INTRODUCTION

1.1 General introduction

Psychiatric disorders have proved to be a major health problem in the recent years. The ‘Global Burden of Disease’ statistics indicate that four out of ten most common diseases worldwide are of psychiatric origin. Kasper, et al. (2008) mentioned that of the various mental disorders, depression, anxiety disorders and adjustment disorders affect about 10% of the population in general. In India the stigma attached to psychiatric disorders and the reluctance to offer depression as a diagnosis may be responsible for the low diagnosis of depressive illness.

The spectre of mental diseases is frightfully enormous. Mental disorders are all pervading, found in people of all regions of the world irrespective of race, gender, age, culture and socio-economic status and are essentially effectively treatable so much so that people with disorders of the mind can lead long productive life along with the main stream of the society.

Statistical studies conducted by the World Health Organization (WHO) have shown that psychiatric disorders in adults have a prevalence of about 10 percent, and it has also been found that one in four families has at least one member suffering from a mental or behavioral disorder at one point of time. About 450 million people were estimated to have been suffering from psychiatric disorders. Major Depressive Disorder is now a leading cause of disability globally and ranks fourth among the leading causes of global burden of diseases (WHO). Depressive disorders were known since the ancient times. As early as the Greek era, depression has been conceptualized in various forms at different points of time. This was primarily because at that time usable research data were not available and also due to frequent variations in occurrence and progress of the disorder.
In 18th century scientists observed that there can be two kinds of clinical presentation of depression. One in which there is an apparent external factor causing depression and in another there is no external factor which causes depression.

Major depressive disorder is a syndrome characterized by recurrent episodes of low mood manifested by persistent alteration of mood for more than two weeks with profound sadness, decreased psychomotor activity, guilt feeling, self blaming, also feeling of hopelessness, helplessness and worthlessness, suicidal ideas, poor sleep and loss of appetite (Freedman 2002).

All of us experience a range of profound emotions in response to stressful life situations. Such emotions may manifest at certain points of life without any perceivable stressful situation. Sadness is of course a normal human emotion and one that is generally unavoidable in the face of stressful and demanding life situations. However, normal sadness waxes and wanes over time and generally lasts for short duration, and people are usually able to come to terms with such situations. In contrast, clinical depression is long lasting and much in excess of what can be explained in context with the stressful life situations.

1.1.1 Types of symptoms

It is customary to divide symptoms of depression in two categories

1. Psychological Symptoms

2. Somatic Symptoms

Psychological Symptoms are

i) Depressed mood or Sadness

ii) Loss of Interest or Pleasure

iii) Loss of energy or fatigue
iv) Loss of Concentration

v) Suicidal thoughts

vi) Guilt/Worthless/Pessimism

vii) Perceptual abnormalities-hallucinations or delusions.

Somatic Symptoms

i) Sleep disturbances

ii) Loss of appetite

iii) Muscle fatigue

iv) Psychomotor retardation

v) Constipation

vi) Menstrual problems

vii) Loss of Sex drive

viii) Agitation (state of restlessness)

ix) Miscellaneous symptoms → headache, backache etc.

1.1.2 Types of depression

There are two core symptoms of depression according to Diagnostic and Statistical Manual of Mental Disorder (DSM-IV TR, A.P.A 2000) namely depressive mood and marked loss of interest and pleasure in most or all activities. To qualify as depression, one of these two core symptoms must be present for at least two weeks along with at least four other depressive symptoms which includes fatigue, poor appetite, weight loss, sleep disturbances, and impairment of memory and concentration. There can be other symptoms
of diagnostic importance like a pervasive sense of hopelessness, helplessness, excessive guilt, self depreciatory thinking, feeling of worthlessness and a feeling that one is being punished by the Almighty or that life is without value. Prominent thoughts about death, death wish and suicidal ideation are strongly associated with depressive illness (Lander M. et al. 2000 and Breibrat et al. 1997).

Both ICD–10 (International Classification of Diseases, WHO 1992) and DSM–IV-TR (Annexure1) conceptualizes depressive episodes in context of their intensity of symptoms as mild, moderate, and severe. Both the systems of classification have specified number of operational criteria for labeling a depressive episode to be mild, moderate or severe (Annexure 2).

Some other types of depression:

1. **Reactive depression** (reaction to stress): A kind of depression in which there is an apparent external adverse factor causing depression.

2. **Endogenous depression** (endo means inside and genous means origin): A kind of depression in which there is no apparent external factor causing depression.

3. **Neurotic depression**: A kind of depression which is mild to moderate and lasts for a long duration with predominant physical symptoms.

4. **Psychotic depression**: A kind of depression which is severe with significant physiological impairment, marked suicidal tendency and generally associated with psychotic symptoms like delusion and hallucination.

5. **Masked Depression**: As many as 50% of major depressive episodes are unrecognized because depressed mood is less obvious then other symptoms of the disorder. Inability to express emotions in words can focus a patient’s attention to physical symptoms of depression such as insomnia, low energy and difficulty in concentrating, without any awareness of feeling depressed. This is also described in literature as ‘Laughing Depression’ or ‘Smiling Depression’.
6. **Dysthymic Disorder**: Dysthymia means “ill tempered”. Dysthymic disorder is a non episodic, chronic depression which last for at least two years. It is generally less severe than the Major Depressive Disorder (MDD).

7. **Anxiety-Depressive Disorder**: The co-occurrence symptoms of anxiety and depression are very common. Kendler et al. (1986) found very high genetic correlations between MDD and generalized anxiety disorder. Anxiety symptoms commonly appear in depressive syndromes and again MDD is frequently found in combination with anxiety disorders.

8. **Resistant Depression**: There is a small percentage of patient suffering from depression, that end up not recovering from depression to any significant extent in spite of being given the best qualitative treatment options for a reasonable long time. This state of depression is called resistant depression. These patients pose a major challenge to the psychiatrist as a large number of them end up committing suicide.

**Suicidal Phenomenon**: The current definition of MDD emphasizes suicidal ideation, thoughts of death and suicidal attempts as the cardinal feature of syndrome of depression. Suicide a feature of depressive disorder carries substantial risk of mortality (Stein et al. 2006). While treating depression, prevention of suicide and immediate intervention when the situation arises assumes much more importance in comparison to the treatment of any other symptoms of depression. A patient with depression who has attempted suicide or is actively contemplating to end his life does require hospitalization as an urgent salvage measure. Suicide is an obvious public health problem that complicates mood disorders more frequently than other conditions. The life time risk of suicide in mood disorders is 10% - 15% (Barklage 1991, Guze and Robbins 1970, Mueller and Leon 1996). The risk of attempted suicide was increased by 41-fold in depressed patients compared to those with other diagnosis in Epidemiologic Catchment Area (ECA) survey (Petronis et al. 1990). Depressive disorders are common and recurrent and are associated with substantial
psychosocial dysfunction and morbidity, in fact approximately 4% – 5% of all depressed patients will commit suicide in the course of time (Kasper, et al. 2008).

