PHARMACOTHERAPEUTICS OF MOOD DISORDERS IN PATIENTS ATTENDING NEURO PSYCHIATRIC CLINIC, AHMADU BELLO UNIVERSITY TEACHING HOSPITAL (ABUTH) ZARIA-NIGERIA

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DECLARATION

I declare that the work in the thesis entitled 'Pharmacotherapeutics of mood disorders in patients attending neuropsychiatry unit, Ahmadu Bello University Teaching Hospital, Shika, Nigeria' has been performed by me in the Department of Pharmacology and Clinical Pharmacy under the supervision of Professor (Mrs.) H.O. Kwanashie, Professor Isa Hussaini 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.

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CERTIFICATION

This thesis entitled "PHARMACOTHERAPEUTICS OF MOOD DISORDERS IN PATIENTS ATTENDING NEURO PSYCHIATRY UNIT, AHMADU BELLO UNIVERSITY TEACHING HOSPITAL, SHIKA, NIGERIA" by AIYELERO, Oyeronke Medinat 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

I specially dedicate this work to Almighty Allah. "All thanks are to Allah the cherisher of the worlds". And also to my parents Alhaji & Alhaja Aiyelero who are always my source of inspiration.

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ABSTRACT

Mood disorders (primary major depressive disorder and bipolar affective disorder) constitute one of the world's greatest public health problems and are associated with significant reductions in productivity, health and longevity. This study involved a retrospective analysis of data obtained from hospital records of patients using this facility for a one year period spanning January 1st 2006 to December 31st, 2006. The study population was 887 patients. This study was carried out to describe prevalence, management, and burden of mood disorders among patients who attended clinic at the neuro-psychiatry unit of Ahmadu Bello University Teaching Hospital, Shika.

Average clinic attendance in year 2006 was 48.47. With respect to relative occurrence, mood disorders (26%) ranked lower than schizophrenia (39.8%) but higher than seizure disorders (12.9%) and anxiety disorders (8.2%). Majority of the patients were female (62.1%), married (57.2%), Hausa (59.3%) and of Muslim faith (77.2%). Most were below thirty (57.2%) and had been attending clinics for five years or less. The mean age of patients was 28.3 years at index episode of mood disorders. More than half of patients with mood disorders (50.7%) were unemployed and 25.5% of these patients had tertiary education. Depression was the most prevalent subtype of mood disorders (52.4%). Bipolar affective disorders (32.4%), hypomania (9.0%) and mania (4.1%) were other subtypes of mood disorders identified. Only 24.8% of patients had record showing family history of mental disorder.

Nearly two-third (64.8%) of patients with mood disorders had co-morbid diagnosis. Non-psychiatric co-morbid disorders (37.2%) were more prevalent than psychiatric co-morbid which were present in 27.6% patients. Malaria (15.7%) was the most commonly-occurring non-psychiatric co-morbid disorder while schizophrenia (9.0%) was the most prevalent psychiatric co-morbid diagnosis.

Signs and symptoms varied and they included insomnia (which were the most prevalent), irrational talkativeness, dysphoric mood, loss of appetite and anxious mood. Haematological investigations (19.8% of patients), serum/urea/electrolyte/creatinine (18.0%), WBC differential (14.8%) was the most frequently requested laboratory investigations. Management of mood disorders involved the use of pharmacotherapy only (35.2%) or a combination of psychotherapy and pharmacotherapy. Drugs employed included amitriptylline (used in 63.4% of patients), imipramine (12.4%) nitrazepam (45.5%), diazepam injection (35.2%) and bromazepam (4.8%). Antipsychotics used included trifluoperazine (in 52.4%), haloperidol injection (45.5%), and chlorpromazine tablets (37.9%) among others. Mood stabilizers used included carbamazepine (in 35.2%) and sodium valporate (in 7.6%). Other drugs used were benzhexol which had the highest usage (83.4%) among patients with mood disorders in this study. Non-pharmacological approaches to treatment included ECT in 46.8% of patients, insight counseling (23.4%) and psychotherapy (7.4%). Drug use was accompanied by side effects which included weakness (13.1% of patients,) headache (8.7%), excessive sleep (8.1%) insomnia (7.2%) and dizziness (1.9%) among others.

Reduction in dosage (in 22.8% patients), use of other drugs to remedy adverse events (22.1%), discontinuation and use of alternative drugs (13.1%), and reduction in frequency of administration (6.2%) were methods employed in management of side effects.

Annual drug cost far outweighed cost of laboratory investigations. An average cost of N15,772.27 per patient per annum was spent on drugs for psychiatric disorders while the mean cost of total drugs was N18,136.04 per year. This is considered high in relation to Nigeria's per capital income of N4.46 as most of these patients (76.2%) were

unemployed and were dependent on caregivers. There was no significant different in cost of drugs as regards type of mood disorders.

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LIST OF ABBREVIATIONS

5-HT	-	5-hydroxytryptamine
ABUTH	-	Ahmadu Bello University Teaching Hospital
Ach	-	Acetylcholine
ACTH	-	Adrenocorticotrophic hormone
AR	-	adrenoreceptors
BAD	-	Bipolar affective disorder
BDNF	-	Brain-derived neurotrophic factor
CNS	-	Central nervous system
CRF	-	Corticotropin-Releasing Factor
CSF	-	Cerebrospinal Fluid
DA	-	Dopamine
DSM-IV	-	Diagnostic and statistical manual of mental disorder-fourth edition
GABA	-	Gamma amino butyric acid
HPA	-	Hypothalamo-pitutary-adrenal axis
ICD-10	-	International classification of diseases and related health disorders- tenth edition
MAOI	-	Monoamine Oxidase Inhibitor
NA	-	Noradrenaline
NOS	-	Not otherwise specified
SSRI	-	Selective serotonin re-uptake inhibitors
TCAD	-	Tricyclic antidepressant
WHO	-	World Health Organization
α	-	Alpha
β	-	Beta
γ	-	Gamma

CHAPTER ONE
INTRODUCTION

1.1 INTRODUCTION

Mental health can be conceptualized as a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community. (WHO, 2007). Mental disorders on the other hand are characterized by some combination of abnormal thoughts, emotions, behaviour and relationships with others. Examples are schizophrenia, mood disorders, mental retardation and disorders due to drug abuse (WHO, 2008).

Mental, neurological and behavioural disorders are common to all countries and cause immense suffering. People with these disorders are often subjected to social isolation, poor quality of life and increased mortality. These disorders are the cause of staggering economic and social costs and thus, are growing public health concern. (WHO 2008, Kohn et al, 2004). These disorders are highly prevalent and exact a high emotional toll on individuals, families, and society. Worldwide, community-based epidemiological studies have estimated rates of lifetime prevalence of mental disorders among adults ranging from 12.2% to 48.6% and 12-month prevalence rates ranging from 8.4% to 29.1% . These rates do not include neurological conditions affecting the brain (Kohn *et al., 2004*).

Hundreds of millions of people worldwide are affected by mental, behavioural, neurological and substance use disorders. Today, 450 million people suffer from mental or behavioural disorder and only a small minority of them receives the most basic treatment (WHO, 2005). Estimates made by WHO in 2002 showed that 154 million people globally suffer from depression and 25 million people from schizophrenia; 91 million people are affected by alcohol use disorders and 15 million by drug use disorders. Mood disorders (including

depression) are estimated to affect some 340 million people at any given time (WHO,2008). A recently published WHO report shows that 50 million people suffer from epilepsy and 24 million from Alzheimer and other dementias. In addition to the above figures, many other disorders affect the nervous system or produce neurological sequelae. Projections based on a WHO study show that worldwide in 2005, 326 million people suffered from migraine; 61 million from cerebrovascular diseases; 18 million from neuroinfections or neurological sequelae of infections. Number of people with neurological sequelae of nutritional disorders and neuropathies (352 million) and neurological sequelae secondary to injuries (170 million) also add substantially to the above burden (WHO, 2008). Some of the common mental conditions prevalent in the African Region include: schizophrenia (occurring in about 3% of the population), epilepsy, organic mental disorders, children's mental health problems (occurring in about 3% of children under nine years of age), post-traumatic stress disorders (which is rife in conflict-affected areas), common mental disorders (occurring at a rate of 20-30% among the population) and psychoactive substance abuse (WHO,1999).

1.2 STATEMENT OF RESEARCH PROBLEM

According to major studies by World Health Organization (WHO 2004), up to half of all people with serious mental disorders in the developed countries (like US and Europe) are not yet receiving treatment and the situation is even worse in some developing countries. The first WHO World Mental Health survey report (WHO 2004) included data from 14 countries (eight developed, six less developed including Nigeria) on prevalence, severity and treatment of mental disorders including mood disorders (WHO 2004). In the Nigerian context, mental illness is still highly stigmatized (Gureje *et al.*, 2005); symptoms of such illness might be embarrassing and therefore such patient finds it difficult to seek out proper treatment.

Mood disorders are among the most prevalent, recurrent and disabling of all illnesses (Costello *et al.*, 2002). Recent surveys of the National Depressive and Manic-Depressive Association (National DMDA) in the USA, have shown that people with mood disorders

often have incorrect information about their illness, that misdiagnosis are frequent, significant physical patients communication gap exist and that non-adherence is wide spread.

For optimal recovery to occur, it is important that the individual receive correct information about their symptoms and treatments and that the physicians, pharmacists and other health care providers understand mood disorders from a patient's perspective. In addition, doctors/pharmacists and patients need to communicate fully throughout the course of treatment about symptoms, side effects and other concerns (Lewis, 2001). Increased awareness and openness about mood disorders can lead to increased acceptance, which, in turn, can lead to more timely diagnosis and treatment (Lewis, 2001).

A publication by the World Health Organization (2001) showed that mental health services were hampered by grossly inadequate personnel and facilities. For example, it has been reported that Nigeria had fewer than 100 psychiatrists for its population of about 114 million persons (Gureje *et al.,* 2005). In the context of our setting therefore, diversion of resources from mild or sub clinical cases to the more severe cases is not the solution. Providing more service to everyone in need may have to be determined by the presence of symptoms and associated impairment rather than by categorical diagnosis. It is also clear that in a setting with few specialists, medical or nursing staff, service can only be realistically provided to the many in need by primary health care workers with basic but relevant training in the identification and treatment of common mental disorders (Gureje *et al.,* 2005).

Effective pharmacotherapy has helped people suffering from mood disorders to recover from potentially devastating episodes of depression or mania and prevent possible relapses. (Kusumakar *et al.,*1997)

The current drug of choice in mood disorders are antidepressants [tricyclics, selctive serotonin re-uptake inhibitors (SSRIs) and monoanine oxidase inhibitors (MAOIs)] for depressive disorders while treatment of mania and depressive disorders with psychotic symptoms include the use of antipsychotic drugs (either typical or atypical). Other drugs used are carbamazepine, sodium valporate and lithium carbonate. In the course of this research

however, availability and affordability of all these drugs will be emphasized. And limitations to use of these drugs like costs, adverse effects, and contra-indications will be looked into. Why, then is this research necessary? The answer is that despite acknowledged progress, emphasis wants to be laid on the statistics of patients treated (that is those responding) and those that still go untreated (that is even after pharmacological interventions are still presenting with psychotic symptoms). Also, irrespective of availability of a reasonably safe and effective pharmacotherapy, are untreated patients associated with profound societal costs?

1.3 JUSTIFICATION OF STUDY

Pharmacotherapy is the area of pharmacy practice that ensures the safe, appropriate and economical use of medicines. Therefore, this research is justifiable in that it will give comprehensive data for rationale of drugs used in patients with mood disorders locally, relative to what obtained elsewhere.

Emphasis will be laid on evaluation of drug efficiency, appropriate changes in pharmacotherapeutic management of patients where it may include the discontinuation of treatment regimen, individualized adjustment of therapy in patients having unstable disease entities or management and monitoring of chronic drug therapy. In addition, this work will show how the physicians and pharmacists interprets the patient data (including medical history, physical findings) to design treatment plan and monitor the patient's response to the recommended dosage regimens.

Adherence to medications by mood disorder patients will be looked into in this work, as mood disorder is a chronic illness with recurrences. It has been noted that non-adherence to medication in mood disorder is common and a major barrier to treatment success (Nicola *et al.,* 2006). Increasing adherence should decrease risk of relapse, improve outcome and lessen cost. Intervention that focuses on the structure of care alongside increasing patient in

treatment have the great potential to improve adherence and hence outcome in mood disorders.

Another important aspect of pharmacotherapy is the economic cost of medications used in treatment of mood disorders. Therefore, the availability and affordability of these medications will be evaluated particularly as Nigeria is a developing country with high percentage of low income earners.

It should be noted that ABUTH where the study is to take place, is a referral hospital owned by the Federal government of Nigeria and a center of excellence by the Federal Ministry of Health. The psychiatry clinic gets referral not only from the different parts of the North but from neighbouring parts of the country. Therefore, data collected from this institution pertaining mood disorders will be highly useful and informative.

1.4 PROJECT AIM AND OBJECTIVES

The overall aim of the current study in which the proposed sample will cover all clinical attendance from January to December 2006, is to study the prescription patterns for patients with mood disorders at Ahmadu Bello University Teaching Hospital (ABUTH) and the type of drugs used. The specific objectives are to:

1. Study the relative occurrence of mood disorders vis-à-vis other psychiatry disorders as well as the subtypes of mood disorders.
2. Document the socio-demographic characteristic of mood disorder patients.
3. Study drug combinations (polypharmacy), the possible drug interactions, rationale behind each combination, dosing and dosing intervals of each drug.
4. Study the adverse effects of drug as seen in patients and how they are managed.

