COMPARISON OF THE PROFILE OF PATIENTS WITH ACUTE AND TRANSIENT PSYCHOTIC DISORDER AND SCHIZOPHRENIA SEEN AT THE UNIVERSITY COLLEGE HOSPITAL, IBADAN, NIGERIA

(2006-2010)

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DEDICATION

This work is dedicated to the God Almighty, my redeemer and king who made it possible.

CERTIFICATION

This is to certify that Oluyomi Babafemi Esan carried out this project in the Department of Epidemiology and Medical Statistics, Faculty of Public Health, College of Medicine, University of Ibadan.

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4/8/12
Date

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SUMMARY

Acute and transient psychotic disorders (ATPD) are distinct from schizophrenia. However very little research has been done on this disorder in low income countries where the magnitude is as much as ten times the incidence in the developed countries. A study that would identify/characterize the sociodemographic and clinical differences between the two disorders would fill some of the gaps in knowledge about the disorders.

To achieve the aforementioned objectives a retrospective review of the records of patients with ATPD and schizophrenia was done. Sociodemographic and clinical data of all new patients with an untreated first episode of ATPD seen at the University College Hospital Ibadan between the first of January 2006 and 31st of December 2010 were extracted using a pro forma. Information collected included age at first episode, sex, marital status at presentation, employment status, family history of mental illness and psychopathology at presentation.

During the five year period, 2604 new patients aged between 18 and 65 years were seen at the Psychiatry clinic. There were 706 subjects with schizophrenia and 208 subjects with ATPD representing 27.2% and 8.0% (Proportional morbidity rate) of all the cases seen respectively. Of these, 243 subjects with Schizophrenia and 124 subjects with ATPD met the inclusion criteria and were recruited into the study. Patients with ATPD (46.8%) were more likely to present below the age of 25 years compared to patients with schizophrenia (30%) ($P<0.01$). Excitement was more common in ATPD (17.2%) compared to schizophrenia (1.2%) ($P<0.01$). suspiciousness was more common in subjects with schizophrenia (20.2%) compared to ATPD (6.5%) ($P<0.01$). The presence of negative symptoms especially blunted affect (18.5% vs. 4.0%, $P<0.01$), emotional withdrawal (10.7% vs. 0.8%, $P<0.01$) passive social withdrawal (26.3% vs 3.2%, $P<0.01$) were highly suggestive of schizophrenia rather than ATPD. Also the presence of anxiety (35.5% vs. 22.6%, $P<0.01$) and uncooperativeness (14.5% vs. 7.0 % $P=0.02$) were significantly more likely to be ATPD than schizophrenia. Poor orientation (32.9% vs. 18.5%, $P<0.01$), disturbance of volition (20.2% vs. 8.1% $P<0.01$), and preoccupation (32.9% vs. 18.5%, $P<0.01$) were more common in Schizophrenia. Mean age of onset was similar between patients with Schizophrenia and ATPD (29.3 vs. 29.5 years, $P=0.2$).

according to religion. presence of the symptoms of delusions . hallucinatory behaviour. conceptual disorganization. grandiosity, hostility . somatic concern .tension . depression active social withdrawal and poor impulse control. Differences which may be important in differentiating between the two included the observation that ATPD were more likely to present below 25 years compared to Schizophrenia. excitement as a symptom was more common in ATPD. The presence of anxiety and uncooperativeness were more suggestive of ATPD than schizophrenia. Suspiciousness was more common in Schizophrenia compared to ATPD. The presence of negative symptoms especially blunted affect. emotional withdrawal and passive social withdrawal was significantly more common in schizophrenia. Poor orientation, disturbance of volition. and preoccupation were more common in schizophrenia than ATPD.

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CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND INFORMATION

Psychosis refers to mental disorders in which the thoughts , affective response, ability to recognize reality, and ability to communicate and relate to others are sufficiently impaired to interfere grossly with the capacity to deal with reality (Sadock and Sadock 2007). In a psychotic state, a person's capacity to recognize reality is impaired (American Psychiatric Association 2000). It also interferes with the individual's capacity to deal with life's demands. Psychosis manifests as hallucinations, delusions or both. The spectrum of psychotic disorders includes Schizophrenia, Schizophreniform disorder, Schizoaffective disorder, Acute and transient psychotic disorders (ATPD) and Delusional disorder (American Psychiatric Association 2000).Schizophrenia is typically chronic and could be recurrent (Marneros et al. 2003),whereas the ATPDs tend to be brief and recurrent. However, their clinical features are frequently indistinguishable when they present acutely for the first time. The fundamental features of Schizophrenia are a mixture of distinguishing signs and symptoms that have been present for a significant portion of the time during a one month period or shorter if successfully treated. These signs and symptoms are associated with marked social or occupational dysfunction. The symptoms involve a range of cognitive and emotional dysfunctions such as perception, inferential thinking , language, fluency and productivity of thought and speech, hedonic capacity, volition, drive and attention (American Psychiatric Association 2000).

The ATPDs present with a sudden onset of at least one of positive psychotic symptoms such as delusions, hallucinations, disorganized speech, or grossly disorganized or catatonic behaviour. An episode lasts at least one day but less than three months and the individual returns back to the previous level of functioning(World Health Organization 1993; American Psychiatric Association 2000). Psychotic disorders contribute significantly to the global burden of disease (World Health Organization 2011) even though they are relatively rare. Lifetime prevalence of psychotic disorders in Finland is about 3.5% (Perala et al. 2007) while the incidence in England is 34.8 per 100 000 person-years (Kirkbride et al. 2006) .The main burden of psychotic disorders is due to Schizophrenia. Firstly, because it usually has its onset in early adulthood. (Sadock and

Sadock 2007) and secondly because of its chronicity and persisting symptoms despite optimal treatment .About 75% of persons with Schizophrenia have relapses and continued disability, and one third fail to respond to standard treatment(Smith et al. 2009).

1.2 PROBLEM STATEMENT

There is a current interest in the contribution of the Non Communicable Diseases (NCDs) to the global burden of diseases. This group of diseases, presently has a status of an epidemic and is the leading cause of death globally, killing more people each year than all other causes combined(World Health Organization 2011). Of the 57 million deaths that occurred globally in 2008, 36 million (about two thirds) were due to NCDs, and over 80% of these deaths occurred in low and middle income countries(World Health Organization 2011).Furthermore, the burden of these diseases is rising fastest among lower-income countries and populations including Nigeria. Over a quarter of these deaths occur before the age of 60years.

Measured in DALYs, in the 2004 WHO Global Burden of Disease report(World Health Organization 2004), Neuropsychiatric conditions accounted for 13.1 % of the global burden of disease, while Schizophrenia alone accounted for 1.1%. Schizophrenia is a serious disease and is responsible for preventable morbidity and mortality. The worldwide prevalence of Schizophrenia is about 1% (Perala et al. 2007). Age of the first episode is lower among men (Sadock and Sadock 2007). The peak age of onset is 10 to 25 years for men and 25 to 35 years for women(Sadock and Sadock 2007). The burden is higher in men, because in this age range majority of male sufferers are unmarried, and would have attained only a modest level of education. A low level of education unfortunately also limits the job opportunities (Kessler et al. 2008; Lee et al. 2010).

Individuals with schizophrenia have a 4.9 % lifetime risk of suicide (Palmer et al. 2005). Mortality is also increased because of medical illnesses, due to a combination of unhealthy lifestyles, side effects of medication, discrimination by medical doctors including psychiatrist (Gray 2002)and decreased health care (Saha et al. 2007).In ATPD, the risk of harm to self and to others increases with each episode of ATPD .(Jorgensen and Mortensen 1990) . Hence in patients with either condition there is an excess mortality risk compared with that of the general

population. This excess morbidity and mortality risk becomes particularly more striking for patients with ATPD in a developing country like Nigeria where studies show that the prevalence of ATPD could be 10 times higher than in developed countries (Susser and Wanderling 1994). Schizophrenia and ATPD patients also experience being stigmatized. This is an additional social burden for sufferers of both conditions and the people who care for them.

Apart from the burden on the individual, there is a major burden of care that family members have to bear because there is no national social welfare and community rehabilitation programmes for the mentally ill in Nigeria. This burden is higher than what care givers of patients with other chronic diseases such as cancer have to bear. This burden is corroborated by a study comparing care giver burden of psychiatric patients and cancer patients in Nigeria. the authors found that caregiver burden was significantly higher among relatives of patients with psychosis(Ohaeri 2001). In financial terms, the mean annual impact of serious mental illness in Nigeria in 2003 was estimated at 60,126 Naira (US$ 463)while at the level of the society the annual impact was 21.6 billion Naira (US$ 166.2 million)(Esan et al. 2012).This suggests that such mental disorders have enormous negative impact on earnings both at the individual and societal level in Nigeria.