1.1.3 Course of depressive disorder

Frank and colleagues (1991) after studying natural course of recurrent depressive disorder have put forward few criteria, pertaining to the change points during the course of illness.

Important change points in the natural course of recurrent depressive disorder are remission, relapse and recurrence.

**Remission** – Remission is a period in which the individual is asymptomatic, does not meet the syndromal criteria for MDD and has no more than minimal symptoms; in clinical practice this remission extends from 2 to 9 months.

**Relapse** – The return of symptoms which meet the criteria of a full episode of MDD and occur towards the end of remission but before recovery is known as relapse.

**Recurrence** – A manifestation of a new episode of MDD that occurs during recovery is known as recurrence.

1.1.4 Risk factors

Numerous studies have investigated the psycho-social environmental and biological risk factor associated with the development of depressive illness. Epidemiological research is the key to the identification of risk factors for mental disorders. Familiarity with the risk factors for major depressive disorders may help to recognize or diagnose this common and serious psychiatric illness. The “depressive guideline Panel” which came up in 1993 consists of certain primary risk factors of depression, viz.

1. History of prior episodes of depression

2. Family history of depressive disorders especially in first-degree relatives.
3. History of suicide attempts

4. Female gender

5. Age of onset before age 40

6. Postpartum period

7. Co-morbid medical illness

8. Absence of social support.

9. Negative, stressful life events

10. Active alcohol or substance abuse.

11. Unmarried, Divorced or Separated status

1.1.5 Factors associated with occurrence of depression

Depression occurs mainly due to stress. Stress can be viewed as an event or situation occurring in a person’s life which compels him to make significant changes in his life situation to adapt to the changing and difficult situation. Stress can be of varying origin as:

1. Social stress – it is a stress induced by various social factors like

   (a). Economic stress – it is the stress related to factors demanding constant adjustment to meet ends. This leads to enormous stress of uncertainty and insecurity. Moreover with expansion of family, financial needs increases while resources remaining limited. This is a major source of stress in economically backward countries.

   (b). Occupational stress – with industrialization and consumerism work related stress is on the rise. So, an individual has to prove himself time and again and thereby work hard to excel and generate more and more to meet the ever escalating target.
(c). Family stress – with break down of joint family structure, more and more families are becoming nuclear. This has led to stress, related to family management like – daily chores, financial management, children education and bearing all responsibilities of the family. Moreover with increasing level of education, employment and financial solvency of individual members of the family, new stresses have started to appear in families like quarrels, increasing breakdown of marital relationship. Again, bereavement caused by death of a near and dear ones and similar life events lead to enormous stress leading to depression.

(d). Migration and minority stress – significant stress is experienced by people who migrate from one habitat to another. This leads to assuming at least temporarily a minority social status to the person shifted to the new place. It generates sense of insecurity and a feeling of being less privileged and thereby become a cause for depression to set in.

2. Co-morbid medical illness - Recent research has convincingly proved that depression is often present with several medical illnesses. It has been shown that heart disease predisposes to depression while presence of depression significantly increases the probability of heart disease. Similarly diabetes and high blood pressure are found to be associated with depression. Stress and anxiety worsen both the conditions. Depression following child birth (postpartum blue) is a well documented entity. It has also been shown that depression often follows diagnosis and treatment of cancer and the presence of depression significantly interferes in body’s own defense mechanism (immunity) which is essential for recovery. Other diseases like viral hepatitis and hypothyroidism often predispose to depression.

3. Alcohol and drug dependence:  It has been proved conclusively that long term abuse of alcohol and other psychoactive drugs increases the possibility of depression and suicide.

4. Social isolation:  Now-a-days most of the elderly people are staying alone as their children are pursuing academic or professional careers away from home. This leads to depression and sense of insecurity aptly termed as the “empty nest syndrome”.

1.1.6 Dimensions of mood disorder

Categorical diagnosis in psychiatry is not as uniform or as useful clinically as is suggested in the diagnostic manual (Nease et al. 1999). Mood disorders are diverse physiologically as well as phenomenologically. Even within the same individual, the presentation and treatment response of affective episodes may vary from one episode to the next.

Within categorical constraints, there are many dimensions of abnormal mood, and the expression of a given type of mood disorder will depend on the net interaction between the factors shown in the figure (1) given below.

**Fig. 1.1 Dimensions of mood disorder**
More categories of depression, and more treatment options, exist in real life than are listed in the textbooks. For example, a classification system based on cluster analysis that included severity as a diagnostic dimension was more useful than DSM diagnosis in predicting impairment of mental and physical health in primary care setting (Nease et al. 1999). As more knowledge accumulates about the importance of specific dimensions of depression, it may become possible to make dimensional as well as categorical diagnoses that suggest more specific treatment options.

1.2 Aims and objectives of the study

The problem of Major Depressive Disorder (MDD) is affecting an ever increasing population day by day. It has lead to significant proportion of premature deaths and it has also resulted in a significant drain in the national revenue in the treatment and loss of manpower. Till date, several epidemiological studies and clinical trials have been carried out on the course, outcome, symptoms, and treatment of MDD by various researchers. Computer friendly statistical modeling has also been applied in the clinical trials involving adequate number of patients in long term follow-up studies.

In this research work our aims and objectives were

- To study the probabilistic behaviour and pattern of the data. This would help to understand the disorder from statistical viewpoint, with an aim to improve the understanding of the disorder by the treating professional.
- Markovian approach has been explored to analyse the data as the behaviour of the depressive patients is highly probabilistic.
- This analysis may be helpful to the psychiatrists as behaviour of various operating characteristics will be presented in this research work.
- To analyse the data pertaining to the patients suffering from Major Depressive Disorder. The data collected is the secondary data from Psychiatry Out patients’ Department (OPD) of Gauhati Medical College and Hospital (GMCH) for a period of ten years.
1.3 Plan of the thesis

A Summary of the Work Done

In the next section of Chapter 1, a brief survey of the work already done on Major Depressive Disorder (MDD) research and on the various concepts and theories which has been applied in this thesis has been presented. This is followed by the definition of mathematical tools used in the thesis.

In Chapter 2, an attempt is made to examine the present scenario of the disease. A study of the world epidemiology of some aspects of MDD from available literature and a subsequent study of the local epidemiological scenario as observed from the collected data has been presented in this chapter. The source of data is the records of the Out patients’ Department (OPD) of the department of Psychiatry of Gauhati Medical College and Hospital (GMCH). The data were collected yearly at random for a period of ten years from 2000 to 2009. In all, records of 518 confirmed patients of MDD attending the OPD were studied. Data has been analysed with respect to socio-demographic variables like age, sex, family history, marital status, education, occupation and socioeconomic status. The next endeavour in this chapter is to estimate the occurrence rate of depressive episodes in the patients studied over the period considered. Here hazard rates, cumulative hazard rates, estimated occurrence density and estimated probability of occurrence of depressive episodes are computed (using excel sheet) and it is observed that the occurrence rate of depressive episodes in the patients is shown to be increasing over the years.