CHAPTER TWO

LITERATURE REVIEW

"Mood" is synonym for affect therefore mood disorders are also termed "affective disorders' because their main features is abnormality of mood, namely depression or elation (Gelder et al, 1999). Mood disorders are also 'brain disorder' meaning they are mediated through the brain, yet they disrupt every facet of a person's life: emotions, thought processes, behaviour and physical health (NIMH).

2.1 Classification of Mood Disorders

The main approaches to classification of mood disorders are International Classification of Diseases and Related Health Problems- Tenth Edition (ICD-10) developed by WHO, and Diagnostic and Statistical manual of mental Disorder-Fourth Edition (DSM-IV) which is developed and published by American Psychiatric Association (APA) (Fraser *et al.*, 2001). 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 compatible diagnosis. The classification of mood disorders given below is drawn from ICD-10. Although criteria used in ICD-10 are partly derive form DSM-IIIR, there are more flexible and clinical friendly, they do not pretend to impose arbitrary precision on the clinical universe of psychiatry (Kaplon and Sadock, 2000). The terms "Mania" and "Severe depression" are used in this classification to denote an intermediate state without delusions, hallucinations or complete disruption of normal activities which is often (but not exclusively) seen as patients develop or recover from mania.

CLASSIFICATION OF MOOD DISORDERS BY ICD-10

F30	Manic episode
F30.0	Hypomania
F30.1	Mania without psychotic symptoms
F30.2	Mania with psychotic symptoms
F30.8	Other manic episode
F30.9	Manic episode, unspecified
F31	Bipolar affective disorder
F31.0	Bipolar affective disorder, current episode hypomanic
F31.1	Bipolar affective disorder, current episode manic without psychotic symptoms
F31.2	Bipolar affective disorder, current episode manic with psychotic symptoms
F31.3	Bipolar affective disorder, current episode mild or moderate depression
.30	Without somatic syndrome
.31	With somatic syndrome
F31.4	Bipolar affective disorder, current episode severe depression without psychotic symptoms
F31.5	Bipolar affective disorder current episode severe depression with psychotic symptoms
F31.6	Bipolar affective disorder, current episode mixed
F31.7	Bipolar affective disorder, currently in remission
F31.8	Other bipolar affective disorders
F31.9	Bipolar affective disorder, unspecified
F32	Depressive episode
F32.0	Mild depressive episode
.00	Without somatic syndrome

.01	With somatic syndrome
F32.1	Moderate depressive episode
.10	Without somatic syndrome
.11	With somatic syndrome
F32.2	Severe depressive episode without psychotic symptoms
F32.3	Severe depressive episode with psychotic symptoms
F32.8	Other depressive episodes
F32.9	Depressive episode, unspecified
F33	Recurrent depressive disorder
F33.0	Recurrent depressive disorder, current episode mild
.00	Without somatic syndrome
.01	With somatic syndrome
F33.1	Recurrent depressive disorder, current episode moderate
.10	Without somatic syndrome
.11	With somatic syndrome
F33.2	Recurrent depressive disorder, current episode severe without psychotic symptoms
F33.3	recurrent depressive disorder, current episode psychotic symptoms
F33.4	Recurrent depressive disorder, current in remission
F33.8	Other recurrent depressive disorders
F33.9	Recurrent depressive disorder, unspecified
F34	Persistent mood (affective) disorders
F34.0	Cyclothymia
F34.1	Dysthymia
F34.8	Other persistent mood (affective) disorders

F34.9	Persistent mood (affective) disorder, unspecified
F38	Other mood (affective) disorders
F38.0	Other single mood (affective) disorder
.00	Mixed affective episode
F39.1	Other recurrent mood (affective) disorders
.10	Recurrent brief depressive disorders
F38.8	Other specified mood (affective) disorders
F39	Unspecified mood (affective) disorder

2.2 Epidemiology of Mood Disorders

Leading causes of years of live lived with disability estimates for year 2000 for unipolar depressive disorders was 11.9% and for bipolar affective disorder (both sexes and all ages) was 2.5% (WHO, 2001).

Depression can vary in severity from mild to very severe. It is most often episodic but can be recurrent or chronic (WHO, 2001). The prevalence of major depression for women is about twice that for men (Schiebe *et al.*, 2003; Gorman 2006; Lucht *et al.*, 2003). Global Burden Diseases (GBD) 2000 estimates the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women and that 5.8% of men and 9.5% of women will experience a depressive episode in a 12 month period. These prevalence figures vary across populations and may be higher in some populations (WHO, 2001). The point prevalence of bipolar disorder is around 0.4% according to GBD 2000 (WHO, 2001).

Studies have shown that depression occurs both at early age of onset (Solis *et al.*, 2006, Philibert *et al.*, 1997 and Schwenk *et al.*, 2004) and at late age of onset (Lavreteky *et al.*,

2005 and Nuyen *et al*., 2007). Bipolar (1) affective disorder on the other hand, has three subgroups based on age at onset which are early (17 years), intermediate (25 years) and late (40 years) (Bellivier *et al*., 2003 and Leboyer *et al*., 2005).

Depending on the study characteristics the relative occurrence of sub-types of depression (mood disorders) varies (Okulate *et al*.,2001). Co-existence of mood disorders with other psychiatric conditions (Merikangas *et al*., 2004; Cerullo *et al.,* 2007; Breiger *et al*., 2005; Harden *et al*., 2002) as well as non-psychiatric conditions (Wildes *et al*., 2006 and Valverde *et al*., 2007) have been studied extensively. Depression and presence of co-morbid medical conditions significantly predicted a low quality of life (Mosaku *et al*., 2008).

2.3 ETIOLOGY OF MOOD DISORDERS

Mood disorders are characterized by depression, mania, or both. In this section, biochemical hypothesis of affective disorders are presented. Depression and mania are thought to be heterogeneous illnesses that can result from dysfunction of several neurotransmitter or metabolic systems. Approaches of biological psychiatry to the affective disorders are summarized in Table 2.1.

Table 2.1 Biological psychiatry and affective disorders

BIOLOGY	Genetics	vulnerability to mental disorders
	Stress	increased sensitivity
	Chronobiology	desynchronisation of biological rhythms
NEUROCHEMISTRY	Neurotransmitters	availability, metabolism
	Receptors	number, affinity, sensitivity
	postreceptor processes	G proteins, 2^{nd} messengers, phosphorylation, transcription
IMMUNONEURO-ENDOCRINOLOGY	hypothalamic-pituitary-adrenocortical system	increased activity during depression
	immune function	different changes during depression

Theoretical and clinical studies have provided evidence that the monoamine neurotransmitter systems are involved in the treatment of affective disorders. These studies have led to a series of hypotheses concerning the mechanism of the action of antidepressant treatments, as well as pathophysiology of depression, that have focused on alterations in brain levels of serotonin and norepinephrine or their receptors.

Studies at the level of neurotransmitters and receptors have not generated a compelling model of antidepressant action or the pathophysiology of depression. For example, common action of antidepressant treatments at the level of monoamines or their receptors was not identified so far. It is possible that there is more than a single mechanism by which antidepressant treatments exert their therapeutic actions.

An updated hypothesis suggests that postreceptor intracellular targets mediate the long-term, therapeutic action of antidepressant treatments.

2.3.1. Neuroendocrine hypotheses

Changes in the activity of the hypothalamic-pituitary-adrenal (HPA) axis or hypothalamic-pituitary-thyroid (HPT) axis were observed during depression. An increased function of the HPA axis was described in more than 50% of depressed patients. Abnormalities of the HPA axis in patients with depression are summarized below

The **dexamethasone suppression test (DST)** is used to determine the sensitivity of the HPA axis to negative feedback. 1 mg of dexamethasone is usually administered at 23:00 h and plasma cortisol is monitored following morning. In healthy subjects dexamethasone suppresses plasma cortisol. DST was suggested as test for diagnosis of major depressive disorder, since increased function of HPA axis can be expressed in reduced decrease of ACTH and cortisol levels after dexamethasone administration. But it was demonstrated that DST test is insufficiently specific.

Abnormalities of the hypothalamic-pituitary-adrenal (HPA) axis in patients with depression includes:

- cortisol hypersecretion
- increased urinary free cortisol
- increased CSF corticotrophin releasing factor
- increased circulating ACTH
- abnormal circadian rhythms of cortisol
- abnormal dexamethasone suppression
- decreased glucocorticoid receptor sensitivity
- decreased release of ACTH to CRF
- increased adrenal gland size

CSF – cerebrospinal fluid, ACTH – adrenocorticotrophic hormone, CRF – corticotrophin-releasing factor (Trimble 1996.)

Neuroendocrine hypothesis of affective disorders were formulated on the base of abnormalities in HPA axis function and disturbed glucocorticoid feedback in depression shown below

Neuroendocrine hypotheses of affective disorders includes

- Endocrine abnormalities associated with depression are results of increased releasing of CRF both in hypothalamus and out of them.
- Disturbed glucocorticoid feedback in depression is caused by lower density of corticosteroid receptors in hippocampus and hypothalamus during depression (i.e. by disturbed regulation of gene expression of these receptors).

2.3.2. Neurochemical hypotheses

There are evidences that signal transmission through chemical synapse is disturbed in the affective disorders. Changes in neurotransmitters, membrane receptors and postreceptor pathways are studied during mental illness and its treatment. The neurochemical parameters studied in affective disorders are summarized in Table 2.2.

Table 2.2. Neurochemical parameters studied in affective disorders

Neurotransmitters	Availability
	Metabolism
Receptors	number or density
	Affinity
	Sensitivity
Postreceptor systems	number and activity of G proteins
	effector enzymes
	2nd messengers systems
	protein kinases
	Phosphatases
	transcription factors

2.3.3. Neurotransmitter hypotheses

Discovery of the tricyclic antidepressant drugs supported hypothesis about significant role for the biogenic amine, particularly NA and 5-HT in the ethiopathogenesis of affective disorders. Reduced activity of the serotonergic and noradrenergic systems has been reported in subgroups of patients with major depression, but this has not been observed in all depressed patients.

Initial neurotransmitter hypotheses were supported by effect of tricyclic antidepressants on reuptake of NA and 5-HT, effect of monoamine oxidase inhibitors (MAOI) on catabolism of monoamine neurotransmitters and effect of reserpine on vesicular transport of neurotransmitters. Reuptake inhibition results in an enrichment of the NA and 5-HT in the synaptic cleft. Similar effect can be achieved with MAO inhibitors. For many years this effect was considered to be the precondition for antidepressant activity. The first major theory about the biological etiology of depression was **monoamine hypothesis** supposing that:

Depression was due to a deficiency of monoamine neurotransmitters, noradrenaline and serotonin. MAOI act as antidepressants by blocking of enzyme MAO, thus allowing

presynaptic accumulation of monoamine neurotransmitters. Tricyclic antidepressants act as antidepressants by blocking membrane transporters ensuring re-uptake of 5-HT or NA, thus causing increased extracellular neurotransmitter concentrations.

Data for neurotransmitter hypothesis

- Tricyclic antidepressants through blockade of neurotransmitter reuptake increase neurotransmission at noradrenergic synapses
- MAOIs increase availability of monoamine neurotransmitters in synaptic cleft
- Depressive symptoms are observed after treatment by reserpine, which depletes biogenic amines in synapse

In addition to the role of noradrenergic and serotonergic systems in depression, cholinergic and dopaminergic and others systems were considered, so, many neurotransmitter hypotheses were formulated below.

Neurotransmitter hypothesis of affective disorders includes:

- catecholamine hypothesis
- indolamine hypothesis
- cholinergic-adrenergic balance hypothesis
- “permissive” hypothesis
- dopamine hypothesis
- hypothesis of biogenic amine
- monoamine hypothesis

Permissive biogenic amine hypothesis persists as part of more recent hypothesis:
A deficit in central indolaminergic transmission permits affective disorder, but is insufficient for its cause; changes in central catecholaminergic transmission, when they occur in the context of a deficit in indoleaminergic transmission, act as a proximate cause for affective disorders and determine their quality, catecholaminergic transmission being elevated in mania and diminished in depression.

However, neither the catecholamine nor the serotonin hypothesis could be confirmed in depressive patients. Clinically, the onset of the antidepressant action differs from the biochemical effects; the uptake inhibition occurs suddenly, whereas the therapeutic effect needs two or three weeks of pharmacotherapy. Furthermore, depletion of 5-HT or NA in healthy individuals does not induce clinically significant depressive symptomatology. These are reasons why receptor and postreceptor events are observed during affective disorders and their treatment at present time.

2.3.4. Receptor hypotheses

The neurotransmitter receptor hypothesis posits that disturbance occurs in function of receptors for the key monoamine neurotransmitters. Such wrong receptor function may be caused by depletion of monoamine neurotransmitters, by abnormalities in the receptor, or by problems with signal transduction on postreceptor level.

The common final result of chronic treatment by majority of antidepressants is the down-regulation or up-regulation of postsynaptic or presynaptic receptors (Table 2.3). The delay of clinical response corresponds with these receptor alterations, hence many receptor hypotheses of affective disorders were formulated and tested.

