A PROSPECTIVE RANDOMISED OPEN LABEL COMPARATIVE STUDY OF EFFICACY AND SAFETY OF ESCITALOPRAM VERSUS SERTRALINE IN MAJOR DEPRESSIVE DISORDER IN A TERTIARY CARE HOSPITAL

Dissertation submitted to

THE TAMILNADU
DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. (PHARMACOLOGY)

BRANCH - VI

DEPARTMENT OF PHARMACOLOGY
CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU - 603 001

MAY - 2018

CERTIFICATE

This is to certify that this dissertation entitled, **A PROSPECTIVE RANDOMISED OPEN LABEL COMPARATIVE STUDY OF EFFICACY AND SAFETY OF ESCITALOPRAM VERSUS SERTRALINE IN MAJOR DEPRESSIVE DISORDER IN A TERTIARY CARE HOSPITAL,** submitted by **Dr.SHARMI.V.J.**, in partial fulfillment for the award of the degree of M.D.(Pharmacology) by The Tamilnadu Dr.M.G.R.Medical University, Chennai is a bonafide record of the research work done by her, under the guidance of **Dr.K.VIJAYARANI,M.D.,** Professor and Head, Department of Pharmacology, Chengalpattu Medical College during the academic year 2015-18 in the Department of Pharmacology,Chengalpattu Medical College, Chengalpattu- 603 001.

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DECLARATION

I solemnly declare that the dissertation entitled **"A PROSPECTIVE RANDOMISED OPEN LABEL COMPARATIVE STUDY OF EFFICACY AND SAFETY OF ESCITALOPRAM VERSUS SERTRALINE IN MAJOR DEPRESSIVE DISORDER IN A TERTIARY CARE HOSPITAL."** is done by me at Chengalpattu Medical College and hospital,Chengalpattu during the period of 2016-2017 under the guidance and supervision of **Dr.K.VIJAYARANI, M.D.,** Associate Professor and Head i/c, Department of Pharmacology, Chengalpattu Medical College. This dissertation is submitted to The Tamilnadu Dr.M.G.R.Medical University, Chennai towards the partial fulfilment of the requirements for the award of **M.D. DEGREE IN PHARMACOLOGY.**

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ACKNOWLEDGEMENT

I express my sincere gratitude to Dean, **Dr.Usha Sadasivan, M.D. Ph.D** Chengalpattu Medical College, for permitting me to undertake this research work as a part of my MD curriculum.

I would like to convey my gratitude to my guide **Dr.K.Vijayarani, M.D.,** Associate Professor and Head, Department of Pharmacology, Chengalpattu Medical College for her unfailing guidance, sincere advice and constant support throughout the study.

I express my sincere thanks to **Dr.K.Baskaran,M.D.,** former Associate Professor, Department of Pharmacology, Chengalpattu Medical College for his enduring encouragement during the study.

I am very thankful to our Associate Professors **Dr.B.Sharmila,M.D. Dr.J.Komathi**, **M.D.,** Department of Pharmacology, Chengalpattu Medical College for their remarkable guidance, continuous suggestions and directions throughout the study.

I would like to convey my gratitude to my co-guide **Dr.S.Sudhakar M.D,** Associate professor, Department of Psychiatry, Chengalpattu Medical College for permitting me to carry out this study in the psychiatry OPD of Chengalpattu Medical College.

I am very much grateful to all my Assistant Professors Dr.T.Ragupathy, M.D.,Dr.T.Siyamaladevi, M.D, Dr.B.Bhuvaneswari, M.D, Dr.R.Ranjini, M.D, Dr.A.Vinoth Kumar, M.D, Dr.S.A.Ayisha, M.D., Dr.D.Nishanthini, M.D., Dr.P.Kalaiselvi, M.D., and Tutors Mr.K.Arumugasamy, M.Sc., Department of Pharmacology, Chengalpattu Medical College for their advice and encouragement.