1.3 JUSTIFICATION

One of the most challenging issues that psychiatrists face is differentiating between ATPD and Schizophrenia when they present acutely for the first time. The need to differentiate between the two conditions becomes particularly important when relatives of patients request information on the prognosis of a sudden onset of a psychotic illness in their relative. Schizophrenia stands out prominently with regards to being stigmatized. Hence making a correct diagnosis is crucial to avoiding stigmatization and discrimination of patients. The duration of follow up treatment is also a reason to be able to differentiate between both mental conditions. Schizophrenia requires long term treatment whereas ATPD requires a shorter duration of treatment. Hence correct diagnosis is important to guide patient care and management. Needless long term exposure to antipsychotics, resulting from a failure to distinguish between the two disorders could be avoided if clinical and epidemiological features are taken into consideration in making a diagnosis. The

need for correct clinical diagnosis is particularly important in Sub-Saharan Africa where health care resources are inadequate and scarce. Thus, it would be beneficial to both the patient and health care provider to distinguish between the two disorders in a low resource setting like Nigeria.

A close study of the difference between both conditions will also aid the implementation of appropriate programs and policy for people living with mental illness. This is apart from the fact that it promotes mental health which is one of the components of Primary Health Care, the health care system of the country.

1.4 AIM

This study aims to identify sociodemographic and clinical differences between patients with ATPD and Schizophrenia.

SPECIFIC OBJECTIVES: The specific objectives are to:

1. Compare the sociodemographic characteristics of the two groups of patients.
2. Compare the distribution of psychopathology between the two groups of patients.
3. Identify sociodemographic and clinical factors associated with schizophrenia and ATPD.

1.5 HYPOTHESES

1. There is no significant difference in age of onset between patients with ATPD and those with Schizophrenia.
2. There is no difference in the sociodemographic characteristics between patients with ATPD and those with Schizophrenia.
3. There is no difference in the distribution of psychopathology between patients with ATPD and those with Schizophrenia.
4. Schizophrenia and ATPD will each have independent predictive factors.

CHAPTER TWO

LITTERATURE REVIEW

2.1 ACUTE AND TRANSIENT PSYCHOTIC DISORDERS

2.1.1 History of Acute and Transient Psychotic Disorders

Acute and transient Psychotic disorders originated from the concept of reactive or psychogenic psychosis. This was widely used through most of the 20th century in the Scandinavian countries for a major group of the so-called "functional psychoses", separate from manic depressive psychosis and schizophrenia. Karl Jaspers described specific criteria for the diagnosis of reactive psychosis, including the presence of an identifiable and extremely traumatic stressor, a close relation between the stressor and the development of psychosis, a generally benign course of the psychotic episode and a tendency to full recovery(Sadock and Sadock 2007).

Ever since the introduction of International Classification of Diseases, Tenth Revision, (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM IV), the reactive psychoses have been reallocated as acute and transient psychotic disorders with associated acute stress and Brief Psychotic Disorder (BPD) respectively.

Currently, The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) describes brief psychotic disorder based primarily on duration of symptoms. DSM-IV defines brief psychotic disorder as an illness lasting from one day to one month, with an eventual return to the premorbid level of functioning.(American Psychiatric Association 2000) Similarly ICD 10 describes the ATPDs as a heterogeneous group of disorders characterized by the acute onset of psychotic symptoms such as delusions, hallucinations, and perceptual disturbances and by the severe disruption of ordinary behaviour. Complete recovery usually occurs within a few months, often within a few weeks or even days. It however states that the disorder may or may not be associated with acute stress(World Health Organization 1993).

Although ATPD has a high concordance with the DSM IV BPD, the ATPDs extends beyond the limits of DSM-IV BPD and includes a subgroup of DSM-IV Schizophreniform disorder.

2.1.2 Epidemiology of ATPD

ATPD is generally considered to be rare based on data from western Europe and the United states (Sadock et al. 2007).In a study that examined a 6-year analysis of readmission patterns of all subjects listed in a Danish psychiatric central register, the incidence of ATPD was 9.6 per 100 000 among patients admitted or treated in outpatient services. (Castagnini et al. 2008). The incidence in developing countries such as Nigeria might not be as low. This is because the incidence in the developing-country setting is about 10-fold the incidence in the industrialized-country setting.(Susser and Wanderling 1994). Nevertheless, the incidence and prevalence of cases that do not come to clinical attention are unknown.

Most studies report that ATPD has a female preponderance (Susser and Wanderling 1994; Marneros et al. 2000; Pillmann et al. 2001; Pillmann et al. 2002; Marneros 2006). In an inpatient study of consecutive patients fulfilling DSM-IV criteria for ATPD in Halle, Germany, 81% of the patients were reported to be females This is at variance with a study in , Qatar (a developing country) by Shaltout et al which found no significant difference in the frequency of ATPD between males and females (Shaltout et al. 2007) Furthermore. Singh et al found the rate of ATPD in men to be almost double that in women with a male to female ratio of 1.87 (Singh et al. 2004).

Individuals with pre-existing personality disorders are predisposed to the development of ATPD. However, the ATPDs are not related to any particular type of Personality Disorder (Jorgensen et al. 1996; American Psychiatric Association 2000; Ungvari and Mullen 2000). ATPDs may be related to Affective Disorders, whereas other evidence suggests that it may be different from both Schizophrenia and Affective Disorders. They are characterized by marked affective disturbances (Marneros et al. 2000; Marneros et al. 2005) and anxiety (Marneros et al. 2005; Lau et al. 2009) within an episode compared with Schizophrenia. The ATPDs are more common in people who have experienced a major cultural change Lau et al..(2009) showed that ATPDs were two times more common in Foreign workers from the Filipines compared to local Chinese women of similar age for this illness (Lau et al. 2009).

ATPDs may appear in adolescence or early adulthood, the average age at onset being between 25 and 35 years (American Psychiatric Association 2000; Pillmann et al. 2002). Age at first episode in ATPD is similar to that of patients with positive symptoms of schizophrenia (Pillmann et al. 2002). The age of onset in industrialized countries are higher than in developing countries (Sadock et al. 2007).

Persons who have gone through major psychosocial stressors and negative life events are at an increased risk of the ATPDs (Beighley et al. 1992; Malhotra 2003; Marneros et al. 2003; Sadock et al. 2007). Marneros et al showed that compared with the normal population patients with ATPD had a significantly higher prevalence of a ''broken home'' situation prior to the onset of ATPD(Marneros et al. 2003). Similarly, Beighley et al found a temporal relationship between the onset of stressors and the development of ATPD among Air Force recruits (Beighley et al. 1992).

While there is evidence to show that no significant difference exists between married and single persons with respect to the development of ATPDs(Shalitout et al. 2007),marital problems have been identified as major stressors in the development of ATPDs (Lau et al. 2009).

2.1.3 Aetiology of ATPD

The cause of brief psychotic disorder is unknown. However ATPDs can be triggered by a distinctly stressful event or by childbirth. It can also occur for no apparent reason at all. There is some evidence that BPD is related to mood disorders; however, this association is considered controversial. People with personality disorders may have a biological or psychological vulnerability for the development of psychotic symptoms especially those with borderline , schizoid, schizotypal or paranoid traits(Jorgensen et al. 1996; American Psychiatric Association 2000; Ungvari and Mullen 2000; Sadock et al. 2007)

The post-partum period is a high risk period for the development of the ATPDs. The frequency of post-partum psychoses is evaluated at 1 to 2 per 1,000 births (Tabbane et al. 1999) . Similarly, antenatal exposure to stress increases the risk of ATPD in the post partum period. Primiparity, previous psychiatric history, antenatal complications, caesarean section, perinatal death and having a female baby have been shown to be associated with high psychiatric morbidity in puerperium (Singh and Kaur 2000).

Some people may have a genetic vulnerability to ATPD(Das et al. 1999; Malhotra 2003) and ATPD occurs more frequently in people with family members who have had ATPD (Malhotra 2003).

2.1.4 Clinical Features of ATPD

The symptoms of ATPDs include an acute onset of delusions, hallucinations, incomprehensible or incoherent speech, or any combination of these. The time interval between the first appearance of any psychotic symptoms and the presentation of the fully developed disorder should not exceed two weeks.(World Health Organization 1992).Labile mood, confusion and impaired attention may be common at the onset of ATPDs compared to other chronic psychiatric disorders such as Schizophrenia. However these should not meet the criteria for organically caused clouding of consciousness and mood disorders respectively. The disturbance cannot be due to the direct physiological effects of a substance or drug (such as a prescription medication, or an illicit drug like cocaine), or a general medical condition (American Psychiatric Association 2000). Characteristic symptoms in the ATPDs include emotional volatility, strange or bizarre behavior, screaming or muteness, and impaired memory for recent events .Some of the symptoms may suggest a diagnosis of delirium and warrant a medical work up.(Sadock et al. 2007).Although there is usually the presence of a stressor, it is not essential in its diagnosis.