Table 2.3. Effect of depression and antidepressant treatment on receptor sensitivity

system	*receptor system*	*treatment by antidepressants*	*depression*
Adrenergic	B_1-AR (postsynaptic, exc.)	↓	
	a_2-AR (presynaptic, inh.)	↓	
	a_2-AR (postsynaptic, inh.)		↓
	a_1-AR (postsynaptic, exc.)		
Serotonergic	5-HT_2 (exc.)	↓	
	5-HT_{1A} (somatodendritic autoreceptors, inh.)	↓	↓?
	5-HT_{1A} (postsynaptic, inh.)		↓
	5-HT_{1B} (terminal autoreceptors, inh.)	↓	
Other	Ach	↓	
	GABA		↓
	DA		↓
	corticosteroid receptors		↓

ACh - acetylcholine, GABA - γ-amino butyric acid, DA - dopamine, AR – adrenoceptors.
↑- increased, ↓ - decreased

When activated by catecholamines, the presynaptic α_2-adrenergic receptors can inhibit NA or 5-HT release. Some antidepressants reduce sensitivity of brain α_2-adrenoreceptors. **Hypothesis about role of presynaptic α_2-AR** was formulated:

There is increased density of presynaptic α_2-adrenergic receptors in high affinity state in depression.

Several lines of evidence indicate that an enhancement of 5-HT neurotransmission might underlie the therapeutic response to different types of antidepressant treatment, so, **general serotonin receptor hypothesis** was suggested:

Depression is connected with these abnormalities in serotonin receptors:

5-HT_2 up-regulation

$5\text{-}HT_{1A}$ desensitisation

Abnormal signal transduction following 5-HT binding to receptor

Very elegant but not confirmed was **receptor catecholamine hypothesis**:

Supersensitivity of catecholamine receptors in the presence of low levels of serotonin is the biochemical basis of depression.

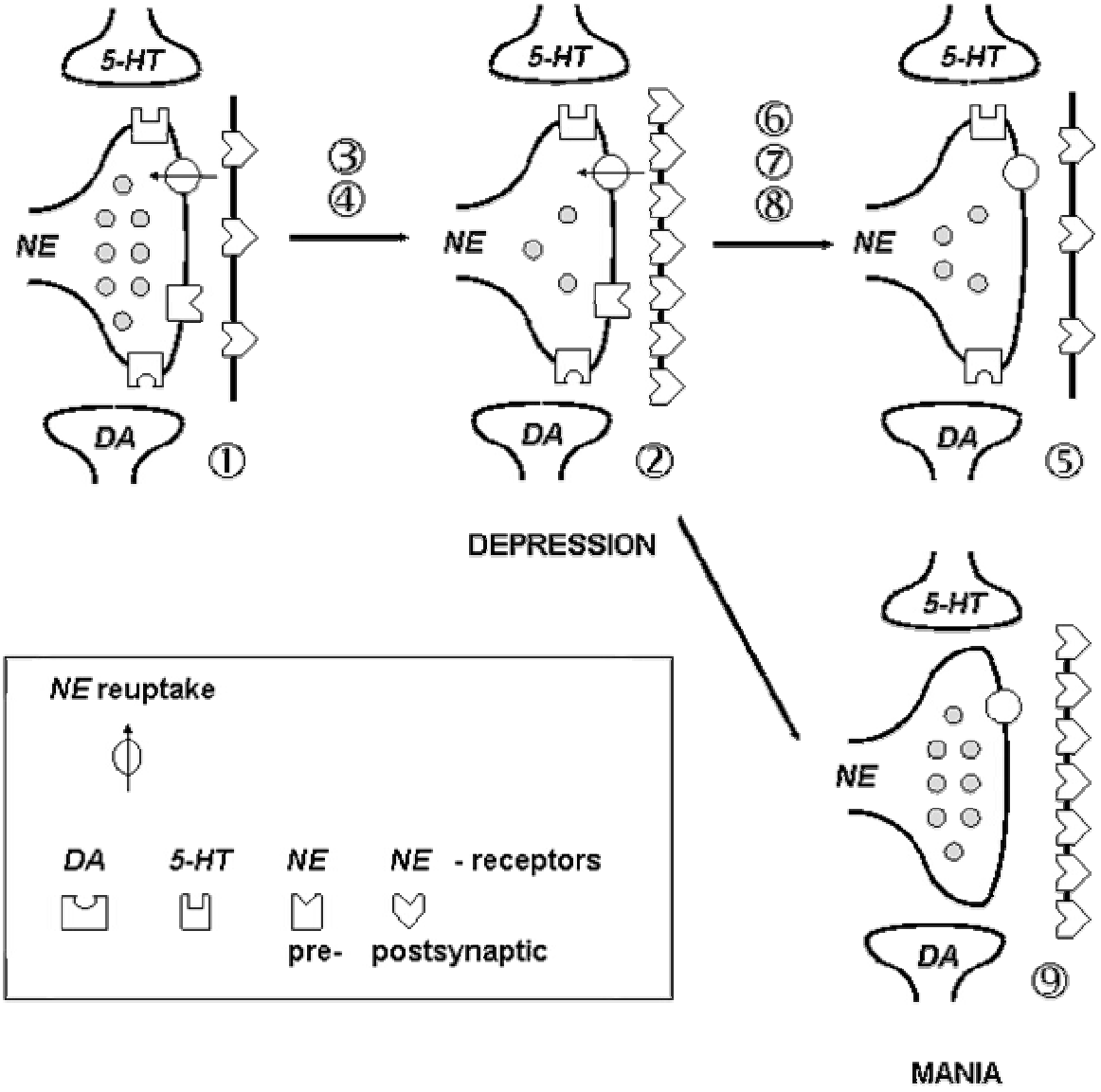
The common result of chronic treatment by majority of antidepressants is the down regulation of β-adrenergic receptors, which can be modulated by interaction with the 5-HT system, DA system, neuropeptides and hormones.

Classical nor adrenaline receptor hypothesis of affective disorders was formulated (Figure 2.1):

There is increased density of postsynaptic β-AR in depression (due to decreased NA release, disturbed interactions of noradrenergic, serotonergic and dopaminergic systems, etc.). Long-term antidepressant treatment causes down regulation of β_1-AR (by inhibition of NA re-uptake, stimulation or blockade of receptors, regulation through serotonergic or dopaminergic systems, etc.). Transient increase of neurotransmitter availability can cause fault to mania.

Apparently paradoxical increase of intracellular cAMP levels were observed at decreased density of β-AR, so increased cAMP system activity seems to be fundamental in therapeutic action of antidepressants. So, postreceptor hypotheses of affective disorders are tested at present time.

Figure 2.1. Classical noradrenergic receptor hypothesis



(Lopez *et al*., 1991)

2.3.5. Postreceptor hypotheses

The introduction of new, more selective antidepressants led to new reflection upon the mechanism of their action. Most promising are recent investigations of the second messenger

systems, the adenylyl cyclase system, the phosphatidylinositol system, G proteins, transcription factors etc. Modulation of receptor sensitivity, either down-regulation or up-regulation, is most probably dependent on the second and third messenger systems. Selected postreceptor hypotheses are shown below.

Postreceptor hypotheses

- **Second messenger dysbalance hypothesis:**

Affective disorders arise from the dysbalance of the two major intrapersonal signal-amplification systems, with depression resulting from a hypofunction of the AC-cAMP kinases pathway together with dominance of the PLC-CaM/C kinases system, and mania resulting from the converse.

- **G protein hypothesis:**

They are changes in either density or function of subunits of G proteins during depression. (e.g. increase of G_s protein)

- **Molecular model of affective disorders:**

Clinical heterogeneity observed at depressed patients can be explained by changes in signal transduction pathways which regulate two or more different neurotransmitter systems and which affect the neuron activity. G proteins, phosphatases and transcription factors are studied mainly.

- **Molecular and cellular theory of depression:**

Transcription factor, cAMP response element-binding protein (CREB), is one intracellular target of long-term antidepressant treatment and brain-derived neurotrophic factor (BDNF) is one target gene of CREB. Chronic stress leads to decrease in expression of BDNF in hippocampus. Long-term increase in levels of glucocorticoids, ischemia, neurotoxins, hypoglycaemia, etc. decreases neuron survival. Long-term antidepressant treatment leads to increase in expression of BDNF and his receptor trkB through elevated function of serotonin and noradrenaline systems.

2.3.6. Molecular and cellular theory of depression

Recent studies have begun to characterize the action of stress and antidepressant treatments on signal transduction at postreceptor level. Long-term antidepressant treatments result in the sustained activation of the cAMP system in specific brain regions, including the increased function and expression of the transcription factor cAMP response element-binding protein (CREB). The activated cAMP system leads to the regulation of specific target genes, including the increased expression of brain-derived neurotrophic factor (BDNF) in hippocampus and cortex.

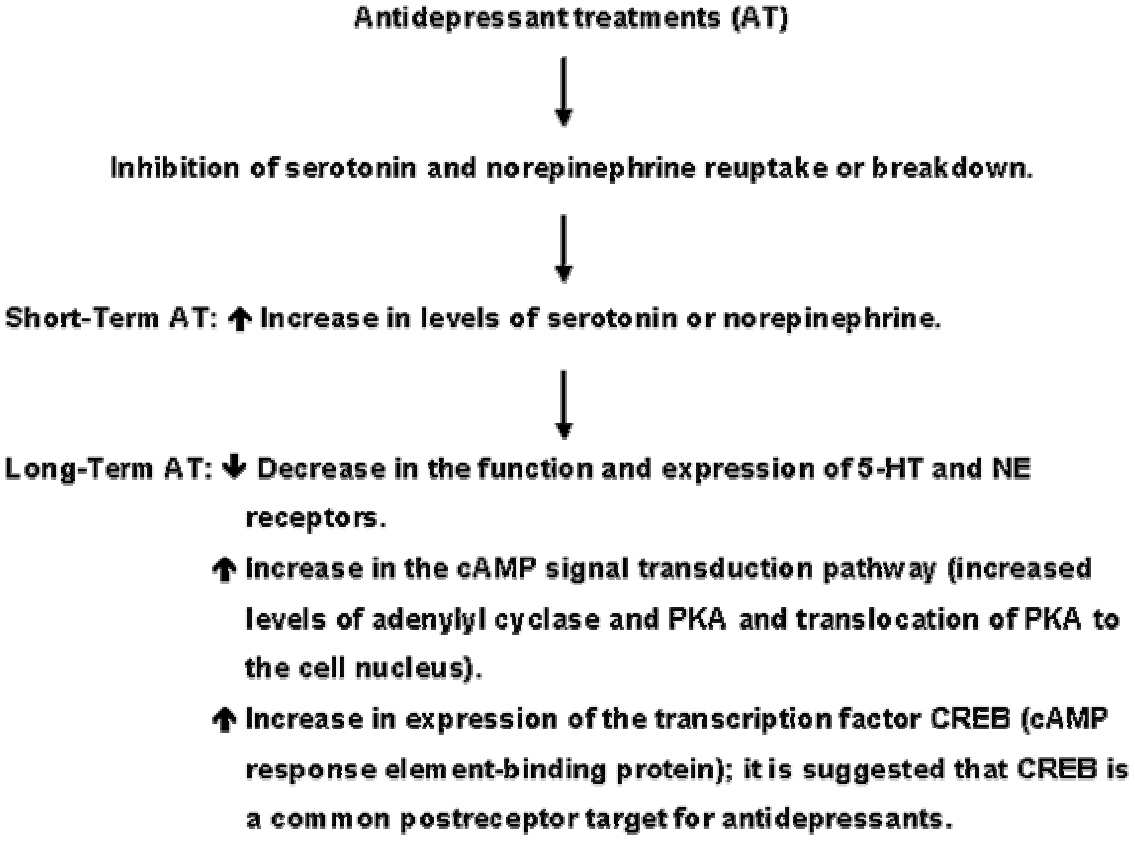
It was found that stress can decrease the expression of BDNF and lead to atrophy of the same populations of stress-vulnerable hippocampal neurons. Decreased size and impaired function of these neurons may be involved in depression; this possibility is supported by clinical imaging studies, which demonstrate a decreased volume of certain brain structures. These findings constitute the framework for **a molecular and cellular hypothesis of depression** which assume that stress-induced vulnerability and therapeutic action of antidepressant treatments occur via intracellular mechanisms that decrease or increase, respectively, neurotrophic factors necessary for the survival and function of particular neurons. This hypothesis also explains how stress and other types of neuronal insult can lead to depression in vulnerable individuals.

2.3.7. Molecular mechanism of action of antidepressants

A model for the molecular mechanism of action of antidepressant treatments is shown on Figure 2.2. Antidepressant treatment causes inhibition of serotonin and noradrenaline re-uptake or breakdown. Short-term antidepressant treatment increase extracellular levels of serotonin and noradrenaline. Long-term treatment leads to decrease in the function and expression of serotonin and noradrenaline receptors, to increase in the cAMP signal

transduction and to increase in expression of CREB. Increased activity of the cAMP signal transduction cascade indicates that the functional output of 5-HT and NA are up-regulated, even though levels of certain 5-HT and NA receptors are down-regulated. Expression of BDNF and its receptor trkB is also increased by long-term antidepressant treatment, so increased neuronal survival, function, and remodelling of synaptic architecture are provided.

FIGURE 2.2. A MODEL FOR THE MOLECULAR MECHANISM OF ACTION OF ANTIDEPRESSANT TREATMENTS



(DUMAN *ET AL* 1997)

2.4 GENERAL CLINICAL FEATURES

2.4.1 DEPRESSION

Sadness is a normal emotion commonly experienced by healthy people in response to misfortunes, especially losses, including grief. It is often accompanied by some anxiety, lack of energy, general malaise and poor sleep.