I have great pleasure in thanking my husband, Dr.P.Parthiban M.D., for helping me in the statistical analysis and giving sustained support. I thank my fellow postgraduates Dr.M.Nandhinipriya, M.D, Dr.M.Nithya Priya, M.D, Dr.S.Sweetlin M.D, Dr.Sanusain M.D., Dr.G.Amutha, Dr.M.Punitha, Dr.M.Firoze, Dr.Devipriya, Dr.Caroline for their help and encouragement throughout this study.

I also extend my sincere thanks to all other staff members of this department for their wholehearted support.

Finally I thank all my patients for they willingly cooperated to undertake and complete this study.

Last but not the least, I sincerely thank my parents, my sister and my family for their continuous encouragement, patience, valuable support and sincere prayers without which I could not have completed this work successfully.

I thank Mrs.Ramalakshmi for her efforts in bringing out the final print of the dissertation.

A prospective randomised open label comparative study of efficacy and safety of Escitalopram versus Sertraline in major depressive disorder in a tertiary care hospital.

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LIST OF ABBREVIATIONS

ADS	–	Anti depressant Discontinuation Syndrome
ACC	–	Anterior Cingulate Cortex
BDNF	–	Brain Derived Neurotropic Factor
BPD	–	Brief PsychoDynamic psychotherapy
BT	–	Behavioural Therapy
CBT	–	Cognitive Behavioural Therapy
Cg25WM	–	Subgenual Cingulate White Matter
CGI-S	–	Clinical Global Impression Severity Scale
CGI-I	–	Clinical Global Impression Improvement Scale
CREB	–	C-AMP Responsive Element Binding Protein
DBS	–	Deep Brain Stimulation
DESS	–	Discontinuation Emergent Signs and Symptoms
DSM	–	Diagnostic and Statistical Manual of Mental Disorders
ECT	–	Electro Convulsive Therapy
GAD	–	Generalised Anxiety Disorder
HAM-D	–	Hamilton Depression Rating Scale
HDRS	–	Hamilton Depression Rating Scale
ICD	–	International Classification of Diseases
IPT	–	Inter Personal Therapy
IRT	–	Item Response Theory
MAO	–	Mono Amine Oxidase

MAOI	–	Mono Amine Oxidase Inhibitors
MT	–	Marital Therapy
MDD	–	Major Depressive Disorder
NET	–	Nor Epinephrine Transporters
OCD	–	Obsessive Compulsive Disorder
OPD	–	Out Patient Department
PTSD	–	Post Traumatic Stress Disorder
Pg ACC	–	Pregenual Anterior Cingulate Cortex
QIDS SR16	–	16-Item Quick Inventory Of Depressive Symptomatology - Self Report
QIDS C16	–	16-Item Quick Inventory Of Depressive Symptomatology - Clinical Rating
rTMS	–	repetitive Transcranial Magnetic Stimulation
SEA	–	South East Asia
Sg ACC	–	Subgenual Anterior Cingulate Cortex
SLI	–	Standard of Living Index Scale
SSRIs	–	Selective Serotonin Reuptake Inhibitors
SERT	–	Serotonin Transporters
SNRIs	–	Selective Serotonin Norepinephrine Reuptake Inhibitors
TCA	–	Tri-Cyclic Antidepressants
WHO	–	World Health Organisation

ABSTRACT

Title : A PROSPECTIVE RANDOMISED OPEN LABEL COMPARATIVE STUDY OF EFFICACY AND SAFETY OF ESCITALOPRAM VERSUS SERTRALINE IN MAJOR DEPRESSIVE DISORDER IN A TERTIARY CARE HOSPITAL.

Background:

Depression is a commonly occuring mental health disorder affecting all sectors of people worldwide. Mental health is equally emphasised as that of physical health. Depression, an exasperating disorder shows alarming hike in the present and recent past. Selective serotonin reuptake inhibitors are first choice of drugs for depression and frequently prescribed. Still it has not been possible to declare one particular drug to be more efficacious than the other. The purpose of this study is to compare two of the drugs from this class of SSRIs, namely Sertraline and Escitalopram, in terms of efficacy and safety among major depressive disorder patients.

Aim:

To compare the efficacy and safety of two anti depressants, Escitalopram and Sertraline in patients diagnosed with major depressive disorder in outpatient department of psychiatry in a tertiary care hospital in Chengalpattu.