In Chapter 3, Regression Analysis is applied to study the impact of the socio-demographic variables (mentioned in Chapter 2) on MDD. Multiple linear regression models have been carried out to study the effect of socio-demographic variables on MDD. To study the affect of these variables on the severity or intensity of the depressive episodes on the patients Ordinal Logistic regression model is used.
The results of multiple linear regression models reveal that:

Sex, socioeconomic status, family history and education contribute significantly to the prediction of the patients suffering from depression. Age, marital status and occupation does not show any significant effect on the occurrence of depression which is in contrast to some common findings. This may be because the sample of the present study has been drawn from the Psychiatry OPD of GMCH which may not be representative of the general population.

The results of ordinal logistic regression models reveal that:

Socioeconomic status and occupation are negatively associated with severity of MDD i.e., for low socioeconomic status and for the unemployed patients the degree of severity is higher. There is no statistically significant affect of age, sex, family history, education and marital status on severity of MDD.

In Chapter 4, the severity of depressive episodes has been ranked as mild, moderate and severe which are mutually exclusive and jointly exhaustive events. To study the probabilities of the variables being affected by mild, moderate and severe depression conditional probabilities have been used which is a consequence of Bayes’ theorem. Here the estimation of odds and indices of diagnostic tests in depression have been computed by applying Bayes’ theorem.

The prior and posterior odds of the socio-demographic variables of the data collected for ten years from GMCH reveal the following:

- Severe and moderate depression in female has been observed to be more whereas mild depression in female is less in comparison to male.
- Severe depression is more likely to occur for those patients who have positive family history.
- Married people suffer more from depression than the unmarried people irrespective of the status of depression.
- Educated people suffer from depression irrespective of the status of depression.
There is a substantial increase of employed people suffering more from mild depression than moderate and severe depression.

People belonging to the middle class suffer less than those of the lower middle class people for every status of depression.

Large number of patients suffers from depression in the age group of less than 45 years.

Bayesian analysis has been used for computing diagnostic values such as sensitivity, specificity and accuracy for a certain diagnostic test and predictive values are obtained to make decisions. In major depressive disorder the diagnosis has been made based on the cluster of symptoms specified by ICD-10 and DSM IV TR. These symptoms are divided as good prognosis and bad prognosis factors. Based on the prognostic factors “Schedule for Assessment of Probable Outcome of Major Depressive Disorder” has been constructed. The reliability and the validity of the schedule have been tested by the senior faculties of the department of Psychiatry, GMCH. Thereby the sensitivity, specificity and accuracy of the schedule have been developed to reassess the reliability of the schedule.

The relevant data collected from 2000 to 2009 for this study have revealed the following:

- Sensitivity = 67.6%. This is percentage of patients remitted with good prognostic factors.
- Specificity = 82.1%. This is percentage of patients not remitted with bad prognostic factors.
- Accuracy = 71.3%. This is percentage of patients correctly assessed and diagnosed.

In Chapter 5, the renewal process has been formulated on the basis of hazard rate of time between two consecutive occurrences of depressive episodes and the corresponding distribution functions may be obtained from hazard rate. This chapter emphasizes the importance of hazard rate and presents the distribution of depressive episodes under
different structures of hazard rate of occurrence. The renewal processes are formulated with

- constant hazard rate
- linearly increasing hazard rate
- hazard rate of distributions which have both IHR and DHR properties
- hazard rate of uniform distribution

The distribution of range i.e. the difference between the longest and the shortest occurrence time to a depressive episode, and the expected number of depressive episodes in a random interval of time are obtained for the distributions under consideration. If the closed form of expression for the waiting time distribution is not available, then the Laplace transformation is used for the study of probabilistic analysis. Hazard rate of occurrence and expected number of depressive episodes have been presented graphically.

In Chapter 6, the occurrence and recovery of a depressive episode follows alternating renewal process. The pattern of the process changes corresponding to the behaviour of the patients. Under different behavioural patterns of the patients the renewal processes have been formulated. The hazard rates under different renewal processes have been obtained. Expected number of renewals per unit of time as time (t) tends to infinity has been obtained and renewal rates have been computed. Hazard rates and renewal rates have been presented graphically.

In Chapter 7, the occurrence of depression has been confined to two specific causes say $A_1$ and $A_2$ which can also be done for multiple causes. The renewal process is a one state process which is renewed after a random interval of time or time epoch but here the renewal may be due to cause $A_1$ or cause $A_2$. The hazard rates of time epochs of depressive episodes for different causes have been obtained. Range of time epochs have also been studied. Here different situations have been studied when the specific causes affect the patients with different hazard rates. For each situation, different distributions
have been formulated to study the pattern of the occurrence of depressive episodes. The hazard rates have also been presented graphically for better understanding at a glance. The pattern of the depressive episodes may be of help to the psychiatrists to predict the time of occurrence of depressive episodes and act accordingly.

In Chapter 8, the joint effect of the simultaneous occurrence of the causes $A_1$ and $A_2$ are considered for a depressive episode to occur. The causes may be independent of each other but their joint effect generates a renewal process corresponding to the occurrence of a depressive episode. The characteristics are obtained under various joint distributions for both independent and dependent time epochs at which depressive episodes occur due to causes $A_1$ and $A_2$. Here a situation has been considered when the time to occurrence of a depressive episode is a linear combination of time to occurrence of depressive episode due to causes $A_1$ and $A_2$ respectively. The parameters responsible for the occurrence of depressive episode serve as weights of the causes. The hazard rate of the linear combination has been obtained and presented graphically. The expected time and correlation between time to occurrence of a depressive episode due to causes $A_1$ and $A_2$ have been obtained and have also been presented graphically.

A summary of the findings and the concluding remarks of the study are depicted in Chapter 9. Efforts were made to form a mathematical concept of the different aspects of MDD and the possible consequences of this work have been presented. Limitations of the present research work have been pointed out. The list of references used for this research work has been provided at the end of the thesis. Directions for possible future research work in this area have also been suggested.

It is hoped that the present study may be of help to the doctors and the researchers in giving a new direction to the study of MDD and in framing treatment strategies for depressive patients.
1.4 Review of literature

**Early history:** Descriptions of variations in moods which go beyond normal limits and are associated with functional impairment are present in the oldest writings of mankind (Goodwin, F. K. and Jamison, R.K. 1990). The ancient Greeks identified that mood disorders are diseases of body, rather than the effects of supernatural spirits and identified the link between elevation of moods and states of depression.