More severe unhappiness is the central symptoms of primary depressive disorder - a syndrome of symptoms associated with low mood, depressive thinking, and (in more severe cases) biological symptoms (Gelder *et al.* 1999).

Features of depression will be described in 3 broad groups which are

i. Mild depressive disorder

ii. Moderately severe depressive disorder

iii. Severe depressive disorder

Mild depressive disorder

Features of mild depressive disorders are :

- symptoms are persistent
- Patients mood and behaviour are seen by others as different to normal character and behaviour.
- Depression
- Anxiety symptoms
- Poor sleep (may be worse in the evenings)
- Pessimism, but not suicidal ideation
- Lack of energy.

The symptoms and signs of moderately severe depressive disorder are:

Appearance

- Sad appearance
- Psychomotor retardation

Low mood

- Misery and unhappiness
- Diurnal variation-worse in morning
- Anxiety, irritability, agitation

Lack of interest and enjoyment

- Reduced energy
- Poor concentration
- Subjective poor memory

Depressive thinking

- Pessimistic and guilty thoughts
- Ideas of personal failure
- Hopelessness
- Suicidal ideas
- Self blame
- Hypochondriacal ideas

Biological symptoms

- Early wakening and other sleep disturbance
- Weight loss
- Reduced sexual drive

Other symptoms

- Obessional symptoms
- Depersonalization etc

Severe depressive disorder

Additional symptoms of severe depressive disorder are:

Delusion of worthlessness

Guilt

Ill-health

Poverty

Nihilism

Persecution

Hallucinations auditory

Rarely visual

2.4.2 Mania

Mania, a syndrome which is in some ways the reverse of depression, occurs as part of so called bipolar disorder. This term implies episodes of both mania and depressive disorder but also include those who, at the time of diagnoses, have only suffered manic illnesses (most patients with mania eventually develop a depressive disorder).

Clinical features of Mania

Mood

- Euphoria
- Irritability

Appearance

- Behaviour
- Over activity
- Distractibility
- Socially-inappropriate behaviour
- Reduced sleep
- Increased appetite

- Increased libido

Thinking and speech

- Flight of ideas
- Expansive ideas
- Grandiose delusions
- Hallucinations

Impaired Insight

The clinical patterns of mania are mild, moderate and severe mania

2.4.3 Mixed and alternating affective states

Occasionally mania and depressive symptoms occur together, as a mixed affective state. For example, an overactive and over-talkative patient may have profound depressive thoughts including suicidal ideas. Occasionally, states of mania and depression follow one another regularly with interval of a few weeks or months between them. This is sometimes called rapid cycling (Gelder *et al.* 1999).

2.4.4 Seasonal affective disorder (SAD)

This is the development of a depressive disorder at the same time of the year. In some cases this timing reflects extra demands on the person at a particular time of year, in other cases there is no such extra demand, and it has been suggested that the cause is related to changes in the season, for example in the length of daylight (Gelder *et al*., 1999).

2.5 Causes and Risk Factors of Mood disorders

In broad terms, affective mood disorders are caused by an interaction between

1. Stressful events
2. Constitutional factors resulting from genetic endowment and childhood experience.

The following are the predisposing or precipitating factors of mood disorders.

- Genetic
- Predisposing environmental factors
- Precipitating environmental factors
- Physical cause
- Personality

Genetics

These have been studied mainly in moderate to severe cases of affective disorder, rather than in mild cases. Parents, siblings and children of severely depressed patients have a higher morbid risk for affective disorder (10-15%) than the general population (1-2%). Twin studies indicate that these high rates among families are due to genetic factors (Gelder *et al.,* 1999). A comprehensive review of the evidence for the role of genetic factors in the etiology of mood disorders have been extensively conducted (Merikangas *et al*., 2002). A finding by Ikeda *et al.,* 2002 showed that genetic factors had an important role in the pathophysiology of mood disorders.

Predisposing environmental factors and precipitating environmental factors can be grouped into exposure to traumatic events.

Exposure to traumatic events

Review of literature suggest relationship between exposure to traumatic life experiences (like during war conflict, poor economic circumstances and unsupportive marriages) has increased prevalence rates of certain mood disorders particularly depression (Thabet *et al*., 2004 and Gelder *et al*., 1999).

2.6 TREATMENT OF MOOD DISORDERS

2.6.1 PHARMACOTHERAPY

2.6.1.1 TREATMENT OF DEPRESSIVE DISORDER

There are three main groups of antidepressants which are

Tricyclic Anti Depressants (TCADs)

The TCADs are classified into two major groups: the dimethylated derivatives also called tertiary amines including amitriptylline, imipramine, doxepin and trimipramine and the monomethylated derivatives also called secondary amines which include nortriptyline, protriptyline, and desipramine. It is hypothesized that these drugs increase concentrations of serotonin or norepinephrine in the central nervous system (specifically in the synaptic cleft between the central nervous system neurones) by blocking re-uptake of the putative neurotransmitter into the pre-synaptic neurone. This hypothesis is based on the assumption that some depressions may be caused by a deficiency of serotonin or noradrenaline in specific areas of the CNS and thus TCADs alleviate these depressions (Aguwa, 2004). Studies have shown that TCADs are effective in treatment of depression, for example the use of reboxetine: a novel antidepressant (Kadhe *et al*., 2003).

Arrthymias, heart block, convulsions, hepatic and haematological reactions are some of the side effects experienced with TCADs use. Others are drowsiness, dry mouth, blurred vision constipation, urinary retention (all of which are associated with its antimuscarinic activity) sweating.

Selective Serotonin Reuptake Inhibitors (SSRIs)

This class includes drugs like paroxetine, citaprolam, fluoxetine, fluvoxamine, sertaline 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” (Aguwa , 2004).

Studies have shown that the number of prescriptions for SSRI has grown in recent years (Hjalmarsson *et al*, 2005) and response rate to SSRI in postpartum depression is high in addition to it, being superior to TCAD in treatment of post partum depression. (Wisner *et al.*, 1999).

Side effects experienced with SSRI include headaches, restlessness, insomnia, palpitations, tremor, confusion, hypotension and hypomania or mania. Others are drowsiness, dizziness, gastrointestinal side effects (eg nausea, vomiting, dyspepsia, diarrhea and constipation), convulsions, fever, sexual dysfunction, sweating, movement disorders, dyskinesia etc. (Aguwa, 2004).

Monoamine Oxidase Inhibitors (MAO-Is)

MAO-Is act by inhibiting monoamine oxidase, an enzyme responsible for intraneuronal breakdown of catecholamines and indoleamine neurotransmitters. Inhibition of monoamine oxidase by these agents is believed to relieve the symptoms of depression by allowing catecholamine and indoleamine neurotransmitters in the presynaptic granules, there by making more of these neurotransmitters available to the post synaptic neurones in the CNS.
MAO-Is are divided into two chemical classes, hydrazines and non-hydrazines. Phenelzine is the most effective of the hydrazine class and tranylcypromine is the most effective of the non-hydrazines (Aguwa , 2004).

Though the list of possible indications for monoamine oxidase inhibitors (MAO-Is) continues to expand, many psychiatrists remain hesitant about prescribing MAO-Is, citing concerns about dietary prohibitions and hypertensive reactions (Sweet *et al.*,1995).

The side effects are dry mouth, blurred vision, orthostatic hypotension, dizziness, delayed ejaculation, constipation and difficulty in urination. MAO-Is may sometimes produce confusion, disorientation and delusions. The most dangerous reaction is acute hypertensive crises that may be caused by interaction with foods containing tyramine (Aguwa, 2004).

2.6.1.2. Treatment of Mania

Lithium Carbonate

The chemical process behind manic-depression is not only unknown but also the mechanism whereby lithium relieves manic states is unknown. However, lithium has been shown to affect electrolyte balance, monoamine metabolism and endocrine system. Thus, it appears that lithium may produce its effect on patients with affective illness by causing a normalization of receptor site sensitivity in the CNS- while others have suggested that lithium ion exerts its antimanic activity through some effects on the ion transfer system of neurotransmitters in the CNS.

Lithium has consistently yielded better results in the treatment of mania than neuroleptics and carbamazepine and equivalent results to divalproex. Lithium also provides benefits in prophylaxis (Bowden,2000). Studies have extensively shown lithium is indicated in treatment of mania (Cookson, 2001 and Kafantaris *et* al., 2004).

Mild adverse effects of lithium are nausea, vomiting, thirst and muscle weakness. Others are weight gain, slurred speech, confusion, vertigo, seizures, stupor, lethargy, coma leading to death.

Antipsychotic drugs

Conventional antipsychotics such as chlorpromazine, haloperidol and depot injections of fluphenazine or flupenthixol have proven value in the treatment of mania (Gelder *et al*., 1999

and Hellewell, 2006). Antipsychotics have long had a place in the clinical treatment of bipolar disorders, in both acute and maintenance phases (Cookson and Sachs, 2000). Atypical antipsychotics like clozapine also play a role in the long term treatment of bipolar disorder (Hellewell, 2006). Antipsychotic agents have been shown to competitively block the dopamine receptors. Areas within the brain where dopamine is concentrated include the substantia nigra and the corpus straitum.

Conventional antipsychotics may induce late dyskinesia, weight gain, sedation, sexual dysfunction. Atypical antipsychotics (other than clozapine) are now rated as first-line agents for adjunctive treatment of mania because they produce less adverse side effect and are strongly preferred when an antipsychotic is required for long term maintenance (Vacheron-Trystram *et al*., 2004).

Use of Anticonvulsant as mood Stabilizers

Three important anticonvulsant drugs valporate, carbamazepine and lamotrigine have been added to the class of drugs with lithium as mood stabilizers. They are useful with the action of preventing mood swings in patients with manic depression or bipolar affective disorders. But the exact mechanisms of action are not yet clear (Aguwa, 2004). Evidence of indications of anticonvulsants as mood stabilizers have been extensively studied (Gray *et al.,* 2003; Kowatch *et al*., 2003 and Haw *et al*., 2005).

2.6.1.3 Polypharmacy in Mood disorders

Polypharmacy is the use of more than one drug to treat the same disorder. In general, polypharmacy should be avoided, but it may be appropriate when the drug combination is more effective or produces fewer side effects than the independent constituents, when its use is safe and for the minimum time necessary (Aguwa,2004).

Bipolar affective illness represents a syndrome not readily treated by single agents. Majority of patients require supplemental antidepressants, antimaniac antipsychotic or hypnotic medications in combinations (Post *et al*., 1996). Many studies report the combination of mood stabilizing agents with conventnional antipsychotics and atypical antisypchotics (Vancheron-Trystram *et al.,* 2004).

2.6.2 NON PHARMACOLOGICAL MANAGEMENT OF MOOD DISORDERS

Psychotherapy

The objective of formal psychotherapy used alone to treat mood disorders are identical to those for medication:

1. Symptom remission
2. Psychosocial restoration and
3. Prevention of relapse or recurrence (Kaplan and Sadock, 2000).

Studies have shown that there is now access to psychotherapy use by some socio-economically disadvantaged groups (Olfson *et al.*, 2002). A review of recently published studies has found that all patients show significant improvement in those with symptoms of depression before treatment with psychodynamic psychotherapy (Bond, 2006).

Forms of Psychotherapy include:

Interpersonal therapy (ITP)

The goals of therapy here are to

i. Reduce the patient's depressive symptoms

ii. Improve the patient's self esteem and

iii. Help the patient develop more effective strategies for dealing with current social and interpersonal relations.

Interpersonal therapy, a short term psychotherapy normally consisting 12 to 16 weekly sessions, was developed specifically to treat non-bipolar psychotic, ambulatory patients suffering from depressive disorder.

Cognitive Behavioural Therapy (CBT)

Goals of therapy are to change the way a person thinks and, subsequently, to alleviate the depressive syndrome and prevent its recurrence. This is accomplished by helping the patient

i. identify the test negative condition

ii. develop alternative, more flexible schemas (stable cognitive structures) and

iii. Rehearse both new cognitive and new behavioural responses.

CBT is a short term structured therapy that involves active collaboration between the patient and therapist in achieving set goals. It is oriented toward current problems and their resolution therapy is usually conducted on an individual basis, although group techniques have been developed and tested, cognitive behavioural therapy may be used in conjunction with pharmacotherapy (Kaplan and Sadock, 2000).

Electroconvulsive Therapy (ECT)

In ECT, an electric current is applied to the skull of an anaesthetized patient to produce seizure activity while the consequent motor effects are prevented with a muscle relaxant. The electrode that delivers the current can be placed with one on each side of the head (bilateral ECT) or with both on the same side (unilateral ECT). ECT is usually given twice a week with a total of 6-12 treatments according to progress (Gelder *et al.,* 2004).

Bilateral ECT is somewhat more effective than unilateral ECT, but it appears to have more cognitive adverse effects (Kaplan and Sadock, 2000). Adverse effects of ECT include headaches, cognitive impairment, and memory problems. There are occasional effects from

the anaesthetic procedure. The teeth, tongue or lips may be injured while the airway is introduced, and, rarely muscle relaxant cause prolonged apnoea.

2.6.3 COMBINING PHARMACOTHERAPY AND PSYCHOTHERAPY

A number of studies have demonstrated comparable benefits of psychosocial interventions and pharmacologic treatment in subgroups of patients with mood disorders. The two treatment modalities are often combined in clinical practice. However, concerns about the cost of health care are paramount (Jindal *et a*l., 2003).