Methodology:

After approval from Institutional Ethical Committee, 120 patients were recruited and randomised into either group A to receive Tab.Escitalopram 10-20mg/day or group B to receive Tab.Sertraline 50-200mg/day.

Demographic details and complete history were recorded during enrolment. Clinical examination, screening with Hamilton depression rating scale and lab investigations were done at baseline. **Efficacy** was measured by response in terms of improvement of symptoms assessed by scoring with Hamilton Depression Rating Scale at baseline, at 4, 8, and 12 weeks. **Safety** was ensured by recording vitals of the patients and laboratory parameters at baseline, 4, 8, 12 weeks of study period. Safety was assessed by recording adverse drug reactions reported voluntarily or observed clinically or changes reported in lab investigation during follow up.

Results:

Mean HAM-D score reduction from 20.77 to 8.75 in group A (Escitalopram) and 20.96 at baseline to 8.65 in group B (Sertraline) after 12 weeks therapy was statistically significant within groups. Response rate assessed by reduction of mean HAM-D score did not show statistically significant difference between two groups. The occurrence of adverse effects in sertraline group was higher than escitalopram group and this difference was found to be statistically significant (P=0.007).

Conclusion:

The study confirms that both Escitalopram and Sertraline are appropriate as first line drugs in treatment for depression. Both drugs showed equal efficacy in producing response and remission. Escitalopram was better tolerated with less number of reported adverse events than sertraline.

Key Words : Depression, Escitalopram, Sertraline, Hamilton Depression Rating Scale

INTRODUCTION

Depression is a common mental health disorder affecting all sectors of people worldwide. WHO defines Health as " a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[(1)]. So Mental health needs to be equally emphasized as physical health. Depression, which increases suicide risk is an exasperating disorder with an alarming hike in the present and recent past.

Depressive disorder is a broad term encompassing major depressive disorder (MDD) (including major depressive episode), persistent depressive disorder (dysthymia), disruptive mood dysregulation disorder, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified and unspecified depressive disorder[(2)]. Of these major depressive disorder (MDD) and persistent depressive disorder comprise major sub categories.

All forms of depressive disorders share common symptoms of mood changes i.e, irritable, sad and empty along with cognitive and somatic features which can cause significant impact on the individual's functional capability and capacity. The distinguishing part in the above spectrum of depressive disorders is the time of occurrence, duration of symptoms or episodes, and the diagnosed etiology[(2)].

Prevalence of depressive disorders has been estimated to show increasing trend, and more studies are done to explore the risk factors, etiology, epidemiology, genetic role, neuro anatomical contributions, biochemical markers, theories of neurotransmission, drugs and diseases commonly associated with depression, current guidelines for managing major depressive disorder, pharmacological and non pharmacological modalities of management, percentage of response to those modalities and safety of various interventions.

Though multiple classes of drugs are available for pharmacological management of depression with evidence of reversing prefrontal cortical and hippocampal atrophy seen in depressed patients, SSRIs are the main stay of treatment for MDD[3]. When the preferred outcome is complete symptom remission, still there is significant group of MDD patients (50%) who are poor responders to drug treatment[3]. Recent studies confirm the fact ,that even with initial or successive treatment ventures, significant proportion of patients do not continue to show adequate therapeutic response. Clinical response mostly tends to fall short of full symptom remission. Depressive disorders turn difficult to treat because of its inherent tendency to recur, relapse and remit, added with under dosing and poor patient compliance[4].

Selective serotonin reuptake inhibitors are first choice of drugs for depression and are frequently prescribed. Still it has not been possible to declare one particular drug in this class to be more efficacious than the

other[5]. The purpose of this study is to compare two of the drugs from this class of SSRIs, namely Sertraline and Escitalopram, in terms of efficacy and safety among major depressive disorder patients, attending psychiatric outpatient department in Chengalpattu Medical College and Hospital.