2.1.5 Diagnosis of ATPD

The diagnosis of the ATPDs is based on the following criteria in the ICD10(World Health Organization 1992).

1 An acute onset of delusions, hallucinations, incomprehensible or incoherent speech, or any combination of these. The time interval between the first appearance of any psychotic symptoms and the presentation of the fully developed disorder should not exceed two weeks.

2. If transient states of perplexity, misidentification, or impairment of attention and concentration are present, they do not fulfill the criteria for organically caused clouding of consciousness.

3. The disorder does not meet the symptomatic criteria for manic episode, depressive episode or recurrent depressive disorder.

4. No evidence of recent psychoactive substance use sufficient to fulfill the criteria of intoxication, harmful use, dependence or withdrawal states.

5. Absence of organic brain disease or serious metabolic disturbances affecting the central nervous system

2.1.6 Treatment of ATPD

There are only a few studies on ATPDs to guide evidence-based treatment recommendations and clinical management .However evidence-based treatments for other psychotic disorders are applicable for the short-term resolution of ATPD symptoms (Kane et al. 2003). Treatment for the ATPDs usually includes psychotherapy, pharmacotherapy or both. Hospitalization may be necessary for evaluation and safety if the symptoms are severe or if there is a risk that the person be a danger to self or to others. Furthermore, long-term monitoring is important to evaluate for relapse, assess for conditions that may precipitate a referral to a mental health professional, and to ensure adherence to treatment.

Medication: Antipsychotics may be prescribed to control psychotic symptoms and terminate an episode of psychosis. Antipsychotics are a chemically diverse but pharmacologically similar class of drugs used to psychotic disorders. Examples include chlorpromazine, clozapine, risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, sertindole, zotepine.

Psychotherapy provides an opportunity to discuss the stressors and the psychotic episode with the sufferer. It also helps in the exploration and development of coping strategies. Psychotherapy: Psychotherapy helps the person identify and cope with the situation or event that triggered the disorder.

2.2 SCHIZOPHRENIA

2.2.1 History of Schizophrenia

The word Schizophrenia was coined by Eugen Bleuler in 1907, but the disorder has probably accompanied humans throughout its whole history. The word was intended to describe the separation of function between personality, thinking, memory, and perception. It was first identified as a discrete mental illness by Emil Kraepelin in 1887, who had used the word dementia praecox to define it. Eugen Bleuler used the word schizophrenia for the first time in 1911.

Schizophrenia historically has been found in many cultures. It can be traced in written documents to the old Pharaonic Egypt, as far back as the second millennium before Christ. Hindu descriptions of schizophrenia dates back to approximately 1400 BC. A Chinese text entitled The Yellow Emperor's Classic of Internal Medicine, written around 1000 BC, described symptoms of insanity, dementia, and seizures. Demonic or supernatural possession was often implicated as the cause of such psychotic behaviours. A study into the ancient Greek and Roman literature showed that although the general population probably had an awareness of psychotic disorders, there was no condition that would meet the modern diagnostic criteria for schizophrenia in these societies. Early theories supposed that mental disorders were caused by evil possession of the body, and the appropriate treatment was then exorcising these demons, through various means, ranging from innocuous treatments, such as exposing the patient to certain types of music, to dangerous and sometimes deadly means, such as releasing the evil spirits by drilling holes in the patient's skull.

The 17th century saw the beginnings of psychiatric hospitals in Europe. With these hospitals came attendants and medical supervisors and the birth of psychiatry.

Beginning in the 18th century, increased importance was placed on thorough and precise descriptions of abnormal mental processes. The 19th century saw a sudden increase of information about the body and mind. Evidence was mounting that mental illness was caused by disease in the brain after a link had been found between general paresis of the insane and syphilis. Biologic aetiologies of mental illness were adopted and separate illnesses identified.

It was in this 19th century that Schizophrenia emerged as a medical condition worthy of study and treatment. Two major figures in psychiatry and neurology who studied the disorder were Emil Kraepelin and Eugene Bleuler. In addition, Benedict Morel a French psychiatrist used the term ''demence precoce'' to describe what is presently known as Schizophrenia .The term denotes deteriorated patients (Dementia) whose illness began in adolescence (Precocious) (Sadock et al. 2007).

2.2.2 Epidemiology of schizophrenia

Several reviews show that there is variability in the prevalence of schizophrenia (Torrey 1987; Saha et al. 2005). In a systematic review by Saha et al which included 1721 prevalence estimates from 188 studies and 46 countries, the median point prevalence, period prevalence and life time prevalence estimates were 4.6, 3.3 and 4.0 per 1000 persons respectively. The authors also reported the lifetime morbid risk of schizophrenia (LMR) as 7.2 per 1000 persons. LMR is the probability of a person developing a disorder during a specified period of their life or up to a specified age. There was at least a fivefold difference between the smallest and the largest values in these estimates. The estimates are higher than the lifetime estimate of 5.5 per 1000 by Goldner et al (2002) but lower than the lifetime estimates of 8.7per 1000 by Perala et al (2007) and 6 per 1000 by Kessler et al (Kessler et al. 1994) although the estimates by Kessler et al included schizophreniform disorder, schizoaffective disorder, delusional disorder and atypical psychosis .

In keeping with the trends of a higher incidence of schizophrenia among migrants, there is a higher prevalence of schizophrenia among migrants(Saha et al. 2005). It has been suggested that the higher prevalence is due to the fact that migrants preferentially receive schizophrenia diagnoses because of cultural misconstruction and/or language difficulties. Nonetheless, proof in support of this belief is not convincing. Follow-up studies have shown no evidence of greater diagnostic instability over time among migrants versus non-migrants (Takei et al. 1998; Harrison et al. 1999).

In contrast to the observed difference in incidence across gender (McGrath et al. 2004), there are no differences in gender with regard to the prevalence of schizophrenia(Saha et al. 2005) . Prevalence estimates have been commonly found to be similar among males and females

Goldner et al (2002). It has been suggested that the disparity between incidence and prevalence could be related to compliance with treatment and higher rates of suicide completion in men than in women Ochoa et al (2012).

Reported prevalence estimates of schizophrenia are less in developing compared to developed countries (Saha et al. 2005) This finding was corroborated by the study by Mcgrath et al (McGrath et al. 2008) who found the median estimates in developed countries compared to less - developed countries to be 3.3 vs. 2.6 per 1000 respectively

There is a significant positive correlation between latitude and the prevalence of schizophrenia. Prevalence estimates from sites in the high-latitude band are significantly higher when compared with lower bands (Saha et al. 2006; Kinney et al. 2009). Some explanations have been proposed for this relationship. First is the pre- or perinatal exposure to some adverse environmental factors that are associated with higher latitudes (Kinney et al. 2009). Another is the trend for patients with schizophrenia to be more prone than controls to be born in the winter, rather than other seasons. The prevalence of schizophrenia increases with latitude and severity of winter climate (Davies et al. 2003) and becomes stronger when factors such as a family history of the disorder(O'Callaghan et al. 1991; Kinney et al. 2000) is corrected for.

2 .2.3 Aetiology of Schizophrenia

Like many non communicable diseases there are many etiological factors associated with schizophrenia. Evidence abounds on the etiology of schizophrenia from the point of view of genetics. Biochemistry, neuropathology, neuroimaging, psychophysiology, immunology, sociological and family dynamics.

Genetics

There is a genetic contribution to all forms of schizophrenia. The odds of a person developing schizophrenia are associated with the closeness of the relationship to an affected relative. As such whereas the prevalence of schizophrenia in the general population is about 1%, the prevalence for a non twin sibling of a schizophrenia patient is 8%, for a dizygotic twin of a schizophrenia patient it is 12% while for a monozygotic twin of a schizophrenia patient it increases to 47%. (Sadock et al. 2007)

Adoptive studies assesses how much genetic influences weigh against environmental influences by examining rates of schizophrenia in adopted-away offspring of schizophrenic and of normal parents. Such studies show that between 10 per cent and 13 per cent developed schizophrenia while none of the adopted offspring of normal parents developed schizophrenia. (Buckley et al. 2005).

Neurochemistry

Dopamine hypothesis postulates that dopamine over activity in mesolimbic pathways is responsible for the development of schizophrenia. Evidence in support of this hypothesis includes the ability of Amphetamine to induce a schizophrenia-like psychosis (Amphetamine increases dopamine release in the brain). Secondly, Antipsychotics block Dopamine receptors .This correlates with the clinical effectiveness of Antipsychotics. Furthermore, post-mortem studies show increased dopamine and dopamine receptors in caudate nucleus and nucleus accumbens of patients with schizophrenia. Apart from Dopamine, Serotonin Nor adrenaline. Gama amino butyric acid (GABA) have been implicated in the etiology of schizophrenia.