2.7 CO-MORBIDITY

Co-morbidities includes co-occurrence (in the same individual) of two or more physical diseases (e.g. cardiovascular 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). Co-morbid disorders may be heterotypic, i.e. between different classes of mental disorders (Anglod et al., 1999), or homotypic, i.e. between different member of a general class of mental disorder (mania and depression). 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.

Co-morbidity of substance use disorder (e.g. alcohol and cannabis) and bipolar type 1 and type II disorder exists with very little treatment research specifically targeting this population (Cerullo *et al*.,2007). Mood disorders co-morbidity with anxiety disorders and substance abuse has been documented (Merikangas *et al*., 2004). Patients with epilepsy are at high risk

for depression (interical depression) which is an under-treated condition because of drug interactions and the risk of exacerbating seizures with antidepressant treatment (Harden *et al*., 2002). Report of co-morbidity of bipolar affective disorder and schizoaffective disorder (Breiger *et al*., 2005) and bipolar disorder with pervasive developmental disorder not otherwise specified (Munesue *et al*., 2008) are also reported.

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).

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 Shika for the period spanning 1st January, 2006 to 31st December, 2006.

The first stage of data collection involved use of attendance registers from the records department of the psychiatric unit. A total of 4,364 attendances were recorded by 887 patients in 90 clinics held within the one year period. Only folders of patients who met the entry criteria (n=145) were selected for the next stage of study i.e. patients diagnosed to have mood disorders.

Socio demographic data, which included; sex, marital status, date of first contact with orthodox facility, age at first contact with orthodox facility, geopolitical zone, 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.

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.

Data obtained were subjected to analysis using statistical package for social scientists (SPSS version 11).

3.2 COST OF ILLNESS

In this study, patients (within the mood disorders patients' population) who had attended clinics regularly between the period of January 2006 and December 2006 (1 year period) and did not default any of their clinic attendance were used. The cost item evaluated in this study is basically the cost of drugs used by patients during this period.

CHAPTER FOUR

RESULTS

TABLE 4.1: NEURO-PSYCHIATRIC CLINIC ATTENDANCE AT AHMADU BELLO UNIVERSITY TEACHING HOSPITAL (ABUTH) ZARIA FROM JANUARY 2006 TO DECEMBER 2006

MONTHS IN 2006	NO OF CLINICS HELD	CLINIC ATTENDANCE NO OF TIMES	% OF ATTENDANCE	ATTENDANCE PER CLINIC
January	6	276	6.32	46.00
February	8	383	8.78	47.88
March	8	350	8.02	43.75
April	6	356	8.16	59.33
May	7	348	7.97	49.71
June	9	465	10.66	51.67
July	9	427	9.78	47.44
August	9	422	9.67	46.89
September	8	354	8.11	44.25
October	6	274	6.28	45.67
November	8	432	9.90	54.00
December	6	277	6.35	46.17
Total	90	4364	100	48.47

Some patient's folders could not be located at the time of study

Schizophrenia, depression and seizure disorders occurred more frequently. Mood disorder which comprises of Hypomania (1.6%) mania (0.9%) Bipolar affective disorder (8.3%) and depression (15.2%) gave a total percentage of 26% of the total patients' population.

DIAGNOSIS OF MENTAL AND NEUROLOGICAL DISORDERS

Table 4.2 Categories of Diagnosis in total Patient's Population at ABUTH for year 2006

DIAGNOSIS	FREQUENCY	PERCENT	CUMULATIVE PERCENT`
Hypomania	14	1.6	1.6
Mania	8	.9	2.5
Bipolar effective disorder	74	8.3	10.8
Depression	135	15.2	26.0
Mixed anxiety/Depressive disorder	9	1.0	27.1
Anxiety Disorder	73	8.2	35.3
Schizophrenia	331	37.3	72.6
Schizoaffective disorder	22	2.5	75.1
Seizure Disorder	114	12.9	87.9
Mental Disability	4	.5	88.4
Organic brain syndrome	14	1.6	90.0
Psychosomatic Illness	16	1.8	91.8
Psychotic Disorder (not otherwise specific)	43	4.8	96.6
Dementia	4	.5	97.1
Delusional disorder	6	.7	97.7
Adjustment Disorder	4	.5	98.2
Substance use disorder	7	.8	99.0
Hypochondriasis	2	.2	99.2
Dissociative disorder	4	.5	99.7
Down's syndrome	1	.1	99.8
Parkinsonism	1	.1	99.9
Hyperkinetic disorder	1	.1	100.0
Total	**887**	**100.0**	

There were more females (62.1%) than males (37.2%) while a patient's gender was not recorded.

Table 4.3: Gender Distribution of Patients suffering from Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

GENDER	FREQUENCY	PERCENT	CUMULATIVE PERCENT
Male	54	37.2	37.2
Female	90	62.1	99.3
Not Recorded	1	.7	100.0
Total	**145**	**100.0**	

The majority of the patients were Muslims (77.2%)

Table 4.4 Prevalence of Mood Disorders by Religion of Patients attending Neuro-Psychiatric clinic at ABUTH in year 2006

RELIGION	FREQUENCY	PERCENT	CUMULATIVE PERCENT
Christian	33	22.8	22.8
Muslim	112	77.2	100.0
Total	**145**	**100.0**	

Eight three (57.2%), forty eighth (33.1%), eight 55%) and six (4.4%) of the patients were married, single, divorced and widowed respectively.

Table 4.5: Marital status of Patients with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

MARITAL STATUS	FREQUENCY	PERCENT	CUMULATIVE PERCENT
Single	48	33.1	33.1
Married	83	57.2	90.3
Divorced	8	5.5	95.9
Widowed	6	4.1	100.0
Total	**145**	**100.0**	

More than half of the patients were Hausa/Fulani (59.3%).

Table 4.6: Prevalence of Mood Disorders by Ethnicity/Tribe of Patients attending Neuro-Psychiatric clinic at ABUTH in year 2006

Ethnicity/Tribe	Frequency	Percent
Hausa/Fulani	86	59.3
Yoruba	24	16.6
Igbo	7	4.8
Jabba	3	2.1
Tiv	3	2.1
Ebira	3	2.1
Igala	2	1.4
Ibibio	2	1.4
Nupe	2	1.4
Non-Nigerian	1	.7
Not Recorded	12	1.4
Others include: Baburi, Tuga, Idoma, Gure, Bassange, Baju, Magavul, Koro, Kagoro, & Kaje	10	6.9
Total	**145**	**100.2**

Patients geopolitical zones were derived from state of origin (not shown) seventy nine of the one hundred and forty four recorded 54.5% were from the North Central. The least percentage (0.79%) was recorded for Abuja. Sixteen patients geopolitical zone were not recorded.

Table 4.7 Prevalence of Mood Disorders by Geopolitical Zones of Patients attending Neuro-Psychiatric clinic at ABUTH in year 2006

Zone	Frequency	Percent	Cumulative Percent
South West	15	11.7	11.7
South East	5	3.9	15.6
South South	3	2.3	17.9
North Central	79	16.7	79.6
North East	3	2.3	81.9
North West	21	16.4	98.3
FCT	1	.8	99.1
Total	144	99.3	99.9
Not Recorded	1	.7	
Total	**128**	**100.0**	

38.6% of the patients were between the ages of 20-29 years at index episode of mood disorders.

Table 4:8 Age Distributions of Patients at Index Episode of Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

AGE	FREQUENCY	PERCENT	CUMULATIVE PERCENT
10-19 Years	27	18.6	18.6
20-29 Years	56	38.6	57.2
30-39 years	20	13.8	71.0
40-49 Years	22	15.2	86.2
50-59 Years	11	7.6	93.8
Above 60 Years	9	6.2	100.0
Total	**145**	**100.0**	

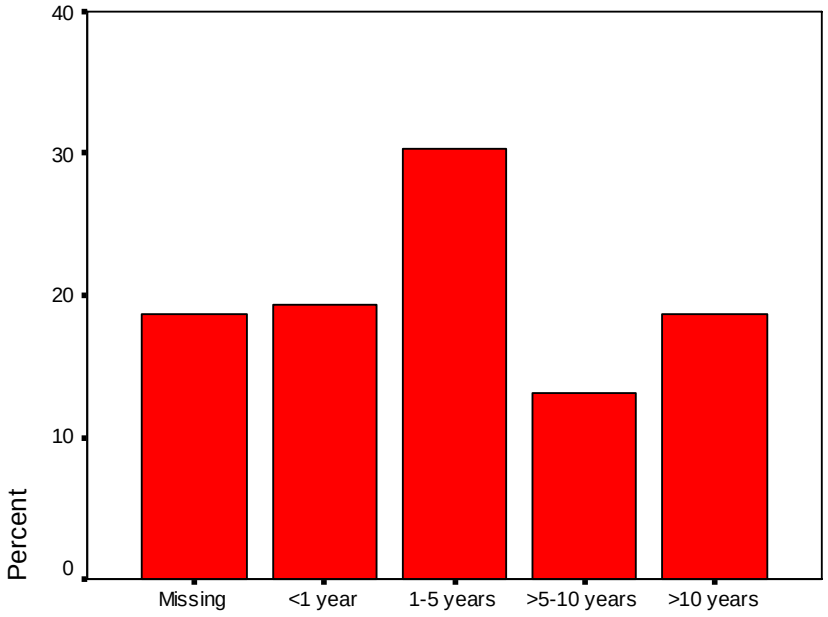


Fig 4.1 Years since First Contact with Orthodox Facility

30% of patients had their first contact with orthodox facility between 1-5 years while 18.6% of patients had no record of first contact with orthodox facility.

More than half of the patients (60.7%) were unemployed and fell into the category of house wife (29.7%) student (24.1%) and unemployed (6.9%). Among the employed majority were self employed which included petty traders, drivers, carpenters, tailors, welders and farmers.

Table 4.9: Occupation of Patients Suffering from Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

OCCUPATION	FREQUENCY	PERCENT	CUMULATIVE PERCENT
House Wife	43	29.7	29.7
Student	35	24.1	53.8
Petty trader	21	14.5	75.2
Other unemployed	10	6.9	60.7
Artisan	8	5.5	80.7
Farmer/Gardner	6	4.1	84.8
Civil Servant	4	2.8	87.6
Health Worker	4	2.8	90.4
Others: Businessman, teachers, Policeman, Navy, Soldier, Doctor, Accountant, Hospital Attendant, Architect, Messenger, Typist, Politician	14	9.7	100.1
Total	**145**	**100.0**	

Fifty four of the hundred and forty five patients (37.2%) had no record of education.

Table 4:10 Highest educational Level of Patients Suffering from Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

HIGHEST EDUCATIONAL QUALIFICATION	FREQUENCY	PERCENT	CUMULATIVE PERCENT
None	10	6.9	6.9
Quranic School	13	9.0	15.9
Primary School uncompleted	3	2.1	17.9
Primary School Completed	6	4.1	22.1
Junior Secondary School Completed	5	3.4	25.5
Senior Secondary School Completed	15	10.3	35.9
Tertiary Education completed	37	25.5	61.4
Postgraduate	1	.7	62.1
Typing school	1	.7	62.8
Not recorded	54	37.2	100.0
Total	**145**	**100.0**	

More than half of the patients (54.5%) were diagnosed with one form of depression (which include mild, moderate, severe, recurrent and depression not otherwise specified).

Table 4.11 Prevalence of Subtypes of Mood disorders of patients attending Neuro-Psychiatric clinic at ABUTH in year 2006

SUBTYPES OF MOOD DISORDERS	FREQUENCY	PERCENT	CUMULATIVE PERCENT
Depression	79	26.2	54.5
Mania	6	4.1	58.6
Hypomania	13	9.0	67.6
Bipolar Affective disorder	47	32.4	100.0
Total	**145**	**100.0**	

Twenty seven female patients had depression (not other wise specified) while only one male patient had recurrent depression.

Table 4.12 Cross tabulation of Sub types of Mood Disorders and Gender Distribution of study Population attending Neuro-Psychiatric clinic at ABUTH in year 2006

MOOD DISORDER	GENDER DISTRIBUTION OF STUDY POPULATION			TOTAL
	MALE	FEMALE	NOT RECORDED	
Depression	18	60	1	79
Mania	4	2		6
Hypomania	7	6		13
Bipolar affective disorder	25	22		47
Total	**54**	**90**	**1**	**145**

Twenty two bipolar affective disorder patients fell into the age of 20-29 years while in the elderly only 3 patients had depression (no otherwise specified)

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Table 4.13 Specific Diagnosis of mood disorders by Age of study Population attending Neuro-Psychiatric clinic at ABUTH in year 2006

	AGE DISTRIBUTION OF PATIENTS AT INDEX EPISODE OF MOOD DISORDERS						TOTAL
PREVALENCE OF SUBTYPES OF MOOD DISORDERS	10-19 YEARS	20-29 YEARS	30-39 YEARS	40-49 YEARS	50-59 YEARS	ABOVE 60 YEARS	
Depression	7	26	13	15	11	7	79
Mania		4	1	1			6
Hypomania	6	4	2	1			13
Bipolar affective Disorder	14	22	4	5		2	47
Total	**27**	**56**	**20**	**22**	**11**	**9**	**145**

Fifteen patients with bipolar affective disorder recorded family history of psychiatric disorder and only one patient with severe depression had family history of psychiatric disorders.

Table 4:14 Cross tabulation of specific diagnosis and family history of Psychiatric Disorder of study Population attending Neuro-Psychiatric clinic at ABUTH in year 2006

	FAMILY HISTORY OF PSYCHIATRIC DISORDERS			
SPECIFIC DIAGNOSIS	YES	NO	NOT RECORDED	TOTAL
Depression	13	50	16	79
Mania	3	3		6
Hypomania	5	7	1	13
Bipolar affective disorder	15	30	2	47
Total	**36**	**90**	**19**	**145**

Some patients (24.8%) reported family history of mood disorder.