REVIEW OF LITERATURE

"Depression is defined as a common mental disorder, characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feeling of tiredness, and poor concentration, for at least two weeks". According to WHO, Depression can be a long term health issue or can be recurrent, ultimately leading to impaired individual's ability to perform his activities at work, school or manage with his day to day life. In its severe form, depression culminates in suicide[6]

Depressive disorder includes two main sub-types:

"Major depressive disorder / depressive episode, which involves symptoms such as depressed mood, loss of interest and enjoyment, and decreased energy; depending on the number and severity of symptoms, a depressive episode can be categorized as mild, moderate, or severe;" and **"Dysthymia,** a persistent or chronic form of mild depression; the symptoms of dysthymia are similar to depressive episode, but tend to be less intense and last longer"[7].

EPIDEMIOLOGY

Global disease burden: As per WHO data, depression ranks the fourth leading cause of disability globally and this scenario is predicted to worsen in 2020 where depression will hike to be the second leading cause[8]. Depression is the most prevalent of all psychiatric disorders and it has

victimised 300 million population around the world, which is about 4.4% of total world's population. As predicted by WHO, among the diseases that contribute to the global disease burden, depression ranks fourth. More than 18% increase in prevalence of depression estimated from 2005 to 2015 is alarming[7].

In 2015, Major depressive disorders caused fifty million years lived with disability (YLD) globally. Middle and low income countries showed higher occurrence ie, 80% of total depressive disorders. WHO regions show differing rates of this non fatal disease burden ranging from 640 years lived with disability in western Pacific regions to more than 850 years lived with disability in European middle and low income countries. Of the total Years Lived with Disability world wide, major depressive disorder alone provides huge contribution of 7.5% [7].

Depression – prevalence in South East Asia And India

Disability secondary to depression has showed increasing trend in South East Asian countries also. Neuropsychiatric diseases has contributed 11% of Disability Adjusted Life Years(DALYs) and 27 % of Years Lived With Disability (YLDs) in these regions. Analysis of epidemiological studies conducted in South East Asian countries revealed the prevalence of depressive disorder in primary care to be 26.3 %. Among patients with major depressive disorder, 23% report health issues and ailments that are severe enough to keep them crippled in bed. As compared to patients in general

medical side, patients with depressive disorder utilise more health care facilities and show increased interpersonal & occupational impairment in terms of cost by lost work days[9].

As estimated by WHO , in India, there are over 56,675,760 cases diagnosed with major depressive disorder which is about 4.5% of total population. Moreover, Depressive disorders are major contributors of health loss and disease burden with 10,050,411 of total YLD which is about 7.1% of total Years Lived with Disability[7]. In a study done in Goa, depressive disorders were about 46.5% in adult patients who attended primary health care facilities.

Epidemiological studies in various regions in TamilNadu throw light on the fact that the prevalence of depressive disorders to be higher than expected. A study done in a health unit of TamilNadu, in women from 18 to 45 years showed the prevalence of MDD to be 20%(10). Another community based study estimated the depression among elderly in rural areas of southern India to be 9.3%[11] all of which show significant disease burden levied by this disorder over the community. A recent large South Indian population based study, overall prevalence of depression is reported to be 15.1%[12].

Prevalence of Depression in adolescents

A study conducted in south India revealed the split up prevalence rates of minimal, mild, moderate, moderate to severe, and severe depression to be

34.4%, 38%, 13.2%, 4.5%, and 1.7% respectively among young adults. This unveils the higher prevalence among young ages too[13]. Prevalence of depression has shown a particular increase during the post pubertal stage due to biological and social changes which characterize the developmental adolescent period . The median 12-month prevalence when estimated for mid to late adolescence was found to be almost identical to the values obtained for adult population, which is 4- 5%. Cumulative probability of depression which is 5% in early adolescence steeply increased to 20% by the end of adolescence[14].

Neuroanatomy of Depression:

Research suggests that brains of people with major depressive disorder is different from that of normal people. Though the role of hippocampus in development of depression is not clearly substantiated, hippocampus is observed to be smaller with less serotoninergic receptors in patients with major depressive disorder[15]. In patients with clinical depression or post traumatic stress disorder and even in animal models of stress induced depression, hippocampus is found to be atrophied with decreased functional integrity. Increased expression of 5HT1A receptors in normal hippocampus and neurogenesis area of dentate gyrus is found to be down regulated in animal models of depression[12].