Neuropathology

There is a decrease in brain weight of patients with schizophrenia compared with normal subjects. There is also a reduction in anterior posterior length of patients with schizophrenia compared with normal subjects. This probably supports a view that schizophrenia is a neurodegenerative disease.

Neuroimaging

Computerized Tomography (CT) studies show non-specific ventricular enlargement and cortical sulcal prominence in subjects with schizophrenia. Similarly, Positron Emission Tomography and Magnetic Resonance Imaging studies show that frontal and temporal lobes are major sites for abnormalities in patients with schizophrenia. Recent proof favors generalized cortical tissue loss and functional disconnectivity in the brains of patients with schizophrenia. Mathalon et al., 2001(Mathalon et al. 2001) found that patients with chronic schizophrenia exhibited accelerated frontotemporal cortical gray matter decline and cortical sulcal and lateral ventricular expansion .This suggests that there may be progressive tissue loss in patients with active schizophrenic

illness. Structural brain anomalies occur in patients with schizophrenia. Even though these anomalies are slight yet they reproducible Shenton et al., 2001 (Shenton et al. 2001) in a review of MRI findings in schizophrenia from 193 peer reviewed MRI studies found ventricular enlargement (80% of studies reviewed) and third ventricle enlargement (73% of studies reviewed). There is also preferential involvement of medial temporal lobe structures (74% of studies reviewed), which include the amygdala, hippocampus, and parahippocampal gyrus, and neocortical temporal lobe regions (superior temporal gyrus) (100% of studies reviewed). When gray and white matter of superior temporal gyrus was combined, 67% of studies reported abnormalities. Family members with high risk of developing schizophrenia also show similar but more subtle brain changes (Lawrie et al. 2002) .

Life Events

There is a strong relationship between the vulnerability in a person and the ability of stressors to either induce or aggravate the symptoms of schizophrenia. This is known as the Vulnerability--stress models of schizophrenia.

Family Dynamics

There is a possible aetiological role of family relational style and development of schizophrenia. Adoptees at high genetic risk are significantly more sensitive to adverse (compared to healthy) rearing patterns in adoptive families than are adoptees at low genetic risk (Tienari et al. 2004).

Developmental Theories

Studies suggest that developmental factors play a role in the etiology of schizophrenia. The season of birth appears to be correlated with the risk of developing schizophrenia. The risk of developing schizophrenia is greatest for individuals born in late winter and early spring.

2.2.4 Clinical Features of Schizophrenia

There are no pathognomonic signs of schizophrenia .However, certain symptoms could suggest schizophrenia. Schneider's First-rank symptoms (FRS), in the absence of organic illness, signify schizophrenia. These include

1. Audible thoughts.

2. Third person hallucinations.
3. Hallucinations in the form of a commentary.
4. Somatic passivity experiences.
5. Thought withdrawal or insertion.
6. Thought broadcasting.
7. Feelings or actions experienced as under the control of an external force.
8. Delusional perception.

Second-rank symptoms have less diagnostic significance they include other disorders of perception, sudden delusional ideas, perplexity, depressive and euphoric changes etc. Schneider's FRS have been very influential, but have limitations first Specificity - occur in other 'functional psychoses' about 20 per cent in psychotic depression and 40 per cent in acute mania. Secondly about 20 per cent of chronic schizophrenics never showed FRS.

2.2.5 Diagnosis of Schizophrenia

The International Classification of Diseases, 10th edition (ICD 10) criteria from the World Health Organization) for diagnosis of includes

A minimum of one very clear symptom (and usually two if less clear-cut) from groups (a)–(d) below, or symptoms from two of the groups (e)- (h), which have been present for most of the time during a period of one month or more:

(a) Thought echo, insertion, withdrawal, and broadcasting.

(b) Delusions of control, influence, passivity; delusional perception.

(c) Hallucinatory voices of running commentary, third-person discussion, or other types of voices coming from some part of the body.

(d) Persistent delusions of other kinds that are culturally inappropriate and completely impossible.

(e) Persistent hallucinations in any modality: daily for weeks/months, or accompanied by half-formed nonaffective delusions, or with persistent overvalued ideas.

(f) Breaks in thought fluency, i.e. incoherence, irrelevant speech, neologisms.

(g) Catatonic behaviour: excitement, stupor, mutism, posturing, waxy flexibility, negativism.

(h) Negative symptoms: apathy, paucity of speech, blunted emotions, social withdrawal: not due to depression or neuroleptic medication

(i) A significant and consistent change in the overall quality of some aspects of personal behaviour (loss of interest, social withdrawal, aimlessness)

2.2.6 Treatment of Schizophrenia

Antipsychotics are the mainstay of the treatment of schizophrenia however , psychosocial interventions psychotherapy enhance the clinical improvement(Sadock et al. 2007). Antipsychotics medications reduce the psychotic symptoms of schizophrenia and usually allow the patient to function more effectively and appropriately. However they do not cure schizophrenia or ensure that there will be no further psychotic episodes. The large majority of people with schizophrenia show substantial improvement when treated with antipsychotic drugs.

Antipsychotic Medications

Antipsychotic medication can be classified broadly into two groups as the conventional (typical) antipsychotics such as haloperidol, chlorpromazine, thioridazine and the newer atypical (second-generation) antipsychotics: such as clozapine, risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, sertindole, zotepine.

Electroconvulsive Therapy (ECT)

Electroconvulsive therapy may be helpful in catatonic states (Tharyan and Adams 2005). The symptoms may improve with the addition of an antidepressant medication.

Psychosocial Treatments

Psychosocial treatments aim to maximize abilities and minimize disabilities(Bustillo et al. 2001). Components include cognitive retraining, crisis management, education, vocational rehabilitation, family therapy, group therapy, social skills training.

Psychotherapy

In the treatment of schizophrenia ,psychotherapy is supportive, practical, problem-oriented, and encourages compliance (Spaulding and Nolting 2006). Cognitive–behavioral therapy is advocated for persistent delusions.

Rehabilitation

Rehabilitation plan in patients being managed for schizophrenia may include vocational counseling, job training, problem-solving and money management skills, and social skills training.

2.3 COMPARISON OF ATPD AND SCHIZOPHRENIA

The ATPDs generally have good outcomes (Marneros et al. 2003; Singh et al. 2004; Pillmann and Marneros 2005). They are also recognized in both The International Statistical Classification of Diseases and Related Health Problems 10th Revision ICD–10 (World Health Organization, 1992) and The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 1994) as distinct from schizophrenia and affective psychoses such as mania or depression with psychotic features.

Unlike Schizophrenia, ATPD is relatively under researched. There is therefore a dearth of information on the disorder especially in the developing countries where it has been shown to be relatively common (Marneros et al. 2003; Shaltout et al. 2007). The results from available studies on ATPD show that it is an infrequent diagnosis in psychiatric facilities (Marneros et al. 2000; Pillmann et al. 2001; Marneros et al. 2003). For example, the study by Pillmann et al among inpatients at a psychiatric facility found that only 4.1% of patients treated for psychotic disorders or a major affective disorder had ATPD. Schizophrenia is a relatively common

psychotic disorder having a lifetime prevalence of about 1% (Perala et al. 2007) , its prevalence is the same in men and women. Prevalence in migrants is usually significantly higher than to native-born individuals, and estimates from less developed countries are also significantly lower than those from both "emerging" and "developed" countries (Saha et al. 2005). ATPD however is not as common as Schizophrenia and it has a lifetime prevalence of 0.05% (Perala et al. 2007). ATPD is also relatively more common in the developing world. The incidence of ATPD in the developing-country setting was found to be about 10-fold the incidence in the industrialized-countries (Susser and Wanderling 1994). ATPD unlike Schizophrenia has a female preponderance (Susser and Wanderling 1994; Marneros et al. 2000; Pillmann et al. 2001; Pillmann et al. 2002; Marneros et al. 2003; Marneros 2006). In an inpatient study of consecutive patients fulfilling criteria for ATPD in Halle, Germany, 81% of the patients were reported to be females. This is at variance with a study in. Qatar (a developing country) by Shaltout et al which found no significant difference in the frequency of ATPD between males and females(Shaltout et al. 2007).

Many studies from high income countries have found patient outcome of ATPD to be better than those of patients with Schizophrenia. (Susser et al. 1995; Malhotra 2003; Marneros et al. 2003; Singh et al. 2004; Shaltout et al. 2007).The few reports from low income countries have found similar results (Guinness 1992; Okasha et al. 1993).