Sporadic and unclear allusions of mood disorders did appear in literature from the time of Hippocrates, Aretaeus (1856) and Galen (131 – 200 A.D) through medieval period to the renaissance. The Hippocrates also identified that the mental disorders were located in the brain. During the renaissance period more clearer description of mood disorder started appearing in writing of Timothy Bright (1551 – 1615), Richard Burton (1577 – 1639) and George Cheyne (1671 – 1743)

In Europe, during the enlightenment of the seventeenth and eighteenth century, reasons and empiricism again emerged. In ‘Anatomy of Melancholy’, published in 1632, Richard Burton provides a comprehensive review of previous writings on mood disorder. Burton clearly makes a link between mood elevation and enhanced creativity, cycling with periods of low mood. He is now recognized as one of the first to localize psychiatric disorders within specific body organs, primarily the brain.

This identification of brain as the location of the involved psychopathology initiated the modern project of the scientific study of serious mood disorder, using contemporarily available scientific methods to generate insights to the understanding of the phenomenon of disturbances of mood.

In 1854, Esquirol described ‘*La folie circulaire*’ which remains a recognizably modern description of bipolar disorder (Esquirol, J.E.D. 1838). At the turn of twentieth century, Kraepelin distinguished *dementia praecox* from manic-depressive insanity (Kraepelin, E. 1896). He emphasized the episodic nature and course of manic-depressive insanity with relatively good prognosis and presence of family history in such cases. Under the influence of such important and valid observations concentrated efforts were made to understand and
conceptualize milder, though still severe enough to cause impairment of functions, forms of depression.

Gradually it became clear that Major Depressive Disorder (unipolar) was the most important cause of disability worldwide (Murray et al. 1997). With the expansion in the scope of mood disorders, it was recognized that there is also heterogeneity in the way in which mood disorder manifest itself. There were debates about the existence of subtypes of depression, often based on the severity of symptoms and hypothesized link to an underlying brain process.

**Clinical features:** The clinical features of mood disorders are dimensional, i.e. distributed according to their severity (Bech, P. 1993). The categorical approach as seen in DSM-IV (A.P.A. 1994) and ICD-10 (W.H.O. 1992) does not, however, preclude dimensional descriptions, because in both classifications the categories or diagnoses are essentially defined by minimum and maximum cut-off scores on the symptomatic states.

**Depressive episodes – Duration and Severity:** DSM-IV and ICD-10 have given a set of symptoms necessary for diagnosis of depressive disorder which to a large extent covers the rating scale dimension. Thus the individual symptom should be present most of the day and nearly every day during one episode. Kendler and Gardner (1998) have shown that the risk of developing a new major depressive episode is as high for patient with depressive symptoms lasting for 5-13 days as for patient with symptoms lasting for 14-59 days. In the study Kendler and Gardner (1998) has also demonstrated that patients with subthreshold quantity of depressive symptoms (i.e. just below five out of nine DSM-IV symptoms given in the table 1 of annexure 1) have the same risk of developing a new major depressive episode as patients fulfilling the symptomatic criteria of major depression. It has been shown that approximately 50% of the patients fulfilling the ICD-10 category of mild depression also fulfill the criteria of DSM-IV for major depression.

Measurements of social behaviour and subjective distress have shown that acute major depression is one of the most disabling and distressing of medical disorders (Bech, P. 1998). The constant mental pain and the suicidal symptoms seriously affect quality of life.
The suicidal risk in major depression is especially high when psychomotor retardation is improving in course of treatment (Gelder et al. 2009). MDD has the highest risk of suicide of all mental disorders, and all patients with major depression should be assessed for the risk of suicide (Gelder et al. 2009).

First episode of depression is often provoked by events like death of dear one, loss of job, retirement, marital separation or divorce. Subsequent episodes are often un-precipitated. Depressive episodes typically increase in frequency and duration as they recur (Goodwin et al. 2007). Recurrent brief depression is a state of major depression lasting 2-3 days. Its diagnosis has not been adopted fully in DSM-IV, but it is included in ICD-10 (Gelder et al. 2009).

Epidemiology:

The Global Burden of Disease, which is a comprehensive assessment of mortality and disability from diseases and injuries in 1990 and projected to 2020, highlights the importance of mood disorders for the world. Using the measure of disability-adjusted life year, it was determined that unipolar major depression was the fourth leading cause of disease burden in the world. It was also projected that, in the year 2020 MDD would be the second leading cause of disease burden in the world. Across the world, 10.7% of disability can be attributed to MDD, and in developed countries MDD contributes to nearly 20% of disease burden in women aged from 15 to 44 years (Murray and Lopez 1996)

The mood disorders have received considerable attention in psychiatric epidemiology over the last 25 years. These received particular attention in the five-site United States National Institutes of Mental Health Epidemiologic Catchment Area Study (ECA), as well as in the epidemiological studies in other countries around the world that used the ECA methodology. Mood disorders also received attention in the National Comorbidity Survey (NCS) in the United States, in the National Psychiatric Morbidity Survey of Great Britain, and most recently in the World Mental Health Survey (WMH) across many countries.
**Prevalence:**

In the ECA, the six month prevalence of MDD across five sites was 2.2%. In another equivalent study it was 5.3%. In the NCS, the one month prevalence of major depressive disorder was 6.1% (Blazer et al. 1994). In the National Psychiatric Morbidity Surveys of Great Britain, the one week rate of a depressive episode was 2.1% (Jenkins et al. 1997). Together these studies would suggest that the rate of MDD to be between 2% to 5%.

The estimates of lifetime prevalence rate of MDD vary considerably. The lowest rate is 4.4% from ECA study, while, in Virginia twins, it was reported as 30%. It is reasonable to believe that the lifetime prevalence of MDD is between 10 to 20%.

Over the past decade, one of the controversial findings in the epidemiology MDD has been whether the rates of depression are increasing, and whether it is occurring at a younger age. Despite methodological concerns about the reliability of the lifetime occurrences of MDD, studies across countries have reasonable consistently documented an increasing rate of MDD with an earlier age of onset (Cross National Collaborative Group 1992).

**Risk factors:**

There is now substantial evidence that genetic factors are of major importance as risk factors for vulnerability to MDD. While the traditional estimates have put the heritability at about 40%, when Kendler et al. (1993) allowed for the moderate reliability of the diagnosis of major depression, the heritability estimate increased to 70%. Of greater interest is that the genes for MDD do not appear to be unique for depression, but overlap with the genes for anxiety and genes for neuroticism (Kendler, et al. 1992, Adrews, et al. 1990).

**Gender:** One of the most consistent findings in the epidemiology of MDD is that the ratio of women to men is approximately 2:1, Kessler, et al. (1998).

**Childhood experiences:** The loss of parent in childhood increased the later risk for major depression. Although many studies have examined this issue, they have inconsistently
found it to be a risk factor for adult depression. However, studies that examine the nature of child-parent attachment using a measure such as the Parental Bonding Instrument have consistently found that a lack of parental care is associated with increased rates of depression (Parker, 1983). More recently, childhood sexual abuse has been established as a risk factor for adult major depression (Gelder, et al. 2009). Moreover, cumulative childhood disadvantage almost certainly poses a greater risk to later depression than any single childhood variable in isolation.