Neuroanatomical studies done to explore the structures in hman brain to locate the anatomical areas involved in the pathogenesis of depression implicate Ventero-medial and Dorso-lateral sectors of prefrontal cortex as main substrates of neural dysfunction for MDD[16]. Also such studies provided scope for emerging pharmacological and non-pharmacological treatment modalities in recent times. Non-pharmacological modalities like Deep Brain Stimulation (DBS) by electrodes placed in subgenual cingulate white matter (cg25WM) showed significant (50%) response among MDD patients in a trial. The lateral habenula, ventral capsule/ventral striatum, and the subcallosal cingulate are other targeted parts for DBS. Vagal nerve stimulation, Electroconvulsive therapy(ECT), and Transcranial magnetic stimulation in regions of prefrontal cortex are the other modalities to treat depression.[17]. A Study has correlated the functional connectivity of Anterior cingulate Cortex (ACC) subregions namely, pregenual ACC (pgACC) and anterior subgenual ACC (sgACC) with the severity of depression. Lesser the connectivity in these regions, more severe is the depression. These subregions of ACC are also implicated in subclinical depression apart from major depression[18].

Physiological and Biochemical Aspects of Neurotransmission in Depression:

Signs and symptoms of cognitive decline associated with aging is accentuated by depression. This is due to disturbance in regulation of

serotonergic activity and hypothalamic-pituitary-adrenal axis, aggravated by depression. Depressed patients show dysregulation of serotonergic neurotransmission in serotonergic raphe neurons of various regions of brain and subsequent commotion in cognitive and other physiological processes. All subtypes of serotonergic receptors are metabotropic receptors except 5-HT3 which is an ionotropic receptor. Subtypes 5-HT 1A, 5-HT 2A, 5-HT 1B and 5-HT 2C are located in brain areas implicated in depression. Serotonergic receptors are found to be of reduced affinity and density in hippocampal, occipital and cortical areas with progression of age correlating to the increased prevalence of depression in elderly.

Antidepressants act directly or indirectly by prolongation of 5HT interaction with its receptors or by preventing the action of 5HT transporters respectively. Prolonged administration of anti depressants in MDD patients have shown to rise hippocampal BDNF and cAMP-responsive element-binding protein (CREB) mRNA levels, which are low in the cerebral cortex of patients with depressive illness[3]. Metabolic end product of sertonin, 5-hydroxyindoleacetic acid (5HIAA) is found to be high in urine of depressive patients which is reduced in patients responding to antidepressant therapy[12].

Pathophysiology in depression

In the understanding of pathophysiology of major depressive disorder (MDD)studies based on positron emission tomography (PET), single photon emission tomography (SPECT), and magnetic resonance imaging (MRI),

reveal that patients with recurrent depressive episodes show evident changes in volume of grey matter and in functions of neurophysiological circuits in the regions of the medial prefrontal cortex (MPFC), the medial and caudolateral orbital cortex, amygdala, hippocampus, and ventromedial parts of the basal ganglia. The findings from such studies had formed basis for development of neurocircuitry models of depression[16].

Neurotransmitter receptor hypothesis in depression explains the delay in achieving therapeutic benefit with antidepressants in treating depressive illness. There is a definitive time lag before therapeutic effect of antidepressants sets in. Mono amine receptor hypothesis of depression explains this by the occurrence of upregulated monoamine receptors in depression, which is downregulated by anti depressants. The blocking of monoamine reuptake pump by anti depressant drugs leads to accumulation of excess neurotransmitter in the synapse. This NT excess produces down regulation of receptors and this receptor adaptive changes explains the time lag of antidepressants to produce their therapeutic effect[19].

Risk Factors and Aetiology of Depression:

Various socio demographic variables are found to influence the incidence of depression. This includes age, sex, marital status, educational status and socio economic class[20]. Depression is more prevalent among younger ages, muslims, low socio economic groups, poor nutritional status, widowers, divorcees, unemployed, low educated, nuclear families and in

urban areas. Stressful events in life, health issues causing chronic illness, low esteemed personality inherited from parents evidenced by family history of depression, postpartum depression, loneliness, alcohol and drug abuse individuals are more prone for depression[21].