Patients with ATPD are more likely to have a family history of ATPD rather than a family history of Schizophrenia (Das et al. 1999; Malhotra 2003) . This probably further substantiates the belief that it is a distinct from schizophrenia. At onset ATPDs have a short prodrome compared to schizophrenia (Marneros et al. 2000; Marneros et al. 2002) and the average duration of the illness of ATPD is typically shorter ,ranging from two to four months (Mojtabai et al. 2000). Most cases of ATPD occur in early adulthood (16-29) years. The study in Qatar reported that no case of ATPD occurred among the 174 in patients treated in a hospital over a seven year period(Shaltout et al. 2007).

Patients with ATPD usually have a better premorbid functioning compared to patients with Schizophrenia (Pillmann et al. 2002; Jager et al. 2003; Marneros et al. 2003; Marneros 2006). Patients with Schizophrenia often have an impaired functioning prior to the onset of the first episode (Strous et al. 2004).It is more common for patients with ATPD to have a negative life

event or stressors preceding an episode of illness, than patients with schizophrenia (Marneros et al. 2002; Malhotra 2003; Marneros et al. 2003). These reported stressors are variable and may range from marital problems, to being a foreigner (Lau et al. 2009).Even though both ATPD and Schizophrenia have many features in common there are differences in psychopathology. The delusions that patients with Schizophrenia exhibit are largely stable; however, the delusions in ATPD are characterized by rapidly changing topics. ATPD also tends to have a higher prevalence of anxiety and presents more often with marked affective disturbances within an episode compared with Schizophrenia (Marneros et al. 2000; Marneros et al. 2005).

CHAPTER THREE

METHODOLOGY

3.1 STUDY SETTING

The study area was the Psychiatry Unit of the University College Hospital (UCH), Ibadan. UCH is an 812 bed teaching hospital located in Ibadan, South-West Nigeria. The estimated population of South West Nigeria is about 28 million (National Population Commission Nigeria 2006). The hospital receives referrals specifically from health facilities in the South West geopolitical zone of Nigeria and frequently from all geopolitical zones of the country .The hospital also provides tertiary and quaternary health care services for the country. The Department of Psychiatry is one of the major specialties in the hospital. It has seven sub-specialties and runs three adult clinics weekly and a 24-hour emergency service. The in-patient facility in the department has two wards operated as a male and female ward and equipped with 64 beds, equally distributed between the two wards. The department has 9 consultants, 17 resident doctors and 32 nurses that run the activities. The Records section of the department is located in the male ward and is manned by five trained records officers who run a 24 hour shift. The Section of Medical Records in the Department of Psychiatry classifies all the psychiatry cases based on ICD-10 diagnoses. Data of all the patients who were admitted in the ward or seen in the outpatient clinics of the department during this period were collected. Only case records reviewed by a consultant psychiatrist were included in the study.

3.2 STUDY DESIGN

This was a comparative study. It was also a case series in which a review of case notes of patients with a first episode of Schizophrenia and ATPD was carried out. All consecutive patients during this period that met the ICD-10 criteria for ATPD and Schizophrenia were recruited into the study.

3.3 STUDY POPULATION

The study population consisted of new male and female adult patients aged between 18 years and 65 years seen during the period from 1st of January 2006 to 31st December 2010. Total sampling was done for all cases that met the criteria for ATPD and Schizophrenia during this period.

3.4 INCLUSION CRITERIA

1. ICD 10 criteria for ATPD or Schizophrenia (Criteria in Sections 2.1.5.and 2.2.5 respectively)
2. Patients in first ever episode of psychotic illness.
3. Patients that have not been treated with antipsychotics.

3.5 EXCLUSION CRITERIA

1. All cases with incomplete records or missing key variables.

3.6 SAMPLE SIZE DETERMINATION

The sample size was calculated to ensure that the number of case records reviewed was adequate to make valid inferences. The formula used was:

$$n = \frac{(Z_\alpha + Z_\beta)^2 \ (\pi_1 (1 - \pi_1) + \pi_2 (1 - \pi_2))}{\delta^2}$$

Where

N is the minimum sample size to be studied in each group.

Z_α is the standard normal deviate corresponding to a type 1 error rate (2 sided level of significance of 5% = 1.96)

$Z_{2\beta}$ is the standard normal deviate corresponding to a one sided beta error of 5% (96% power) = 1.645

π_1= proportion of females in schizophrenia=50% (Saha et al. 2005)

π_2= Proportion of females in ATPD=78.6% (Marneros et al. 2003)

Calculation:

Z_α 1.96

$Z_{2\beta}$ (at 96% power) = 1.645

π_1 50% = 0.5

π_2 78.6% = 0.786

δ 0.286

$Z_\alpha + Z_{2\beta}$ 1.96+1.645 = 3.605

$(Z_\alpha + Z_{2\beta})^2$ = 3.605^2 = 12.995

$$n = \frac{(Z_\alpha + Z_\beta)^2 \ (\pi_1 (1 - \pi_1) + \pi_2 (1-\pi_2))}{\delta 2}$$

$$n = \frac{13.00(0.5(1-0.5) + 0.79(1-0.77)}{0.29^2}$$

66.2

To adjust for non-response.

$$N(s) \quad \frac{1}{1-r}$$

r = estimated non- response rate = 10% or 0.1

at 10% = $\frac{66 \times 1.0}{0.9}$

=73.3

Hence minimum sample size was =73.

3.7 DATA COLLECTION

Sociodemographic and clinical data were extracted from the case notes of patients using a case record form. The case record form collected data on age at first episode, sex, marital status at presentation, employment status, family history, psychopathology at presentation. Sociodemographic data were extracted by two research assistants after three weeks of training by -

the Principal Investigator. The clinical data were extracted by the investigator. Data was collected over a period of 10 weeks from February 1 to April 14, 2012.

3.8 DATA MANAGEMENT AND ANALYSIS

Data cleaning and coding was done daily by the investigator. Data entry and analysis was done using the Statistical Package for the Social sciences (SPSS) version 16.0.

Descriptive statistics such as means and standard deviations were used to summarize quantitative variables such as age at onset, while frequencies and proportions were used for qualitative variables. Chi-Square test and Student-t test were used to test for significance between qualitative variables and differences between means respectively. Logistic regression was used to identify independent factors associated with schizophrenia and ATPD.

CHAPTER FOUR

RESULTS

Between 1st of January 2006 and 31st of December 2011, 2604 new patients aged between 18 and 65 years were seen at the Clinic. There were 706 subjects with schizophrenia and 208 subjects with ATPD representing 27.2% and 8.0% of all the cases seen respectively. Subjects who had received some treatment or who were not first episode cases were excluded. For the patients with schizophrenia, 233 patients were not first episode patients while 230 patients of the remainder although were first episode, had been treated at other mental health facilities before presentation at the UCH. As such, 463 subjects were excluded from the schizophrenia group (Appendix 1). For the subjects with ATPD, of the 208 new patients, 54 were not first episode, while 30 though first episode patients had received prior treatment; as such these 84 patients were excluded. Following the exclusion, 243 subjects with Schizophrenia and 124 subjects with ATPD were recruited into the study. This represented 9.3% and 4.8% of the number of new patients that were seen at the department respectively i.e. proportional morbidity rate for schizophrenia and ATPD respectively.

4.1 SOCIO-DEMOGRAPHIC CHARACTERISTICS.

Table 1 describes the sociodemographic characteristics of the subjects with ATPD and Schizophrenia respectively. Over 70% of all the cases seen in both ATPD the Schizophrenia group were between the ages of 15 and 34 years. There were about equal proportion of males and females in both groups (P=0.91). Majority (72.6%) of the subjects with ATPD had the first episode of ATPD between the ages of 20 and 39 years. Likewise, majority (79.5%) of the subjects with schizophrenia had the first episode of illness at the age of 20-39years. A significantly higher proportion of subjects who had ATPD (46.8%) presented below the age of 25 years compared to those that had schizophrenia (30.0%) (P<0.01). There was a significant association between occupation and diagnoses (P<0.01). A significantly higher proportion of subjects with schizophrenia (16.9%) were unemployed compared to patients with ATPD (4.2%) (P<0.01) There was also a significant association between marital status and diagnosis (P<0.01).

Subjects with Schizophrenia had a significantly higher proportion of subjects who were divorced, widowed or separated (11.9%) compared to subjects with ATPD (3.2%) (P<0.01). In both groups about 60% of the subjects were single. Majority of the patients with Schizophrenia (51.1%) had at least tertiary education while most of the ATPD (58.1%) group had at most a secondary education. In both groups over 75% of the subjects were Christians (P=0.73).

Table 1 Comparison of the sociodemographic characteristics of subjects with untreated first episode of ATPD and Schizophrenia seen at the University College Hospital Ibadan between January 2006 to December 2010.