**Personality:** There has been a long history of interest in the likelihood that people with certain personality traits are more vulnerable to depression than others. It is likely that those individuals who are unduly anxious, impulsive, and obsessional may have increased rates of later MDD (Freedman, et al. 2002).

**Social environment:** There has been considerable interest in the role of marital status as a risk factor for MDD. For men it appears clear that married men have lowest rate of depression, while separated or divorced men have highest rates of MDD. In women the association is less clear, but in ECA study the same findings applied for women as for men (Stein et al. 2006).

In the classic work of George Brown (1978) on working class women, having three or more children, a lack of paid employment, and lack of confidence were risk factors for the development of an episode of depression.

It is well established that adverse life events, particularly those characterized by loss increases the risk of an episode of MDD. The increased risk to an episode of depression appears to last for a period of two to three months following an adverse event. Kendler, et al. (1997) proposed that genetic factors influence the risk of onset of depression by effect of stressful life events.

**Course and prognosis:**

Ever since Kahlbaum’s monograph (Kahlbaum, K. 1863) the course and outcome of mental disorders have played important roles as criteria and validators of psychiatric
classification. The description of course includes the age of onset, episode length, recurrence of episodes, residual symptoms between episodes and outcome i.e. remission, chronicity or death.

**Stability of diagnosis:** Mood disorders can be roughly sub-classified as unipolar mania, bipolar disorder, and unipolar depression (Angst, J. 2007). The three groups differ significantly as regards family history, personality, course and outcome, including mortality. The diagnosis of unipolar depression is always uncertain. Many depressives are hidden bipolar patients. A long term follow-up study over 27 years showed a constant rate of diagnostic change from depression to hypomania of 1.25% per year of follow-up.

**Onset of episode:** MDD may start at any time of life and has therefore a later mean age of onset. In the United Kingdom a mean age of onset of 33 years was found in hospitalized patients. In a large United States study of outpatients the mean was 29.4 years, but in 53% of cases the onset was before the age of 21. The distribution of the age of onset is bimodal, with peaks in the 30s and 50s.

**Length of episodes:** The length of depressive episodes is log normally distributed. Compared to bipolar disorder, episodes of depressive disorders last about one month longer (median duration of 5.4 months), and about 18% to 25% of patients develop chronic depression with a minimum duration of two years. In the general population, among whom there are many untreated cases of depression, episodes were found to be shorter, the 25th, 50th and 75th percentiles were 4, 8, and 16 weeks respectively for recurrent episodes (Gelder et al. 2009).

**Recurrence of episodes:** MDD is recurrent in about 85% of cases, compared to bipolar disorders; however, depressive patients experience only half as many episodes over their lifetime. The cycle length (time from the start of an episode to the start of a subsequent episode) is consequently longer than in bipolar disorders. There is also a systematic shortening of cycle length with the increasing number of episodes. In a recent large representative record study in Denmark of 20350 first admissions unipolar depressive
patients had strikingly lower recurrence rates than the bipolars, the rates for both correlating with the number of previous episodes (Kessing et al. 1998).

Residual symptoms represent a strong risk factor for further recurrence; a survival analysis by Paykel et al. (1995) found a three-fold higher risk of recurrence (76%) in patients with residual symptoms than in those without (25%). This sub-threshold depressive morbidity is clinically relevant and a clear risk factor for future recurrence and suicidality, especially in the elderly.

**Outcome of episodes:** In long term follow-up studies, 43 to 52% of depressed outpatients became symptom-free between their episodes, and the other half continued to suffer from dynamically fluctuating residual syndromes or symptoms. These sub-threshold statuses may be diagnosed as dysthymia, recurrent brief depression, minor depression, residual symptoms, or as full recovery. Initial severity and comorbidity are positively correlated with poor outcome in terms of poorer functioning and incomplete remission. In a British study residual symptoms of MDD defined by a score of eight or more in the 17-item HAM-D scale, were found in 32% of 60 patients 12-15 months after remission (Paykel et al. 1995). In a cross-cultural study of 968 patients conducted over nine months, between 25 to 48% of cases experienced complete remission, rates which also depended on the severity of depression and co-morbidity (De Almeida Fleck et al. 2005). Severe residual symptoms correlate with long-term morbidity, impaired social functioning at work and in relationship and suicidal behaviour especially in elderly, amongst whom remission is present in only about one third of cases.

Recent evidence from a 30-month prospective community-based cohort study of 75 year old subjects suggests that a history of depression may increase the risk of senile dementia which is compatible with findings from Denmark that recurrence (number of hospital admissions) increases the risk of dementia (Andersen et al. 2005).

**Mortality due to episodes:** Depressive patients have twice the mortality risk in comparison to the general population. The standardized mortality ratio (SMR) for suicide is 21 for males and 27 for females (Osby et al. 2001). Many other causes of death are also
common in depressives than in the general population. The frequently quoted suicide rate of 12 to 19% is only valid for selected hospitalized patients.

**Socio-demography variables**

In terms of socio-demographic variables, an overview of the research in depression in India and abroad has shown that depression is more common in women, (Poongothai, et al. 2009, Ramachandran, et al. 1982). Kessler, et al. (1998) reported that depression occurs twice as frequently in females compared to males. Ponnudurai, et al. (1981), Phookun and Sarmah (2010) found that depression manifests more in the age group 15-45 years. Kessler, et al. (1997), Poongothai, et al. (2009), Mohandas (2009), reported depression to be common in low socioeconomic status. Weissman et al. (1996), Poongothai, et al. (2009), Nandi et al. (1997), Sharma et al. (1985) found that those who are divorced or widowed are more depressed than married and single. Depression is also very common in unemployed condition, low educational level, in subjects living in nuclear family or living alone (Tiwari, 2000, Jain et al. 2007, Ramachandran, et al. 1982, Sharma et al. 1985). It is reported by Tsuang, M. and Faraone, S. (1996) that depression is very common in subjects having family history of depression.

**Regression analysis**

Application of regression analysis to study different aspects of MDD has been amply cited in literature. Many medical scientists have developed multiple linear regression analysis to study the various aspects of MDD and its effects. Some of the studies using multiple linear regression analysis are as follows:

Golding, J. M. et al. (2002) used it to study that low socio-economic status and social isolation contribute to depressed mood independent of MDD. Skodol, A.E et al. (2011) examined the effects of specific personality disorder, co morbidity on the course of MDD in a nationally represented sample. Sadowski, H et al. (1999) studied that multiple family disadvantages in childhood substantially increase the risk of suffering a MDD in
adulthood. Guajardo V.D. et al. (2011) examined that loss of interest and depressed mood were associated with significant decrease in health related quality of life (H-RQOL). Hierarchical multiple regression model was developed by Kathleen Myers et al. (1991) to assess the potential risk factors for suicidality among the age group 7 to 17 years of age. Fava, M. et al. (1997) studied that there is no association between the subtypes of MDD and in treatment outcome. Andrea, H et al. (2009) examined the main and interactive effects of gender and MDD. Pepper, C.A et al. (2009) investigated the role played by Post Traumatic stress disorder in relationship between MDD and borderline personality disorder.