Age: Normal stress of adolescent age is found to be the main attributing factor for depression in adolescents. A study in western population estimated that 8.3% of older adolescents and 20% of young adolescents show signs and symptoms attributing to depression. Depression in adolescents often go unnoticed or misdiagnosed to be of substance abuse and attentional disorders. However this can result in increased suicidal rates among teen aged population. Suicidal rates among teens have shown three times increase in past 50 years. Depressive illness of onset at early age onset often turn chronic, severe and relapse in later ages. Major Depressive Disorder tend to be 2 to 3 times higher in adulthood when they have had earlier subclinical depression during their teens. Hence early and appropriate diagnosis, effective intervention and preventing complications in early ages may help reduce the incidence of this disease in adult population[22]. A study conducted among geriatric population of 60 years and older has revealed depressive illness to be the commonest psychiatric condition prevailing in that elderly age group[12]. Health issues and poverty are detrimental while good family and social support is salvaging from depression in elderly age groups. A study in rural south India has shown increased geriatric prevalence of depression[23].

Though many estimates are being done among various age groups, depression is proven to be more in later part of life[24].

Gender: Depression is more prevalent among women with 5.1% than in men with 3.6%[7]. Based on the report on Global Burden of Disease, the point prevalence of unipolar depressive episodes in men is estimated to be 1.9% and in women to be 3.2%. One-year prevalence in men and women is estimated to be 5.8% and 9.5% respectively. Rate of depressive disorders were greater in women with 704/1000 population[12]. Hence, women are twice more likely to be affected by depression than men[20]. Prevalence of depression among women in child bearing age is very high with 20%. Lifetime risk of developing depression in women varies from 10 to 25%[25].

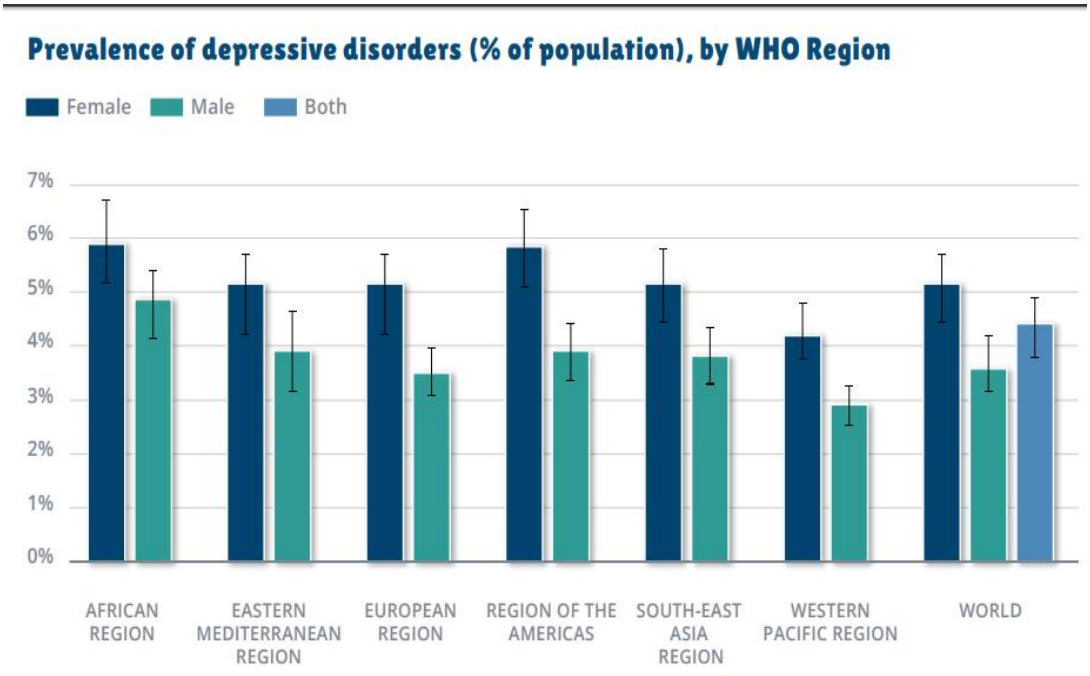


Figure - 1 Shows sex related differences in prevalence of depression in WHO regions.