Table 4.15 Family History of Psychiatric Disorders of patients with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

FAMILY HISTORY	FREQUENCY	PERCENT	CUMULATIVE PERCENT
Yes	36	24.8	24.8
No	90	62.1	86.9
Not Recorded	19	13.1	100.0
Total	**145**	**100.0**	

Patient's relationship with family history had 35.7% recorded for parent, 28.6% of siblings while 2.4% recorded for wife or children or distant relative.

Table 4.16 Family History of Psychiatric Disorders: Relationship of patients with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

RELATIONSHIP	NO OF PATIENTS	PERCENT
Parents	15	35.7
Sibling	12	28.6
Uncles/Aunties	6	14.3
Grandparents	3	7.1
Cousins/Niece/Nephews	3	7.1
Wife	1	2.4
Distant relatives	1	2.4
Children	1	2.4
Total	**42**	**100**

Ninety one patients had no non-psychiatric co-morbid disorders. Seventeen females had hypertension.

Table 4.17 Cross tabulation of Prevalence of Non-psychiatric Co-morbidity and Gender Distribution of study Population attending Neuro-Psychiatric clinic at ABUTH in year 2006

	GENDER DISTRIBUTION OF STUDY POPULATION			
PREVALENCE OF NON PSYCHIATRIC CO-MORBIDITY	MALE	FEMALE	NOT RECORDED	TOTAL
Patients without co-morbidity	40	50	1	91
Malaria	7	16		23
Typhoid fever	3	1		4
Diabetes		1		1
Hypertension	2	17		19
Asthma		1		1
Ulcer		1		1
Allergic	1			1
Conjunctivitis				1
Recto-cuntaneous fistula	1			1
Skin rash		1		1
Sub acute appendicitis		1		1
Worm infestation		1		1
Total	**54**	**90**	**1**	**145**

One hundred and five patients had no psychiatric co-morbid disorders while 9 males had co-morbid schizophrenia and 9 females had co-morbid psychosomatic disorder.

Table 4.18 Cross tabulation of Prevalence of Psychiatric Co-morbidity and Sex Distribution of Study Population attending Neuro-Psychiatric clinic at ABUTH in year 2006

PREVALENCE OF PSYCHIATRIC CO-MORBIDITY	SEX DISTRIBUTION OF STUDY POPULATION			
	MALE	FEMALE	NOT RECORDED	TOTAL
Patients without co-morbidity	37	67	1	105
Schizophrenia	9	4		13
Organic brain syndrome	2			2
Anxiety		6		6
Dementia		2		2
Drug substance abuse	3	1		4
Psychosomatic disorder	2	9		11
Adjustment disorder	1			1
Schizoaffective disorder		1		1
Total	**54**	**90**	**1**	**145**

One hundred and twenty six patients (86.9%) had no record of the use of psychoactive substance.

Table 4.19 Psychoactive substance used by patients with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

PSYCHOACTIVE SUBSTANCE USED	FREQUENCY	PERCENT
Alcohol consumption	8	5.5
Tobacco use	6	4.1
Marijuana (Indian hemp) use	4	2.8
"Solution"	1	0.7
None	126	86.9
Total	**145**	**100.0**

Forty six patients had no record here. Seventy five patients (75.7%) sought for medical intervention in less than a year of their index episode and eleven patients (7.6%) did after 4 or more years of index episode.

Table 4.20 Duration between index Episode of Mood Disorders and Medical intervention of Study Population attending Neuro-Psychiatric clinic at ABUTH in year 2006

PERIOD OF INDEX EPISODE	FREQUENCY	PERCENT	CUMULATIVE PERCENT
0-1 month	33	22.8	33.3
1-6 months	34	23.4	67.7
6-8 months	5	3.4	72.7
8-11 months	3	2.1	75.8
1-2 years	9	6.2	84.8
2-4 years	4	2.8	88.9
> 4 years	11	7.6	100.0
Not Recorded	46	21.7	
Total	**145**	**100.0**	

Table 4.21 Signs and Symptoms presented by Patients Diagnosed with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

SIGNS/SYMPTOMS	NO OF PATIENTS	PERCENT
Insomnia	106	14.8
Irrational Talk	67	9.4
Dysphonic Mood	66	9.2
Loss of appetite	47	6.6
Anxious mood/worries/Pessimistic	50	7.0
Headaches	31	4.3
Intrusive thoughts	25	3.5
Weakness	22	3.1
Palpitations	21	2.9
Disoriented	19	2.7
Aches and Pains	18	2.5
Psychosomatic Complaints	15	2.1
Memory impairment	14	2.0
Over activity	14	2.0
Grandiosity	14	2.0
Dizziness	13	1.8
Poor concentration	13	1.8
Inappropriate guilt	12	1.7
Euphoric Mood	11	1.5
Suicidal tendency	12	1.7
Excitability	10	1.4
Auditory Hallucinations	10	1.4
Weight loss	9	1.3
Night mares	6	0.8
Sweating	6	0.8
Pounding sounds in head	5	0.7
Pressured speech	5	0.7
Abnormal behaviour	4	0.6
Easy distractibility	4	0.6
Fatigue	4	0.6
Chest pain	4	0.6
Dry mouth	3	0.4
Indecisiveness	3	0.4
Self withdrawal	3	0.4
Increased appetite	2	0.3
Poorly groomed	2	0.3
Nausea and vomiting	2	0.3
Impotence	2	0.3
Abdominal fullness	2	0.3
Diarrhorea, constipation, Persecutory ideas, aggressiveness	1 (each)	0.3 each

The most common laboratory investigations carried out on the patients included general hematological investigations, serum urea/ electrolyte/ creatinine, WBC differential, serum glucose, stool and urine microscopy.

Table 4.22 Laboratory investigations carried out by patients Diagnosed with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

LABORATORY INVESTIGATIONS	NO OF PATIENTS	PERCENT
General hematological investigations	56	19.8
Serum urea /electrolyte /creatinine	51	18.0
WBC differential	42	14.8
Serum Glucose	39	13.8
Stool Microscopy	29	10.2
Urine Microscopy	25	8.8
Malaria Parasite	8	2.8
Urine analysis	11	3.9
EEG	4	1.4
Widal test	4	1.4
ECG	3	1.1
Culture and Sensitivity	3	1.1
X-ray	2	0.7
HIV Screening	2	0.7
Liver Function test	2	0.7
Pregnancy test, CT Scan	1 each	0.4 each
Total	**283**	**100**

Table 4.23 Psychiatric Drugs routinely used in Patients with Mood disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

DRUG PRESCRIBED	PHARMACOLOGICAL BASIC FOR THEIR USE	CLASS/SUBCLASS	NO. OF PATIENTS USING DRUG	%
Amitriptylline	Antidepressant	Tricyclic anti-depressant	92	10.9
Benzhexol	For extra pyrimadal effects	An inootropic agent	121	14.4
Biperidine	For extra pyrimadal effects	An inootropic agent	3	0.4
Bromazapam	Sedative/anxiolytic effect	Benzodiazepines	7	0.8
Carbamazepine	Mood stabilizer	Iminostibenes	51	6.1
Tabs Chlorpromazine	Antipsychotic	Phenothiazines	55	5.6
Inj Chlorpromazine	Antipsychotic	Phenothiazines	52	6.2
Clonazepam	Sedative/anxiolytic effects	Benzodiazepines	9	1.1
Tabs Diazepam	Sedative/hypnotic effects	Benzodiazepines	21	2.5
Inj Diazepam	Sedative/hypnotic effects	Benzodiazepines	51	6.1
Flunitrazepam	Hypnotic effects	Benzodiazepines	2	0.2
Inj flupenthixol	Antipsychotic	Thioxanthene	14	1.7
Inj Fluphenazine	Antipsychotic	Phenothiazine	20	2.4
Tabs Haloperidol	Antipsychotic	Butyrophenone	66	7.8
Inj Haloperidol	Antipsychotic	Butyrophenone	5	0.6
Imipramine	Antidepressant	Tricyclic antidepressant	18	2.1
Lorazepam	Sedative/anxiolytic	Benzodiazepines	5	0.6
Moclobomide	Antidepressant	(MAOI)	11	1.3

Olanzapine	Antipsychotic	Thienobenzodiazeine	2	0.2
Paroxetine	Antidrepressant	(SSRI)	9	1.1
Ris[eridine	Antipsychotic	Heterocyclic Compounds	3	0.4
Fluspirilene	Antipsychotic	Diphenylbutylpiperidine	5	0.6
Sodium Valporate	Mood stabilizers	Valporic acid	11	1.4
Thioridazine	Antipsychotics	Phenothiazines	44	5.2
Chlormezanone	Anxiolytic/hypnotics	Discontinued	1	5.2
Trifluoperazine	Antipsychotic	Phenothiazines	76	9.0
Trimipramine	Antidepressant	Tricyclic anti depressant	5	0.6
Nitrazepam	Sedative/hypnotic	Benzodiazepine	66	7.8
Cloimipramine	Antidepressant	Tricyclic antidepressant	6	0.7
Sulpiride	Antipsychotic	Benzamides	2	0.2
Chlordiazepoxide	Anxiolytic/Sedative	Benzodiazepines	3	0.4
Pyrintol	CVA Disorder	Inootropic	2	0.2
Setraline	Antidepressant	(SSRI)	4	0.4
Fluoxetine	Antidepressant	(SSRI)	1	0.1
Total			**842**	**100.1**

Non-pharmacological management was not recorded for fifty one patients while forty four patients (46.8%) had ECT and seven patients (7.4%) each had either counseling with family or psychotherapy.

Table 4.24 Non Pharmacological Management of Patients with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

NON-PHARMACOLOGICAL MANAGEMENT	NO. OF PATIENTS	PERCENT
Electroconvulsive therapy (ECT)	44	46.8
Insight Counseling	22	23.4
Counseling with family	7	7.4
Psychotherapy	7	7.4
Counseling on follow-up	14	14.9
Total	**94**	**100.0**

Alternative therapy of seventy two patients (49.7%) was not recorded while 20% of patients used traditional medicine and 5.5% religious intervention.

Table 4.25 Alternative Therapy Patients with Mood Disorder Used

Therapy	No of patients	%
None	36	24.8
Traditional Medicine	29	20
Religious intervention	8	5.5
Not Recorded	72	49.7
Total	145	100.0

Seventy five patients (51.7%) had poor adherence while seventy (48.3%) patients had good adherence to their medications.

Table 4:26 Report of Drug Adherence by Psychiatrists in Patients with Mood disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

ADHERENCE	FREQUENCY	PERCENT	CUMULATIVE PERCENT
Poor	75	51.7	51.7
Good	70	48.3	100.0
Total	**145**	**100.0**	**100.0**

Table 4.27 Adverse effects experienced by Patients Managed with Pharmacotherapy while attending Neuro-Psychiatric clinic at ABUTH in year 2006

ADVERSE EFFECTS	NO. OF PATIENT	PERCENT
Weakness	42	13.1
Headache	28	8.7
Excessive sleep	26	8.1
Insomnia	23	7.2
Forgetfulness	18	5.6
Drowsiness	16	5.0
Irritability	15	4.7
Extra pyrimidal side effect	14	4.4
Crawling sensation	10	3.1
Tremors	10	3.1
Upward rolling of eyes	10	3.1
Blurred vision	8	2.5
Dryness of the mouth	8	2.5
Emotional upset	8	2.5
Sensation in the ear	8	2.5
Palpitations	7	2.2
Restlessness	7	2.2
Dizziness	6	1.9
Epigastric pain	6	1.9
Pruritis	6	1.9
Amenorrhea	6	1.9
Behavioral change	5	1.6
Dry irritating cough	5	1.6
Poor Appetite	5	1.6
Agitation	3	0.9
Excessive salivation	3	0.9
Weight gain	3	0.9
Confusion	2	0.6
Nausea and vomiting	2	0.6
Erectile dysfunction	2	0.6
Skin Rashes	2	0.6
Numbness in the hand	2	0.6
Nasal Congestion	2	0.6
Hypersensitivity	1	0.3
Dermatitis	1	0.3
Galactorrhea	1	0.3

Forty eight patients (33.1%) had no record of management of adverse effects. Nineteen (3.1%) patients discontinued and used alternative drugs and only 2.7% of patients were counseled on adverse effects.

Table 4.28 Management of adverse effects of patients with Mood Disorders attending Neuro-Psychiatric clinic at ABUTH in year 2006

MANAGEMENT OF ADVERSE EFFECTS	NO. OF PATIENTS	PERCENT
Discontinuation and use of alternative drugs	19	13.1
Use of other drugs to remedy side effect	32	22.1
Reduction in dosage	33	22.8
Reduction in frequency of administration	9	6.2
Counseling	4	2.7
Not recorded	48	33.1
Total	**145**	**100.0**

Only 5 patients (3.4%) had contact with the law

.