Logistic regression analysis has been extensively used in mental health. Some of the studies performing logistic regression analysis are elaborately used by Durdle, H et al. (2008), Egede, L.E et al. (2003), Lee, L.C. et al. (2005), Rissanen, et al. (2011), Rohde, P. et al. (2000), Melville et al. (2010) to name a few.

The use of ordinal logistic regression in mental health has been reviewed and it is observed that it is rarely used in case of MDD. Some of the studies using ordinal logistic regression analysis in health sector are as follows:

Agresti, A. (1989) used logit and log linear model building technique for nominal data is generalized for use with ordinal data. Ordinal logistic regression models were used to analyse a cross-classification table relating mental impairments and parents’ socioeconomic status. Among the ordinal models, the proportional odds model (POM) is outstanding due to its parsimony, provided the proportional odds assumption is not violated for the data (Mery Natali Silva Abrue et al 2008) and they used the model for analyzing data with quality of life measurements as the response. The POM, known as the cumulative logit model, is indicated when an originally continuous response variable is later grouped (Lall R et al. 2002), (Ananth C.V, Kleinbaum D.G 1997). The cumulative logit model was originally proposed by Walker and Duncan (1967) and later called the proportional odds model (POM) by McCullagh (1980), Ananth and Kleinbaum (1997), Hosmer and Lemeshow (2000), Agresti (2007). Degenhardt, L. et al. (2001) carried out the
psychosis scores, including demographic, mental health and drug use variables by using ordinal logistic regression model. Adeleke, K.A. et al. (2010) studied the factors viz. environmental, behavioral and demographic that affected the outcomes of pregnancies. Bender, R. and Grouven, U. (1997) have given some recommendations for the use and assessment of ordinal logistic regression models in medical research. Das, S. and Rahman, R. (2011) applied ordinal logistic regression to identify the determinants of child malnutrition. Crane, P.K. et al. (2006) presented an ordinal logistic regression model for identification of items with differential item functioning and applied this to Mini-Mental State Examination dataset. Pahwa, P. et al. (2009) used ordinal logistic regression models to the longitudinal data to investigate the association between respiratory diseases and mental distress adjusting for other covariates of interest. Schorr, G. et al. (2009) used ordinal logistic regression model to examine the association between daily smokers’ mental health with stage of change, processes of change, smoking cessation self efficacy and decisional balance. Raman, R. and Hedeker, D. (2005) described a three level mixed effects regression model, and used ordinal logistic regression model to allow for explanatory variables to have varying effects on the cumulative logits of the model. Pluddemann, A. et al. (2010) used ordinal logistic regression analysis to show methamphetamine (drug) use in the past year was significantly associated with higher aggressive scores, mental risk scores and depression scores. Guterman, N.B. et al. (2002) used ordinal logistic regression model to find the degree of to which adolescents receive personal victimization needed professional mental health supports in the wake of serious violence exposure. Ordinal logistic regression’s use is demonstrated by Ashby, D. et al. (1989) to model the association of dementia with demographic characteristics, and then to explore possible reasons for a rise in the prevalence of dementia. Corvin, A. et al. (2001) to determine whether smoking is associated with psychosis in bipolar affective disorder used ordinal logistic regression analysis to test the relationship between smoking severity and psychotic symptomatology. Barnett, A.E. and Robbins, C. (2008) examined the association of three sources of women’s aging anxiety – declining attractiveness, health and fertility with social contexts of their lives by using ordinal logistic regression.
Bayes’ Theorem

Bayes’ theorem is used elaborately in research which is due to Rev. Thomas Bayes (1763). Several solutions have been proposed by Savage (1962), Jeffreys’ (1961), Zellner (1971), Raiffa and Schlaifer (1961), Hartigan (1964), among others to select a prior. Foxcroft, D. et al. (2009) used Bayes’ theorem to demonstrate an approach to estimate the difference in prevalence of alcohol use disorder in two groups. Mitnitski, A.B. et al. (1997) estimated the probability distribution for the etiologically heterogeneous dementia diagnosis based on Bayes’ approach. Thomsen, I.S. (1994) described a method of demonstrating syndromes by means of Bayes’ with correction for redundancy. Elwood, R.W. (1993) reviewed the measures based on Bayesian probabilities with specific application to neuropsychological assessment. Prince, M.J. (1996) used Bayes’ theorem approach to develop a test package for Alzheimer’s disease that consists of some simple cognitive tests combined with age and family history of dementia. According to Lindgaard, G. et al. (2008) Bayes’ theorem can be applied fruitfully to provide diagnostic support for human decision makers and e-health mental intervention system. Furukawa, T. et al. (1997) used Bayes’ theorem to overcome the shortcomings regarding the validity of popular self rating scales for depression both in community and clinical settings. Bayes’ theorem was used by Alegria, M., Mcguire, T. (2003) to find conditional probabilities of disorders and symptoms. Gilbody, S., Barkham, M. (2006) used Bayes’ theorem to find that brief self-rated questionnaires are as good as clinician administered instrument in detecting depression. Winkler, R.L., Smith, J.E. (2004) considered the situation in which there is uncertainty about the prior probability and about the sensitivity and specificity of a diagnostic test of a disease in a patient. To calculate posterior probabilities of disease under such uncertainty standard Bayesian formula can be used. Okeh, U.M. and Ugwu, A.C. (2008) presented a brief intuitive development of probability and the statement about Bayes’ theorem with emphasis on obtaining diagnostic values from which positive or negative predictive values are achieved.
Renewal Theory

Renewal theory in discrete time has been thoroughly discussed by Feller (1957). Cox (1962), Ross (1989) and Medhi (1994) concentrated on renewal theory in continuous time. Heyde (1967) suggested some renewal theorem in discrete time for a sequence of independent and identically distributed random variables. Smith (1958) has given an excellent account of the general mathematical theorems of renewal theory, and has given a number of advanced developments, especially concerning problems about electronic counters. According to Feller (1949) renewal theory is important for studying wide class of stochastic processes. Owen (1949) and Skellam and Shenton (1957) have discussed the number of renewals in an interval not starting at the origin. Skellam and Shenton (1957) gave many exact results for the distribution of number of renewals for a fixed interval of time. Cox (1960) has considered the number of renewals in a random time interval. Feller (1941) gave the first rigorous proof of the convergence of the renewal density to a limit. Smith (1960) has given a remarkable necessary and sufficient condition for convergence. Recurrence time problems which are generally important in stochastic processes was discussed by Bartlett (1955). Cane (1959) and Page (1959) have considered applications of alternating renewal processes respectively, to animal ethology and the maintenance of electronic computers. Cox and Smith (1953b) and Smith (1961) have studied renewal theory when the failure-times, although independent, are not identically distributed. Chow and Robbins (1963) have suggested a renewal theorem for dependent and non-identically distributed random variables for continuous time. A model of failure with wear is discussed by Bovaird (1961).