Variable	Dependent Variable (% within diagnosis)		X^2	P- value
	ATPD n (%)	SCHIZOPHRENIA n (%)		
Age at presentation (Years)				
<20	9 (7.3)	11 (4.5)	13.94	<0.01*
20-29	71 (57.3)	116 (47.7)		
30-39	19 (15.3)	80 (32.9)		
40-49	20 (16.1)	26 (10.7)		
≥50	5 (4.0)	10 (4.1)		
Gender				
Male	61(50.8)	125 (51.4)	0.01	0.91
Female	63 (33.8)	118 (48.6)		
Occupation				
Skilled	35(29.70)	51(25.40)	16.41	<0.01*
Semiskilled	22(18.60)	51(25.00)		
Unskilled	12(10.20)	12(6.00)		
Unemployed	5(4.20)	34(16.90)		
Student	44(37.30)	53(26.40)		
Level of Education				
No Formal Education	5 (4.00)	6(2.60)	5.91	<0.12
Primary	17(13.70)	28(11.90)		
Secondary	55(44.40)	81(34.50)		
Tertiary	47(37.90)	120(51.10)		
Marital Status				
Single	73 (58.90)	150(61.70)	10.67	<0.01*
Married	46(37.90)	64(26.30)		
Divorced/ Widowed/ Separated	5 (3.20)	29(11.90)		
Religion				
Christianity	94(75.80)	185 (77.74)	0.12	0.73
Islam	30(24.20)	54(22.60)		

Table 2 shows the comparison of means. The mean age at presentation for the ATPD and Schizophrenia groups were 29.5 (S.D 9.6) and 30.8 (S.D 8.8) respectively (P =0.2).There was no significant difference in the age at onset between ATPD and schizophrenia in males 29.61(S.D.9.46) vs. 31.75(9.16) (P=0.14) and also in females 29.38(S.D.9.79) vs. 26.96(S.D.7.57) (P =0.06). The mean age of onset of the subjects with ATPD was 29.5 (SD 9.6) years while for the schizophrenia subjects it was 29.3 (S.D 8.7) (P=0.20).

Table 2 Comparison of means between subjects with untreated first episode of ATPD and first episode of Schizophrenia seen at the University College Hospital Ibadan between January 2006 to December 2010.

VARIABLES(Years)	ATPD Mean(S.D.)	SCHIZOPHRENIA Mean (S.D.)	T-TEST	P-VALUE
Age at presentation	29.50(9.60)	30.9(8.80)	-1.29	0.20
Age at onset (All)	29.50(9.60)	29.3(8.70)	0.21	0.20
Age at onset (Male)	29.61(9.46)	31.75(9.16)	-1.47	0.14
Age at onset (Female)	29.38(9.79)	26.96(7.57)	1.87	0.06
Numbers of years of education	11.50(4.40)	12.0(4.80)	-1.04	-0.53

4.2 CLINICAL CHARACTERISTICS

Thirty one subjects (27.2%) of the patients with ATPD had a relative with a family history of mental illness, while in the subjects with schizophrenia, a similar proportion (25.2%) had a family history of mental illness (P=0.71). In both groups a majority (64.5% and 82.5% respectively) of those that had a family history of mental illness were first degree relatives(p=0.10).

Table 3 shows the distribution of positive psychotic symptoms in both groups. In both groups the majority had delusions and conceptual disorganization as part of the presenting symptom. A significantly higher proportion of subjects with schizophrenia had excitement(17.7%) as part of the presenting symptom compared to subjects with ATPD (1.2%)(P<0.01).Grandiosity was present in 12.1 % of the subjects with schizophrenia compared to 6.6 % of the subjects with ATPD. Suspiciousness was three times more common in the patients with schizophrenia (20.2%) compared to the patients with ATPD (6.5%) (P<0.01).

Table 3 Comparison of Positive Psychotic Symptoms between subjects with untreated first episode of ATPD and Schizophrenia seen at the University College Hospital Ibadan between January 2006 to December 2010.

Positive Psychotic Symptoms	ATPD n (%)	SCHIZOPHRENIA n (%)	X^2	P value
Delusions	77 (62.10)	156 (64.20)	0.16	0.69
Conceptual Disorganization	82 (66.10)	142 (58.40)	2.04	0.15
Hallucinatory Behavior	61 (49.20)	124 (51.00)	0.11	0.74
Excitement	22 (17.70)	3 (1.20)	35.24	<0.01*
Grandiosity	15 (12.10)	16 (6.60)	3.23	0.07
Suspiciousness	8 (6.50)	49 (20.20)	11.77	<0.01*
Hostility	44 (35.50)	93 (38.30)	0.27	0.60

Table 4 shows the comparison of negative psychotic symptoms between both groups. A significantly higher proportion of subjects with schizophrenia 18.5% (45) had blunted affect compared to 4.0% (5) of subjects with ATPD. This association was significant (<0.01). A significantly higher proportion of subjects with schizophrenia 26.3 % (64) had passive social withdrawal compared to subjects with ATPD 3.2% (4).

Table 4 Comparison of Negative Psychotic Symptoms between subjects with untreated first episode of ATPD and Schizophrenia seen at the University College Hospital Ibadan between January 2006 to December 2010.

Negative Psychotic Symptoms	ATPD n (%)	SCHIZOPHRENIA n (%)	X^2	P value
Blunted Affect	5 (4.0)	45(18.5)	14.64	<0.01*
Emotional withdrawal	1(0.8)	26(10.7)	11.80	0.01*
Passive social withdrawal	4 (3.2)	64 (26.3)	29.052	<0.01*
Lack of spontaneity	1 (0.8)	9 (3.7)	2.6	0.11
Stereotyped thinking	2 (1.6)	6 (2.5)	0.28	0.60

Table 5 shows that patients with ATPD presented more commonly 35.5% (44) with symptoms of anxiety compared to patients with schizophrenia 22.6% (55). This difference was significant (P 0.01). Also patients with schizophrenia presented more commonly (20.2%) with disturbance of volition than patients with ATPD (8.1 %) (P<0.01).

Table 5 Comparison of General Symptoms between subjects with untreated first episode of ATPD and Schizophrenia seen at the University College Hospital Ibadan between January 2006 to December 2010.

General symptoms	ATPD (%)	SCHIZOPHRENIA (%)	X^2	P value
Somatic concern	12(9.7)	19 (7.8)	0.37	0.55
Anxiety	44(35.5)	55(22.6)	6.88	0.01*
Tension	19(15.3)	22(9.1)	3.25	0.07
Depression	11(8.9)	31(12.8)	1.22	0.27
Uncooperativeness	18(14.5)	17(7.0)	5.38	0.02*
Unusual thought content	9(7.3)	31 (12.8)	10.90	0.11
Disorientation	13(10.5)	49 (20.2)	5.48	0.19
Poor attention	59 (16.1)	79 (21.5)	7.94	0.01*
Lack of judgment and insight	79(63.7)	171 (70.4)	1.68	0.2
Disturbance of volition	10 (8.1)	49 (20.2)	8.91	<0.01*
Poor Impulse control	42 (33.9)	113(46.5)	5.37	0.20
Preoccupation	23 (18.5)	80 (32.9)	8.40	<0.01*
Active social avoidance	3 (2.4)	7 (2.9)	0.66	0.79

4.3 FACTORS THAT INDEPENDENTLY PREDICT SCHIZOPHRENIA

Table six shows the factors that are independently predictive of schizophrenia following logistic regression. Subjects above 25 years are about three times more likely to have schizophrenia compared to those below the age of 25 .This was statistically significant (P=0.02). There was a significant relationship between occupational status and schizophrenia. Subjects who had semiskilled occupation were twice likely to have schizophrenia than to those who were engaged in a skilled occupation. Subjects who were unemployed were four times more likely to have schizophrenia than to those who had skilled employment (P=0.04). With regards to the symptomatology of schizophrenia, subjects with suspiciousness, emotional withdrawal, and preoccupation were more likely to be schizophrenics than those who were not. Also, subjects who had excitement poor attention were less likely to be schizophrenics than those who were not.

Table 6: Factors that were predictive of Schizophrenia after logistic regression.