Table 4.29 Documenting Patients' Contact with the Law

Contact with law	Frequency	Percent	Cumulative Percent
Yes	**5**	**3.4**	**3.4**
No	**139**	**95.9**	**99.3**
Not recorded	**1**	**0.7**	**100.0**
Total	**145**	**100.0**	

Table 4.30 Cost of Mood Disorders-Socio Demographic Data, Diagnosis and cost of Drugs for Year 2006

S/N	MENTAL COMORBIDITY	NON MENTAL COMORBIDITY	DIAGNOSIS	AGE AT FIRST CONTACT WITH ORTHODOX FACILITIES	OCCUPATION	NO OF CLINICS ATTENDED	COST OF LAB. INVESTIGATIONS (₦)	TOTAL COST OF DRUGS USED (₦)	TOTAL COST OF DRUGS USED PARTICULARLY FOR PSYCHIATRIC DISORDERS (₦)
1.	None	None	B.A.D.	34	House Wife	8	None	6,050.34	5,051.31
2.	None	None	Severe Depression	25	House wife	8	1,250	9,374.10	9,010.10
3.	None	Hypertension	Depression	50	Unemployed	5	None	15,833.65	5,038.60
4.	None	None	Moderate depression	50	House wife	8	720	10,148.30	9,749.30
5.	None	Malaria Hypertension	Recurrent Depression	60	Unemployed	3	2,770	13,674.36	4,869.20
6.	None	Malaria	B.A.D.	27	Unemployed	4	1,650	32,434.62	31,546.62
7.	Anxeity	None	Depression	17	Student	3	1,370	28,811.10	28,75510
8.	None	None	Recurrent Depression	35	House wife	4	None	9,326.20	9,272.20
9.	None	None	Moderate depression	30	House wife	2	520	12,988.90	12,260.90
10.	Schizophrenia	None	B.A.D.	31	Gardener	3	None	6,791.84	6,541.84
11.	Schizophrenia	Malaria	B.A.D.	18	Student	4	400	15,007.09	15,007.09
12.	None	Hypertension	Depression	not recorded	House wife	5	None	22,431.50	19,337.50
13.	Schizophrenia	Malaria	B.A.D	21	Student	9	720	46,801.44	46,513.94
14.	Hypochondriasis	None	Depression	42	Trader	4	1,000	9,482.20	9,118.20
15.	Psychosomatization	Hypertension	Moderate depression	38	House wife	5	1,650	28,793.10	9,214.80
16.	None	None	Severe depression	44	Health worker	4	320	5,527.20	5,527.20

17.	None	None	Severe depression	48	Big businessman	3	1,370	9,482.20	9,118.20
18.	None	None	Depression	Not recorded	House wife	5	1,770	9,558.58	9,558.58
19.	None	Malaria hypertension	Malaria	32	House wife	5	2,770	34,349.80	33,476.80
20.	None	Malaria	B.A.D	25	Messenger	8	1,250	14,702.59	13,974.59
21.	None	Malaria	Depression	21	House wife	14	1,650	39,287.64	38,265.64

KEY

B.A.D - Bipolar Affective Disorder

CHAPTER FIVE

DISCUSSION

5.1 CLINIC AND PATIENT ATTENDANCE

This study conducted at the Neuro Psychiatry unit of Ahmadu Bello University Teaching Hospital (ABUTH) Shika, was designed to access characteristics, management and cost of mood disorders among patients who attended psychiatry clinic during a one year period from January to December, 2006.

Clinics were held twice per week (Mondays and Thursdays) and a total of 104 clinics were expected in a year. However, in this study only 90 clinics were held and the short fall was due to public holidays and resident doctor's strikes. It was observed that the months of June, July and August had the highest number of clinics (9) in year 2006 while January, April, October and December had the least of 6 clinics in each of these months. The 4,364 attendances were made by 887 patients who attended clinics from 1-14 times. Patients who are clinically stable are usually given appointments at interval not less than 4 months (i.e. 3 times per year) (Table 4.1).

5.2 CATEGORIES OF DIAGNOSIS

Based on the 887 patients whose diagnosis records were complete, schizophrenia had the highest percentage of 37.3%. Patients diagnosed of depression, seizures, bipolar affective disorders, anxiety disorders were 15.2%, 12.9%, 8.3% and 8.2% respectively (Table 4.2). This is not similar to a finding by Moscicka *et al* 2001 who reported that the following disorders were most common in a group of subjects under study: neurotic, stress-related and somatoform disorder (32.9%), mental and behavioural disorders due to psychoactive

substance use (26.5%, 11.8%-nicotine dependence) and mood (affective) disorders (16.5%).

High percentage of schizophrenic patients in this study could be due to the fact that, the disorder requires prompt medical attention as compared to some other mental disorders e.g. depression and alcohol abuse disorder.

5.3 FEATURES OF MOOD DISORDERS

There were more female patients with mood disorders (62.1%) than male (37.2%)-see Table 4.3. This is similar to what was obtained in some past studies globally, indicating that there are higher incidences of mood disorders in female than male. (Scheibe *et al*., 2003; Lucht *et al*., 2003; Gorman, 2006 and Rouillon, 2008).

Majority of the patients (77.2%) were of Muslim faith see Table 4.4, and this may be explained by the fact that ABUTH is located in northern Nigeria where Islam is the prevalent religion. Over 57.2% of these patients were married while 33.1% were single and 9.6% were either divorced or widowed at first presentation (Table 4.5). This is not surprising since 52.4% were in their twenties and thirties (Table 4.8). The mean age for patients diagnosed with mood disorders is 28.3 years which was higher than the median age of mood disorders (26 years) (WHO 2000). As previously indicated 52.4% of patients suffering from mood disorders are below thirty of age, therefore this data shows that mood disorders were predominant among the productive class of the society.

Based on data calculated from date of first registration until December 31st, 2006, majority of patients with mood disorders (49.6%) have been attending clinics for 5 years or less,

13.1% have been attending clinics between 6 and 10 years while 18.6% had no record (See fig. 1).

Findings from analysis of data on the prevalence of mood disorders at ABUTH by tribe/ethnicity shows mood disorders were ubiquitous, with a Hausa/Fulani majority (59.3%). Other tribes/ethnic groups include Yoruba 16.6%, Igbo 4.8%, Jabba, Tiv, Ebira 2.1% each. For the geopolitical zone (i.e. origin of patients) North central had 54.5% (Table 4.6 and 4.7).

More than half of the patients were unemployed (60.7%) falling into the category of housewife (29.7%), students (24.1%) and other "unemployed" (6.9%). This can be explained by the fact that mood disorders is more common in women and they belong to the group of housewife. This is consistent with a finding by Okulate 2001 who reported that depressed female were less educated and more likely to be married. The percentages of the students and unemployed can be explained by the fact that most patients age fall between the productive age (which is twenties and thirties) (Table 4.9).

Due to the fact that majority of patients were in their twenties and thirties (Table 4.8), data for level of education of patients diagnosed as having mood disorders showed that 26.2% (Table 4.10) had tertiary education. However 37.2% of patients had no record of their educational level. This is consistent with a study conducted in Canada by Akhtar-Danesh *et al.,* 2007 who found that the highest rates of depression are seen among individuals with 'other post-secondary' education. In addition, a total of 36.6% of patients in this study (Table 4.10) had low level of education i.e. 'below post-secondary education. This is

however not similar to a finding conducted in Nigeria by Ihueze *et al* 1986 who reported that majority of depressed patients had low level of education.

Depression (including mild, moderate, severe, recurrent, and not otherwise specified (NOS)) 54.5% was the most common sub type of mood disorder reported. This finding is consistent with a publication by Mclntype *et al*., 2007 who reported that depression had the highest prevalent diagnosis among patients diagnosed of mood disorders. Bipolar affective disorder (32.4%), hypomania (9.0%) and mania (4.1%) were also reported (Table 4.11).

Only 24.8% of the patients had records indicating family history of mental disorders (Table 4.15). Records were not available for 13.1% while 62.1% said they had no history of such occurrence in their families. This is not in agreement with available literatures which show familial aggregation among mental disorders (Hetema et al., 2001 and Nemi *et al.*, 2004).

5.3 CO-MORBIDITY

Co-morbid disorders were present in 64.8% of patients. This result is consistent with the findings of Nuyen *et al* (2005) in which co-morbidity have been shown to exert opposite effect on under diagnosis of mood disorders by general practitioners. The prevalence of non-psychiatric co-morbid disorders (37.2%) was observed to be higher than that of psychiatric co-morbid disorders (27.6%) Malaria was the most frequently occurring non psychiatric co-morbid disorder (15.9%) (Table 4.17) This high prevalence is not surprising as malaria occurs very frequently in this part of the world. Hypertension is the second most prevalent co-morbid non-psychiatric disorder (13.1%). This is consistent to results published by Kinzie *et al* (2008) who reported that there was strong public health concern

for cardiovascular disease in psychiatric patients. The most frequently reported psychiatric co-morbid disorder was schizophrenia (9.0%) (Table 4.18). This result is consistent with the findings of Breiger *et al* (2005) who observed similar coexistence between mood disorders and schizophrenia. Psychosomatic disorder (7.6%) was second only to schizophrenia. Others were anxiety disorder (4.1%) and are consistent with findings by Middeldrop *et al*., 2005 and Kendler *et al.,* 2007 who reported that there were high levels of co-morbidity between major depression and generalized anxiety disorder and that these disorders were closely related genetically. Other psychiatric co-morbid disorders reported are organic brain syndromes and substance abuse both of which occurred each in 1.4% of patients. Understanding co-morbidity patterns is essential for accurate differential diagnosis, for understanding how co-morbidity influences illness course and severity as well as for developing rational plan for treatment (Goisman *et al*., 1995).

Data regarding lifestyle behaviours such as alcohol and tobacco use were very scanty (records were unavailable for 86.9% of patients). Available records show that alcohol (5.5%) consumption predominated. (Table 4.19). The extent to which these behaviours influenced the course and management of mood disorders could not be determined because of deficiency of records and the retrospective design of this study. This finding is different from past studies which showed that co-morbidity of mood disorders and psychoactive substance use disorder (PSUDs) was highly prevalent (Salloum *et al.,* 2000) . In addition that co-occuring substance use disorders are correlated with negative effects on illness outcome including more frequent and prolonged affective episodes, decreased compliance with treatment, a lower quality of life and increased suicidal tendencies. (Cerullo *et al.*, 2007). Duration between index episode of mood disorders and medical intervention was

recorded for 99 patients (Table 4.20). 22.8 % of patients sought for medical intervention within one month of index episode. 23.4% of patients sought medical intervention within six months, 3.4% of patients within six-eight months, 6.2% of patients within 1-2 years while 7.6% of patients after 4 years of index episode of mood disorders.

5.4 MANAGEMENT OF MOOD DISORDERS AT ABUTH

Signs and symptoms

Signs and symptoms of mood disorders frequently reported by physicians were insomnia and other sleep disorders (difficulty in falling or staying asleep, nighmares), irrational talk, dysphoric mood, loss of appetite, anxious mood (worries pessimistic), cardiovascular complaints (palpitations), euphoric mood, gastrointestinal complaints (Nausea, vomiting, diarrhorea, constipation etc), psychosomatic complains, grandiosity and a host of others. (Table 4.21). This finding was in consistent with a study by Toros *et al*., 2004 who reported that most common symptoms of mood disorders were feelings of guilt, sadness, irritability and somatic disorder.

Laboratory investigations

Frequently requested investigations include, general hematological investigations (19.8% of patients); serum/urea/electrolyte/creatinine (18.0%), WBC differential (14.8%), serum glucose (13.8%), stool microscopy (10.2%) and urine microscopy (8.8%) (Table 4.22)

The frequent request for general haematological investigations may have been necessitated by the significant number of cardiovascular complaints and the high prevalence of co-morbid hypertension among mood disorder patients. Psychiatrists involved in the patients

care explained the frequent requests of laboratory investigations thus, that diagnosis of mood disorders involves a process of exclusion. Laboratory investigations are required to exclude disorders that are similar or mimic mood disorders.

Pharmacotherapy and Psychotherapy

Patients were managed either with pharmacotherapy (35.2%) or pharmacotherapy plus psychotherapy (64.8%).

Anti depressants used in pharmacotherapy include TCADs, amitriptylline in 63.4% patients, imipramine in 12.4% patients, MAOI (moclobomide) in 7.5% patients. SSRI used include paroxetine in 6.2% patients, sertaline in 2.7% patients and fluxetine in 0.6% patients.

Mood stablizers used included carbamazepine in 35.2% patients and sodium valporate in 7.5% patients. Antipsychotics used were trifluoperazine in 52.4% patients, haloperidol tablets in 45.5% patients, sulpiride in 1.3% patients etc. (see table 4:20) Anxiolytics used were benzodiazepdines which include nitrazepam in 45.5% patients, diazepam injection in 35.2% patients and flunitrazepam in 1.3% patients among others. Drugs used for prophylaxis of extrapyramidal side effect were benzhexol in 83.4% patients and biperidine in 2.1% patients.

Newer SSRIs which have been proven to be more effective and were better tolerated were rarely prescribed probably due to their prohibitive cost. Tricyclic anti-depressants (TCAD)

achieved their effect by inhibiting re-uptake of 5-HT and nor-adrenaline (some e.g. desipramine inhibits just noradrenaline). Their sedative side effect is due to blockade of histamine receptors (this makes them useful in treatment of insomnia, a presenting symptom in a large number of patients with mood disorders presenting at the clinic).

Reports of abnormalities in GABA receptors system of patients with mood disorders favour the use of benzodiazepines in the management of mood disorders as they are viewed as offsetting an underlying abnormality. Benzodiazepines act at γ-aminobutyric acid type A (GABA-A) receptor, where they increase neurotransmission produced by endogenous neurotansmitter, γ-amino butyric acid (GABA), the major inhibitory neurotransmitter in the brain.