Renewal process is also a particular case of counting process. Counting process methodology has been applied in survival analysis. The approach first developed by Allen (1975) and later on it was well exploited by Andersen et al. (1993), Fleming and Harrington (1991). Barthakur and Sarmah (2007) have considered a renewal process in discrete time in a dependent and non-identical set up. In this thesis, a renewal process in continuous time in an independent and identical set up is considered to study some aspects of major depressive disorder.
Cause specific

There are many studies regarding cause specific depression. According to Lorant et al. (2003) low socioeconomic status was the specific cause of depression. Cacioppo et al. (2006) found out that loneliness is specific risk factor for depressive symptoms. Meyer, B. et al. (2007) studied the causes, the depressed patients report for their depression. These causes are therefore thought to be important predictors of theory process and treatment. According to Hallas, J. (1996) many cardiovascular drugs have been implicated as causes of depression. Khan, T.M. et al. (2009) confirms the association of socio-demographic factors like education, gender, race and socioeconomic status as the main or specific causes of depression. Findings of Fergusson, D.M. et al. (2006) suggest that abortion in young women may be considered as an important cause of depression. Due to Robert, R.E. et al. (2003) obesity at baseline was associated with increased risk of depression. Haider, V.S. et al. (2008) confirmed in their study that use of cannabis can be considered as a specific cause of depression. In this thesis the cause specific depression is studied from a different perspective. When the patient is under the influence of a specific cause of depression then it is of interest to find out how the causes affect the patient with different types of hazard rate. When the patient is under the influence of two specific causes then the characteristics are obtained under various joint distributions of both the causes.

1.5 Mathematical tools used:

The Hazard Rate (or failure rate) is defined by -

\[ h(x) = \frac{f(x)}{1 - F(x)}, \]  

… (1.1)

where \( x \) is a random variable and \( f(x) \) & \( F(x) \) are density function and distribution function of \( x \).

Multiple linear regression model:
Suppose that we have 'k' independent variables $x_1, x_2, \ldots, x_k$ and 'n' observations $y_1, y_2, \ldots, y_n$ each of which can be expressed by the equation

$$Y_i = \beta_0 + \beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_k x_{ki} + \varepsilon_i \quad \ldots \quad (1.2)$$

this model essentially represents 'n' equations describing how the response values are generated in the scientific process. Using matrix notation we can write the equation as –

$$y = X\beta + \varepsilon$$

Where, $y = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix}_{n \times 1}$, $X = \begin{bmatrix} 1 & x_{11} & x_{12} & \cdots & x_{1k} \\ 1 & x_{21} & x_{22} & \cdots & x_{2k} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ 1 & x_{n1} & x_{n2} & \cdots & x_{nk} \end{bmatrix}_{n \times p}$, $\beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_k \end{bmatrix}_{p \times 1}$, $\varepsilon = \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}_{n \times 1}$

**Ordinal Logistic regression model:**

The proportional odds model is now the most commonly used logistic regression model for ordinal response. With this model a comparison is made with the probability of an equal or smaller response, $Y \leq k$, to the probability of a larger response, $Y > k$,

$$C_k(X) = \ln \left[ \frac{P(Y \leq k \mid x)}{P(Y > k \mid x)} \right]$$

$$= \ln \left[ \frac{\phi_0(x) + \phi_1(x) + \cdots + \phi_k(x)}{\phi_{k+1}(x) + \phi_{k+2}(x) + \cdots + \phi_{p-1}(x)} \right]$$

$$= \tau_k - x'\beta \quad \ldots \quad (1.3)$$

for $k = 0, 1, \ldots, p - 1$, (Hosmer and Lemeshow, 2000) and where $\tau_k$ are the thresholds or cutpoints between the categories, and $\phi_i(x)$ is the probability of being in class $i$ of given
covariates \( x \). \( \tau_k \) are the unknown intercept parameters, satisfying the condition
\[
\tau_0 \leq \tau_1 \leq \ldots \leq \tau_{p-1}
\]
and \( \beta = (\beta_0, \beta_1, \ldots, \beta_{p-1}) \) is a vector of unknown regression coefficients corresponding to \( x \)

**Order Statistics:**

Let \( X_1, X_2, \ldots, X_n \) be a random sample from a p.d.f \( f(x, \theta) \).

Suppose that the \( n \) observations are arranged in ascending order so that
\[
X_{(1)} \leq X_{(2)} \leq \ldots \leq X_{(n)},
\]
where \( X_{(1)} \) is the smallest observation and \( X_{(n)} \) is the largest.

Then \( X_{(1)} \) is called the first order statistic, whereas \( X_n \) is called the \( n^{th} \) order statistic. In general \( X_{(r)} \) is called the \( r^{th} \) order statistic, and it has \((r-1)\) observations preceding it.

The random samples of size \( n \) from an infinite population has the value \( f(x) \) at \( x \), the probability density of the \( r^{th} \) order statistic \( Y_r \) is given by
\[
g_r(y_r) = \frac{n!}{(r-1)! (n-r)!} \left[ \int_{-\infty}^{y_r} f(x)dx \right]^{r-1} \left[ \int_{\infty}^{y_r} f(x)dx \right]^{n-r} \text{ for } -\infty < y_r < \infty \quad (1.4)
\]

In particular, the sampling distribution of \( Y_n \), the largest value in the random value of size \( n \), is given by
\[
g_n(y_n) = n \left[ \int_{-\infty}^{y_n} f(x)dx \right]^{n-1} f(y_n) \text{ for } -\infty < y_n < \infty
\]

The sampling distribution of \( Y_1 \), the smallest value of size \( n \), is given by
\[
g_1(y_1) = n \left[ \int_{y_1}^{\infty} f(x)dx \right]^{n-1} f(y_1) \text{ for } -\infty < y_1 < \infty
\]
**Stochastic Process:**

Families of random variables which are functions of say, time or space, are known as stochastic processes. (J.Medhi, 2009)

A stochastic process \( \{X(t), t \in T\} \) is a collection of random variables \( X(t) \) defined for each \( t \) belonging to the parameter set or index set \( T \). The index set \( t \) is often interpreted as time and thus, \( X(t) \) is the state of the process at time \( t \).

When \( T \) is a countable set, the stochastic process is said to be a discrete-time process and is denoted by \( \{X_n, n = 0, 1, 2, \ldots\} \).

When \( T \) is an interval of the real line, the stochastic process is said to be a continuous time process and denoted by \( \{X(t), t \geq 0\} \).