	Odds ratio	95% CI of Odds Ratio		P-Value
Age at presentation				
Below 25(REF)	1.0			
Above 25	2.46	1.18	5.15	0.02*
Occupation				
Skilled(REF)	1.00			
Semiskilled	2.32	1.02	5.27	0.04*
Unskilled	0.95	0.29	3.15	0.94
Unemployed	3.60	1.05	12.26	0.04*
Student	0.85	0.33	2.17	0.73
Marital Status				
Single(REF)	1.00			
Married	0.58	0.27	1.19	0.13
Divorced/widowed/separated	2.36	0.64	8.67	0.20
Symptoms of schizophrenia				
Excitement	0.07	0.01	0.34	<0.01*
Suspiciousness	3.29	1.29	8.42	0.01*
Blunted	5.00	1.60	15.61	0.07
Emotional withdrawal	38.83	1.90	795.62	0.02*
Passive social withdrawal	15.04	4.08	55.48	<0.01*
Anxiety	0.60	0.31	1.12	0.11
Uncooperativeness	0.42	0.15	1.17	0.10
Poor attention	0.48	0.27	0.88	0.02*
Disturbance of Volition	1.01	0.37	2.73	0.99
Preoccupation	2.04	1.02	4.10	0.04*

4.4 FACTORS THAT INDEPENDENTLY PREDICT ATPD.

Table seven shows the factors that are independently predictive of ATPD following logistic regression. Subjects above 25 years are about three times less likely to have ATPD compared to those below the age of 25 .This was statistically significant (P=0.02). There was a significant relationship between occupational status and ATPD. Subjects who had semiskilled occupation were twice less likely to have ATPD compared to those who were engaged in a skilled occupation. Subjects who were unemployed were four times less likely to have ATPD than to those who had skilled employment. With regards to the symptomatology, subjects with excitement, and poor attention more likely to have ATPD than those who did not have such symptoms. Similarly subjects who were suspicious, had blunted affect, passive social withdrawal or who had preoccupation were less likely to have a diagnosis of ATPD than those who did not have such symptoms.

Table 7: Factors that were predictive of ATPD using logistic regression.

Variable	Odds Ratio	95.0% C.I. for Odds Ratio		P- Value
Age at presentation				
Below 25	1.00			
Above 25	.406	0.19	0.85	0.02*
Occupation				
Skilled (REF)	1.00			
Semiskilled	.43	.19	0.98	0.04*
Unskilled	1.05	0.32	3.48	0.93
Unemployed	0.28	0.08	0.95	0.04*
Student	1.18	0.46	3.03	0.73
Marital status				
Single (REF)	1.00			
Married	1.76	0.84	3.69	0.13
Divorced/widowed/separated	0.42	0.12	1.55	0.20
Symptoms of ATPD				
Excitement	15.30	2.91	80.40	<0.01*
Suspiciousness	0.30	0.12	0.78	0.01*
Blunted affect	0.20	0.06	0.62	0.01*
Emotional withdrawal	0.03	0.02	0.53	0.02*
Passive social withdrawal	0.07	0.02	0.25	<0.01*
Anxiety	1.70	0.90	3.22	0.11
Uncooperativeness	2.38	0.86	6.59	0.10
Poor attention	2.07	1.14	3.75	0.02*
Disturbance of Volition	1.00.	0.37	2.68	1.00
Preoccupation	0.49	0.24	0.98	0.04*

CHAPTER FIVE

DISCUSSION

5.1 SOCIODEMOGRAPHICS

This sample of untreated first episode ATPD and Schizophrenia represents the clinical patient population of patients with ATPD and Schizophrenia respectively in UCH respectively. It included all consecutively diagnosed cases of untreated first episode of ATPD and Schizophrenia seen during a five year period in a Nigerian teaching hospital. About 5% of all new patients that were seen at the department had ATPD. This is in sharp contrast to findings from Europe and North America where ATPD has been shown to be a rare occurrence (Marneros et al. 2003; Marneros et al. 2003; Sadock et al. 2007). About 10% of all the new cases seen were untreated first episode of schizophrenia while 27.2% of all the new cases were diagnosed as schizophrenia. Healy et al (2012) that found 64% of subjects admitted in North Wales were schizophrenia or schizoaffective disorder. Although the study (Healy et al. 2012) focused on admitted patients and included schizoaffective disorders. The figures reiterate the enormous burden of schizophrenia on the society and especially in a low economy country like Nigeria.

Over 70% of the subjects in both groups had the first episode of illness between the ages of 20 and 39 years. This age at onset in the ATPD subjects was similar to the commonest age range of presentation of 16-29 years by Shaltout et al (2007) in a Qatar a developing country like Nigeria. Similarly the modal age range of onset in the schizophrenia group was within the peak age onset of 15 to 35 years commonly reported (Sadock and Sadock 2007). In line with previous studies that found no significant differences between ATPD and Schizophrenia with regards to the age of onset (Pillmann et al. 2002; Marneros et al. 2003; Marneros et al. 2005) this study also found no significant difference in the age of onset between patients with ATPD and patients with Schizophrenia .The mean age of onset of the subjects with ATPD was 29.5 years while for the schizophrenia subjects it was 29.3 years. However, compared to the result in this study the authors of both studies (both conducted in Europe) found a higher mean age of onset of 35.8 years and 35.3years for ATPD and Schizophrenia respectively. Nevertheless the same trend of a slightly higher age of onset of ATPD above Schizophrenia was observed in our study. As such age at onset did not differentiate between ATPD and schizophrenia. The public health

implications of the lower age of onset of both schizophrenia and ATPD compared to that in Europe are a high prevalence of psychotic disorders on the society since schizophrenia is a chronic disorder. The implication of this is increased demand and utilization of mental health facilities, increased mental health needs by the populace with a consequent increased spending of scarce resources on mental health.

Unlike the age of onset, the age at presentation in this study discriminated between ATPD and Schizophrenia. With respect to a first episode of illness, ATPD was significantly more likely to present below the age of 25 years compared to Schizophrenia. This finding is in keeping with the epidemiology of schizophrenia with an average age of onset of 15-35 years.(Sadock et al. 2007). Following the desegregation of age of onset by sex, neither ATPD nor schizophrenia showed a differentiation in age of onset by sex. This is at variance with reports of a higher age of onset of schizophrenia in females.

Contrary to previous studies that found marked female preponderance in ATPD (Susser and Wanderling 1994; Marneros et al. 2000; Pillmann et al. 2002; Marneros et al. 2003). This study found an equal gender representation in both groups. The finding of an equal frequency of ATPD between males and females is however in keeping with the reports by Shaltout et al (2007) in a study carried out in Qatar. A common factor to all the studies that found a preponderance of females in ATPD is that they were all conducted in Europe or in the United States. This finding adds weight to the findings of cross-cultural differences in the incidence of ATPDs (Sartorius et al. 1978; Susser and Wanderling 1994). It may also suggest that epidemiology of ATPD may differ with geographic sites. Whether this is true needs further exploration; However it has been shown that comparable to the relationship between latitude and the incidence of certain disorders such type I diabetes (Holick 2004) there is a significant positive association between latitude and the incidence of certain psychotic disorders (Saha et al. 2006). Schizophrenia however, unlike ATPD does not show gender differentiation with regards to incidence (Leung and Chue 2000).

A comparison of the occupational status between ATPD and schizophrenia revealed some minor differences. A significantly higher proportion of subjects with schizophrenia(16.9%) were unemployed at the time of presentation compared to ATPD (4.2%).This trend was also found among subjects at follow up in a study by Pillmann et al (2002) (Pillmann et al. 2002) No significant differences were observed with regards to educational level. This result confirms the

findings from earlier investigations by Marneros et al (2003) and Pillmann et al (2002) that educational level did not distinguish between schizophrenia and ATPD. With regards to employment and education .Guinness (1992) found an over-representation of education and paid employment in the ATPDs compared with schizophrenia (Guinness 1992).In keeping with the findings by Guinness, subjects with ATPD in the current study had a higher proportion of subjects in employment compared to subjects with schizophrenia.

Patients with schizophrenia have lower rates of marriage (Watt and Szulecka 1979) In this study subjects with schizophrenia were more likely to be single, while ATPD subjects were more likely to be married. This is however at variance with the study by Pillman et al (2002) that showed that being married did not differ significantly between the ATPD group and schizophrenia group. A bivariate analysis in the current study showed that compared to ATPD, subjects with schizophrenia were significantly more likely to be divorced, widowed or separated. This could be due to the fact that patients with schizophrenia have poor social skills and are less likely to be in or maintain a heterosexual relationship(Watt and Szulecka 1979). Separation and divorce could also be a consequence of the illness when partners cannot cope with the stress associated with being married to spouses with mental illness.