Advantages of the use of benzodiazepines include, rapid on set of action, they improve sleep onset and its subjective quality, a feature which is often disrupted in mood disorder. Drawbacks in their use include, risk of developing tolerance, dependence and or withdrawal symptoms.

Non-pharmacological therapy was usually undertaken in conjunction with drug therapy. The forms of non pharmacological therapy (in 64.8% of patients) prescribed were ECT (46.8%), insight counseling (23.4%), psychotherapy (7.4%) and counseling on follow-up (14.9%) (Table 4.24). 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 (2000) 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 reduced health-care cost, as successfully treated patients reduce their utilization of health care services.

49.7% of patients had no record of alternative therapy while 20% and 5.5% patients used traditional medicine and religious intervention respectively (Table 4.25). This is not similar to a finding conducted in USA by Roy-Byrne *et al*., 2005 who reported that the rate of use of herbal medicine in depressed patients was 11%. In another study, it was revealed that 39.9% of patients who attended a mental health service in Nigeria (Ilorin) had first contacted traditional or religious healers when they became mentally ill (Abiodun, 1995).

Table 4.26 shows that 51.7% of patients had poor adherence to drug medications, the consequences of poor adherence to long term therapies for chronic illnesses are poor health outcomes and increased health care costs. The assessment of drug adherence is consistent with a finding by Woltmann *et al.*,2007, who reported that pharmacy data could be used to identify partially adherent patients.

Adverse effects and their management

Frequent complaints included weakness (13.1%), headache (8.7%), excessive sleep (8.1%), insomnia (7.2%), and dizziness (1.9%) among others. (Table 4.27) 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 drug therapy make it difficult to tie adverse events to any particular drug use.

Use of other drugs to remedy adverse events (22.1% of patients), reduction in dosage (22.8%), discontinuation and use of alternative drugs (13.1%), and reduction in frequency of administration (6.2%) were methods identified for management of adverse events (Table 4.28).

3.4% patients had contact with law (Table 4.29) which is lower than a finding by Munetze *et al*., 2001 who reported that 7.9% of severely mentally disabled patients had at least one incarceration in a county jail and that diagnosis were predominantly in the schizophrenia spectrum. A different report by White 2005 said 60% of patients with affective (mood) disorders were discharged to prison, court or local hospital within one year of their admission to special secure care.

5.5 COST OF MOOD DISORDERS TREATMENT

The patients whose data were tabulated on table 4.30 are patients who were regular in the clinic from January 2006 to December, 2006 (100% clinic attendance). This criterion was used in order to assess the amount they spent on their drug during one year course of treatment as required for cost prevalence studies. This method was well described in chapter three of this thesis. The minimum years since contact with orthodox facilities were 0.05 years and maximum of 25 years. The minimum clinic attendance was 2 clinics and maximum was 14.

Patients were either self-employed or civil servant while seventeen were unemployed (housewife and students) who depend on their parents or husband for financial support. This implies that the cost of treatment is solely responsibilities of their care-givers (dependants). Ohaeri (2001) reported that in Nigeria, as there is no national social welfare and community rehabilitation programmes for the mentally ill, therefore families have to bear the major burden of care. The minimum cost of drugs used for mood disorders was N4,869.20 and maximum was N46,513.94, the mean annual cost for mood disorders drugs was N15,772.27. However, the minimum total cost of drugs including drugs for non-psychiatric co-morbid disorders was N6,050.34 and maximum was N46,801.44. The mean cost of total drugs taken is N18,136.04. For the cost of laboratory investigation, the minimum was N320 and maximum was N2,770. Based on national per capital income (which is N4.46 according to 2004 Central Bank of Nigeria bulletin), the patients or their caregivers were really affected financially. It is not worthy that cost items which include; direct cost (hospital in-patients and out patients service, are by physician and other practitioners, rehabilitation service, transport fare, special equipments used, home services and others) and indirect cost such as unemployment (patients or caregivers), underemployment, loss of productivity of patients and caregivers, decrease house-hold work and so on, were not used in this study.

CHAPTER SIX

CONCLUSION

6.1 CONCLUSIONS

Currently few data were available on mood disorders, 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 mood disorders will continue to increase as incidence increase with progressive years.

From this study, there were more female patients with mood disorders than male; up to half of the patients were less than 30 years at index episode of mood disorders, indicating that mood disorders is prevalent at productive class of the society. Half of the patients were married and most were of Muslim faith. Mood disorders showed no geopolitical, ethnic or tribal barriers and most of the patients had been attending clinic for five years or less. Depression was the most prevalent subtype of mood disorder encountered.

Signs and symptoms presented by patients varied and insomnia was the most dominant. Hematological investigations were the most requested laboratory investigations. Patients were managed either with pharmacotherapy or psychotherapy plus pharmacotherapy. Drug preferences were for amitriptylline, trifluoperazine and benzhexol. Other drugs include haloperidol injection, nitrazepam, chlorpromazine (tablets and injection) and carbamazepine.

Drugs 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 effect or reduction in dosage. Non-pharmacological approaches used included ECT and insight counseling.

With regards to patient expenses, drug cost far out weighed cost of laboratory investigations. The cost of drugs used by patients with mood disorders per year was high in relation to Nigeria per capital income as most of these patients were unemployed.

6.2 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) Cost of mood disorders in Nigeria which will include various cost items (mentioned earlier in chapter two) is essential so that the economic impact of mood disorders can be

made known to the government, in order that commitment of resource for mood disorders treatment can be from the government and international health organizations.

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APPENDIX
MOOD DISORDERS DATA FORM

PART I: GENERAL INFORMATION AND SOCIO-DEMOGRAPHIC DATA

Q1. Unit Number

Q2. Gender
01-Male
02-Female
99-Not recorded

Q3. Age (in years) (last birthday): _____

Q4. Nationality
01-Nigerian
02-Non-Nigerian
99-Not recorded

Q5. Geopolitical zone (of origin, not of residence)
01-South West
02-South East
03-South South
04-North Central
05-North East
06-North West
07-FCT
08-Not Applicable (i.e. if non-Nigerian)

Q6. Ethnicity/Tribe

01-Hausa	08-Tiv	15-Igala
02-Yoruba	09-Gure	16-Ibibio
03-Ibo	10-Ebira	17-Kagoro
04-Baburi	11-Bassange	18-Nupe
05-Tuga	12-Baju	19-Kaje
06-Jabba	13-Magvul	
07-Idoma	14-Koro	

Q7. Religion
01-Christainity
02-Islam
03-Traditional African Religion
99-Not recorded

Q8. Marital Status
01-Single
02-Married
03-Seperated
04-Divorced
05-Widowed

Q9. For married men only, Number of wives:

1-01
2-01
3-03
4-04
5- >4 Specify.-
07-Not applicable (i.e. Single, never married)
09- Not applicable (Female). .
99-Not recorded

Q10. Highest educational level attained

1-None (i.e. never been to school)
2-Koranic school
3-Pre primary school
4-Primary school uncompleted
5-Primary school completed
6-Junior secondary school completed
7-Senior secondary school completed
8-Tertiary (i.e. higher education after secondary school)
9-Postgraduate
10-Adult literacy
11-Others Specify _____
99-Not recorded

Q11. Occupation

1-Farmer
2-Petty trader
3-Big business man / contractor
4-Driver/mechanic/artisan/carpenter
5-Civil servant
6-Teacher / Lecturer
7-Policeman / Soldier / Navy
8-Health worker
9-Doctor
10-Lawyer
11-Student
12-Child
13-House wife
14-Unemployed
15-Retiree
16-Accountant
17-Hospital Attendant
18-Achitect
19-Messenger
20-Typist
21-Politician

PART II: MEDICAL HISTORY

Q12. Presenting compliant(s): _____

_____

Q13. Examination (signs and symptoms)

1-Abdominal fullness
2-Aches and pains
3-Anxious mood / worries / pessimistic
4-Chest pain
5-Constipation
28-Loss of appetite
29-Memory impairment
30-Nausea / vomiting
31-Nightmares
32-Overactivity
33-Palpitations

6-Dysphoric mood
7-Diarrhoea
8-Disoriented
9-Dizziness
10-Dry mouth
11-Dysmenorrhoea
12-Easy Distractability
13-Excessive worries
14-Excitability
15-Faintness
16-Fatigue
17-Fear (non specific)
18-Fears (of darkness, being alone, strangers, etc)
19-Grandiosity
20-Headaches
21-Inappropriate guilt
22-Indecisiveness
23-Irrational talkativeness
24-Euphoric mood
25-Impotence
26-Insomnia
27-Intrusive thoughts
34-Poor concentration
35-Pounding sounds in the head
36-Pressured speech
37-Psychosomatic complaints
38-Restlessness
39-Shortness of breath
40-Suicidal tendency
41-Sweating
42-Tachycardia
43-Tension / cries easily
44-Trembling
45-Urinary incontinence/lost of sphincter control
46-Weakness
47-Weight loss
48-Loss of sexual drive
49-Hallucination
50-Persecutory ideas
51-Aggressiveness
52-Self withdrawal
53-Poorly groomed
54-Abnormal behaviour
99-Not recorded

Q14. Specific Diagnosis :

1-Depression
2-Mania
3-Hypomania
4-Bipolar affective disorder

Q15. Family history of psychiatry disorders I: Disorder

1-Yes Specify disorder_____
2-No
99-Not recorded

Q16. Family history of psychiatry disorders II: Relationship

1-Father/Mother
2-Sibling
3-Uncles/Aunties
4-Ground Parents
5-Cousins/Nieces/Nephews
6-Distant relatives
7-Wife
8-Children
9-Not applicable (i.e. 'No' to Q 15)
99-Not recorded

Q17. Age at index episode: _____

Q18. Date of index episode: _____

Q19. First contact with mental health institution: _____

Q20. Other alternative therapy patient had ever used

0-None
1-Traditional medicine
2-Religious intervention (deliverance)
99-Not recorded

Q21. Performance in school

1- Dropped out because of inability to concentrate
2- Cannot go to school (formal education)
3- Slow learning
4- Dropped out at primary school
5- Dropped out at secondary school
6- Dropped out at tertiary school
7- Not affected –doing well
8- Not recorded
9- Poor academic performance
10- Not applicable (neither pupil nor student)

Q22. Co-morbid (i.e. co –existing) psychiatry conditions.

1-Schizophrenia
2-Organic brain syndrome
3-Anxiety
4-Dementia
5-Drug / substance abuse
6-Somatic complain
7-Adjustment disorder
8-Schizoaffective disorder
99-None

Q23. Co-morbid (i.e. co-existing) non- psychiatry conditions.

1- Malaria
2-Typhoid fever
3-Diabetes
4-Hypertension
5-HIV / AIDS
6-Tuberculosis
7-Asthma
8-Ulcer
9-Allergic conjuctivitis
10-Recto-cutaneous fistula
11-Sub-acute appenditis
12-Worm infestations
99-None

Q24. Any contact with the law:_____

Q25. Psychoactive substance use:

1-Alcohol consumption
2-Tobacco use (e.g. cigarette smoking)
3-Marijuana (Indian hemp) use
4-Solution
99-None

Q26. Laboratory investigations carried out

1-Culture and Sensitivity
2-Electro encephalogram (EEG)
3-General haematological investigations
4-HIV Screening test
5-Liver function test
6-Malaria parasite
7-Serum glucose
8-Serum urea/electrolyte/creatinine
9-Stool microscopy
10-Urinalysis
11-Urine microscopy
12-WBC and differential
13-Widal test
14-Electro cardiogram (ECG)
15-CT Scan
16-Xray (chest)
17-Pregnancy test
99-None

PART III: DRUG TREATMENT HISTORY AND NON-DRUG ASPECTS OF MANAGEMENT

Q27. Psychiatry drugs used.

Q28. Side effects experienced with drugs used

1-Anemia
2-Agitation
3-Ataxia
4-Behavioral change
5-Blurred vision
6-Confusion
7-Crawling sensation
8-Dizziness
9-Drowsiness
10-Dry irritating cough
11-Dryness of mouth
12-Emotional upset
13-Epigastric pain
14-Excessive sleep
15-Forgetfulness
16-Headache
17-Insomnia / poor sleep
18-Irritability
19-Lethargy
20-Nasal congestion
21-Nausea /vomiting
22-Palpitations
23-Poor appetite
24-Pruritus
25-Restlessness
26-Sensations in the ear
27-Skin rashes
28-Tremors
29-Upward rolling of eyes
30-Weakness

31-Amenorrhea
32-Galactorrhea
33-Extra pyrimadal symptoms
34-Excessive salivation
35-Weight gain
36-Erectile dysfunction
37-Hyper sensitivity
38-Dermatitis
99-Not recorded

Q29. Management of side effects

1-Discontinuation and use of alternative drugs
2-Use of other drugs to remedy side effects
3-Reduction in dosage
4-Reduction in frequency of administration
5-Counseling
99-None (i.e. no specified management)

Q30. Reasons for drug discontinuation

1-Side effects
2-Therapeutic failure
3-Non-compliance / adherence
4-Prohibitive cost
99-None

Q31. Assessment of drug adherence

1-Poor 2-Good

Q32. Non pharmacological management

1-Electro-convulsive therapy (ECT)
2-Insight counseling
3-Counseling with family
4-Group counseling
5-Psychotherapy
6-Cognitive behaviour therapy
7-Counseling on follow-up
99-None

UNIT NUMBER:_____

DRUG TREATMENT SUMMARY

DRUG NAME	DOSE/ FREQ	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU	DOU

KEY:
DOU – Duration of Use