The **state space** of a stochastic process is the set of all possible values that the random variables \( X(t) \) can assume.

**Poisson Process:**

The family of random variables \( \{N(t), t \geq 0\} \) is a stochastic process. Here the time ‘\( t \)’ is continuous, the state space of \( N(t) \) is discrete and integral-valued and the process is integral-valued. One of the most important integral-valued processes is Poisson process.

Under certain condition \( N(t) \) follows Poisson distribution with mean \( \lambda t \) (\( \lambda \) being constant) and the corresponding stochastic process \( \{N(t), t \geq 0\} \) follows the Poisson law.

**Counting Process:**

A stochastic process \( \{X(t)\} \) with integral valued state space associated with counting (one by one) of an event, such that as \( t \) increases, the cumulative count can only increase is called a counting process or point process. Poisson process is a counting process.
Renewal processes in continuous time:

Renewal process is a generalization of the Poisson process. Renewal process is also a particular case of counting process.

Let \( \{X_n, n=1, 2, \ldots\} \) be a sequence of non-negative independent variables. It is assumed that \( \Pr\{X_n = 0\} < 1 \), and that the random variables are identically distributed and are continuous with a distribution function \( F(\cdot) \). Since \( X_n \) is non-negative, it follows that \( E\{X_n\} \) exits and it is denoted by

\[
E(X_n) = \int_0^\infty xdF(x) = \mu, \quad \text{where } \mu \text{ may be infinite.}
\]

Whenever \( \mu = \infty \), \( \frac{1}{\mu} \) shall be interpreted as zero.

Let \( S_0 = 0 \), \( S_n = X_1 + X_2 + \cdots + X_n \), \( n \geq 1 \)

and let \( F_n(x) = \Pr\{S_n \leq x\} \) be the distribution function of \( S_n \), \( n \geq 1 \):

\[
F_0(x) = 1 \text{ if } x \geq 0 \text{ and } F_0(x) = 0 \text{ if } x < 0.
\]

Define the random variable

\[
N(t) = \sup\{n : S_n \leq t\}. \quad \text{.... (1.5)}
\]

The process \( \{N(t), t \geq 0\} \) is called a renewal process with distribution \( F \) or generated or induced by \( F \).

Laplace Transform:

Laplace Transform is a generalization of generating function. Laplace Transformation reduces a linear differential to an algebraic equation.
Let \( f(t) \) be a function of a positive real variable \( t \). Then the Laplace transform (L.T.) of \( f(t) \) is defined by

\[
L\{f(t)\} = \int_{0}^{\infty} e^{-st} f(t) \, dt 
\]

for the range of values of ‘s’ for which the integral exists.

**Exponential distribution:**

A continuous random variable \( X \) is defined to have an exponential distribution with parameter \( \lambda > 0 \) if its p.d.f. is given by

\[
f(x, \lambda) = \begin{cases} 
\lambda e^{-\lambda x}, & 0 < x < \infty, \quad \lambda > 0 \\
0, & \text{otherwise}
\end{cases}
\]

…. (1.7)

The c.d.f. is

\[
F_x(x) = \begin{cases} 
1 - e^{-\lambda x}, & x \geq 0 \\
0, & \text{otherwise}
\end{cases}
\]

…. (1.8)

The mean and variance of this distribution are \( \frac{1}{\lambda} \) and \( \frac{1}{\lambda^2} \) respectively.

**Rayleigh Distribution:**

A continuous random variable \( X \) is defined to have a Rayleigh distribution with parameter \( \lambda > 0 \) if its p.d.f. is given by

\[
f(x, \lambda) = \lambda x e^{-\lambda^2 / 2}, \quad \text{where } x \geq 0, \lambda > 0
\]

…. (1.9)

The c.d.f. is given by
\[ F(x) = 1 - e^{-\frac{\lambda x^2}{2}} \quad \text{where} \quad x \geq 0, \lambda > 0 \] .... (1.10)

**Weibull distribution:**

A continuous random variable \( X \) is defined to have a Weibull distribution with parameter \( \lambda > 0, p > 0 \) if its p.d.f. is given by

\[ f(x) = p \lambda x^{p-1} e^{-(\lambda x)^p} \quad \text{where} \quad x \geq 0, \lambda > 0 \] .... (1.11)

The c.d.f. is given by

\[ F(x) = \left[ 1 - e^{-(\lambda x)^p} \right] \quad \text{where} \quad x \geq 0, \lambda > 0. \] .... (1.12)

The mean and variance of the distribution are

\[ E(X) = \Gamma \left( 1 + \frac{1}{p} \right) \quad \text{and} \quad V(X) = \Gamma \left( 1 + \frac{2}{p} \right) - \left\{ \Gamma \left( 1 + \frac{1}{p} \right) \right\}^2 \]

The parameter \( p \) determines nature of rate of occurrence of depressive episode.

**Uniform Distribution:**

A random variable \( X \) is said to have a continuous uniform (rectangular) distribution on the interval \([a,b] \quad (-\infty < a < b < \infty) \) if its p.d.f. is given by

\[ f(x; a, b) = \begin{cases} \frac{1}{b-a}, & \text{if} \quad a \leq x \leq b \\ 0, & \text{otherwise} \end{cases} \] .... (1.13)

\( a, b \) are the parameters of the distribution. The c.d.f. is
Chapter -1: Introduction

The mean and variance of the distribution are $\frac{a + b}{2}$ and $\frac{(b-a)^2}{12}$ respectively.

**Jacobian transformation:**

If independent continuous random variables $X$ and $Y$ by the transformation $u = u(x, y)$, $v = v(x, y)$ where $u$ and $v$ are continuously differentiable functions for which Jacobian of transformation

$$J = \frac{\partial(x, y)}{\partial(u, v)} = \begin{vmatrix} \frac{\partial x}{\partial u} & \frac{\partial y}{\partial u} \\ \frac{\partial x}{\partial v} & \frac{\partial y}{\partial v} \end{vmatrix} \neq 0 \quad \text{at all points } (x, y)$$

The inverse transformation is uniquely given by $x = x(u, v)$ and $y = (u, v)$.

**Statistical package used: SPSS**

SPSS (Statistical Package for Social Sciences) is among the most widely used programs for statistical analysis in social science. It is used by market researchers, health researchers, survey companies, government, education researchers, marketing organizations and others. The original SPSS manual (Nie, Bent and Hull, 1970) has been described as one of “sociology’s most influential books”.

\[
F_x(x) = \begin{cases} 
0, & x \leq a \\
\frac{x-a}{b-a}, & a < x < b \\
1, & x \geq b 
\end{cases} \quad \text{.... (1.14)}
\]
SPSS is a full-featured data analysis computer program that offers a variety of applications including data base management and reporting, statistical analysis, and graphics. The SPSS program runs on a wide variety of mainframe, mini and microcomputers.