A comparison of the psychotic features between both groups revealed that delusions and hallucinations were frequent in both groups. This is expected because both symptoms define a psychotic disorder. It was also not surprising that there were no significant differences in both groups with regards to the proportion that presented with hallucinations and delusions. Excitement was significantly more common among subjects with ATPD this included features such as agitation, pressured speech, excessive arousal and hyperactivity. Similarly suspiciousness was significantly more common in schizophrenia compared to ATPD (20.2% vs. 6.5%). Features classified here included distrustfulness, persecutory ideas, hypervigilance, delusions of persecution. Both Excitement and Suspiciousness constituted some of the most important differences regarding the phenomenology of ATPD and Schizophrenia in this study. Expectedly , and in keeping with previous studies, negative psychotic symptoms such as blunted affect ,emotional withdrawal ,passive social withdrawal were significantly more common in Schizophrenia This corroborates the findings by Jager et al (2003). This feature reiterates the importance of negative psychotic symptoms in the diagnosis of schizophrenia in both the ICD-10

and DSM-IV where the presence of negative symptoms is highly suggestive of schizophrenia (World Health Organization 1993; American Psychiatric Association 2000)

A comparison of general (non psychotic) symptoms between the two groups revealed some differences. Anxiety and uncooperativeness were significantly more common in the ATPD group while poor orientation, disturbance of volition, preoccupation were significantly more common in the Schizophrenia group. Similarly, a five year prospective study that explored psychopathological differences between ATPD and Schizophrenia Marneros et al (2005) concluded that the most important differences between ATPD and schizophrenia were a higher frequency of rapidly changing delusional topic, a rapidly changing mood and anxiety in ATPD compared to schizophrenia. This study corroborates this finding as well. It is however important to note that differences in psychopathology are not sufficient to distinguish between ATPD as an entity and schizophrenia.

Logistic regression identified certain factors as predictive of schizophrenia. Symptoms such as emotional withdrawal, passive social withdrawal are part of the symptom cluster known as negative symptoms of schizophrenia (American Psychiatric Association 2000). As such it was expected that such symptoms would predict schizophrenia. Scully et al (2002) showed that the average age at presentation of first episode of schizophrenia was 31.4 years. This is in keeping with the findings in this study that showed that age of presentation above 25 years was predictive of schizophrenia. It is well established that people with schizophrenia have markedly high rates of unemployment. There is also evidence of associations between high rates of unemployment and greater symptomatology (Ramsay et al. 2012).Similarly, in this study unemployed subjects were four times more likely to be schizophrenics than subjects who have skilled occupation. Whisman and Baucom showed that relationship discord is associated with mental ill health. Furthermore,it was shown that married people have better mental and physical health than their non married counterparts (Whisman and Baucom 2012; Whisman et al. 2012).In this current study, subjects who were Widowed, divorced, separated were twice more likely than those who were single to have schizophrenia. Conversely, being married was protective against schizophrenia .This however did not attain statistical significance.

The factors that were predictive of ATPD included excitement and poor attention. Subjects who had these symptoms were more likely to receive a diagnosis of ATPD compared to those who

did not have such symptoms. Excitement is an affective symptom. This finding is in keeping with reports by Marneros et al (2000) that ATPD showed marked affective symptoms compared to schizophrenia.

Mental ill health such as ATPD and schizophrenia has a significant impact on a range of outcomes. This includes reduced educational accomplishment, greater risk of suicide.substance misuse, antisocial behaviour, and early pregnancy. Individuals with mental illness also experience increased levels of physical illness and reduced life expectancy. In economic terms, psychotic disorders matter significantly. At the national level, treatment expenses can be high and the loss of labour due to its chronicity can make a substantial dent in a country's productive capacity. .

One strength of this study is that it has used a relatively large sample size for the ATPD group. Previous studies used much smaller sample sizes for example in Germany, Pillmann et al (2002) used 26 patients, also in Germany, Pillman et al (2001) used 42 patients, in Denmark, Jorgensen et al (1996) used 51 patients, in India. Susser et al (1995) used 46 patients (Susser et al. 1995) .As such this study has more power to detect a difference compared to the earlier mentioned studies. Secondly, since ATPDs are common in the less developed countries the findings of this study are more generalizable in Africa compared to previous studies which were done in Europe and America. Hence this is one of the first studies on ATPD in Africa.

The results of this study should be considered in the context of its limitations. First, this was a review of case notes as such missing information is not uncommon with such studies. However for subjects who had lengthy follow up at the clinics or who had more than one episode of illness and presented at our clinics, several sociodemographic data were obtained from the case note at such follow up and latter episodes Consequently there were very few missing sociodemographic data. Secondly, the diagnosis of ATPD and Schizophrenia were not made with standardized diagnostic research instruments. These are structured and semi structured interviews based on diagnostic criteria such as ICD10 criteria for Schizophrenia. They help to standardize a subject cohort. An example is the Structured Clinical Interview for DSM IV (SCID). However each case of ATPD or Schizophrenia recruited into the study was reviewed by

two specialist, firstly during the first episode and secondly, at the commencement of this study by the principal investigator. Cases that did not meet the criteria were excluded.

Thirdly it is possible that some cases of ATPD were classified as schizophrenia and vice versa. Random misclassification results in an underestimate of the difference between the two groups while differential misclassification can either overestimate or underestimate the true difference between the two groups depending on the situation. This type of bias was minimized by ensuring a good method of ensuring diagnosis by two specialists as earlier stated.

5.2 CONCLUSION

This five year comparative review of case notes of patients with a first episode of schizophrenia and those with a first episode of ATPD revealed that 9.3% and 4.8% of the new patients seen at the department of psychiatry UCH were untreated first episodes of schizophrenia and ATPD respectively. Over 70% of this new untreated first episode cases were between the ages of 15 and 34 years. The mean age at presentation for patients with Schizophrenia and ATPD were similar.

ATPD and Schizophrenia were alike in many ways. This similarity included the age of onset, gender distribution of the disorder, mean number of years of formal education, distribution according to religion, presence of the symptoms of delusions , hallucinatory behaviour, conceptual disorganization, grandiosity, hostility , somatic concern ,tension , depression active social withdrawal and poor impulse control. Differences which may be important in differentiating between the two include the observation that ATPD were more likely to present below 25 years compared to Schizophrenia, excitement as a symptom was more common in ATPD. The presence of anxiety and uncooperativeness was more suggestive of ATPD than schizophrenia. Suspiciousness was more common in Schizophrenia compared to ATPD. The presence of negative symptoms especially blunted affect, emotional withdrawal, passive social withdrawal was significantly more common in schizophrenia. Poor orientation, disturbance of volition, and preoccupation were more common in schizophrenia than ATPD.

5.3 RECOMMENDATIONS

The following recommendations were made based on the results of this study

1 Clinicians should bear in mind that compared to Europe and America, in Nigerians, ATPD has a slightly differential pattern of risk of illness compared to schizophrenia. This includes a lower mean age of onset, an equal pattern of risk for ATPD in women. These differences should be taken into consideration when discussing prognosis of an acute onset of a first episode of psychotic disorder with family members of a sufferer.

2 There is need for further cross-cultural research on the ATPD in Africans .There is also the need to replicate the findings of this study using a prospective approach.

3 Public health physicians need to sensitize the populace on the differences in the signs and symptoms between ATPD and schizophrenia. This is important in predicting the course, devising long term treatment, promoting mental health and reducing stigma.

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APPENDIX 1

A COMPARISON OF THE PROFILE OF PATIENTS WITH ACUTE AND TRANSIENT PSYCHOTIC (ATPD) DISORDER AND SCHIZOPHRENIA AT THE UNIVERSITY COLLEGE HOSPITAL IBADAN (2006-2010).

1 Study Number					
2 Hospital Number					
3 Diagnosis					
4 Date of assessment/ presentation					
5 Age at presentation					
6 Age at onset					
7 Gender	1 Male	2 Female	9–Not Stated		
8 Employment status	1 Employed	2. Unemployed	8 Not Stated		
9 Occupation					
10 Marital status	1.Single/ Never married		4.Divorced		
	2.Married		5.Widowed		
	3.Cohabiting		6.Separated		
11 Religion	1.Christianity				
	2.Islam				
	3.Others(Specify)				
12 Highest level of education	1.No Formal Education	2.Primary	3.Secondary	4.Post secondary	5.University
13 Number of years of education					
14 Admission status	Inpatient		Outpatient		
15 Date of onset of symptoms		17.1 Duration of illness before presentation			
16 Date of onset of psychotic episode.		18.1 Duration of psychosis before presentation			
17 Date of admission(If admitted)		19.1 Duration of admission			
18 Date of remission					
19 Date of discharge(If Admitted)					
				Diagnosis	

20 Family history of similar MentaHllness	Yes/ No	Who?	1	
			2	
			3	

21Psychopathology at presentation	Psychopathology
22 Mental State Examination	

Parameter				
1 Appearance				
2Mood				
3 Affect				
4 Speech				
5 Thought				
a)Form				
b)stream				
c)content				
d)Possession				
6 Perception				
7 Orientation				
a)Time				
b)Place				
c)Person				
8 Attention /Concentration				
9 Abstraction				
10 Memory				
11 Intelligence				
		Average	Below average	Above average
12 Judgement				
		Normal	Impaired	
13 Insight				
		No Insight	Partial Insight	Full Insight

APPENDIX 2

Flow chart showing patients recruitment procedure.