Marital status of an individual significantly influence the development of depression. Single ie, divorced and widowed individuals show increased prevalence. However, prevalence of depression based on marital status did not show any sex differences[20].

Socio-economic status and depression : People belonging to Lower socio economic class show higher prevalence of depression than among people from higher socioeconomic class. Prevalence rises with decreasing socio economic status[20].

Maternal health and depression : Women diagnosed with major depressive disorder during their antenatal period take poor care of themselves, many engage in alcohol and drug abuse that is detrimental to the fetus. All these culminate in decreased or abnormal development in the fetus, increases complications like pre eclampsia during the pregnancy and delivery, leading to low birth weight, malnourished and chronically ill babies. Perinatal depression also affects language, social and cognitive development of the offspring. Even after adjusting the confounding factors of socio economic status and others, mothers with perinatal depression have five times more risk of producing infants with stunted growth which become evident by 6 months of age[9]. Children born to mothers with depression have 5 times more risk of developing depression by 16 years of age than the adolescents born to non depressed mothers[25]. Role of hormonal changes involving progesterone,

estrogen, TSH that is drastic during pregnancy and nutritional influence on development of depression requires further evidence[25]. Depression is found to be significantly high among women during perinatal period and incidence of depression during postnatal period is estimated to be 11%[12].

To sum up the epidemiological prevalence, depression shows higher incidence among women, older age groups, poor socio economic background, among persons with declined nutritional status, in single, divorced or widowed, in unemployed, and those living in urban areas and nuclear families than in joint families[12].

Genetic risk factors for depression

Family based studies and twin studies show strong genetic influence on development of depression as evidenced by recurrent illness and young age onset. Unexpected discontinuation or loss of pregnancy is identified as significantly major single risk factor leading to depression[26].

Drugs causing depression

- Cancer chemotherapy is a long course with many side effects and by itself can lead to depression. Chemotherapeutic agents like asparaginase, azathioprine, vincristine, vinblastine and bleomycin in addition have a direct role in causing depression.

- Cardiovascular drugs like ACE inhibitors, calcium channel blockers, digitalis and clonidine are also found to precipitate depression in

susceptible individuals. Statins widely prescribed in most of atherosclerotic or degenerative disorders too have a role as a cause of depression.

- Anti hypertensive drug, methyl dopa often used for treating PIH in pregnant women is also implicated in causing depression.

- Other drugs that can produce depression includes are anti-parkinsonian drugs like amantadine, levodopa and bromocriptine. anti-psychotics like haloperidol, anti epileptics like phenytoin, ethosuximide, tiagabine, vigabatrin.

- Anti microbials like ampicillin, chloroquine, dapsone, anti-tubercular drugs like isoniazid, ethambutol. Anti retroviral drugs like atazanavir, efavirenz,saquinavir, zidovudine also cause depression.

- NSAIDS, antihistaminics like ranitidine, and cholinergic drug physostigmine, are known to cause depression[27].

- Hormonal agents like oral contraceptive pills and tamoxifen can cause depression. Prednisolone and Reserpine simulate endocrine and neurochemical changes similar to the changes observed in endogenous Major Depressive Disorder. Prednisolone causes hypercortisolism, while reserpine deplete mono amine transmitters which in turn precipitates a Major Ddepressive Episode in vulnerable population [26]

Diseases commonly associated with depression

There are certain physical illnesses that are often associated with occurrence of depression and that includes malignancy, diabetes mellitus, post stroke, epilepsy, alzheimer's disease, multiple sclerosis, hypothyroidism, hyperthyroidism, parkinsonism and other degenerative brain disease[27]. Various health conditions including endocrine disorders like cushing's syndrome, neurological disorders like parkinsonism, huntingtons disease, wilsons disease, tumors, infarcts and injury of frontal lobe, striatum and medial mesotemporal cortex all make the susceptible individuals develop depression. Patients with Parkinsons disease show four times higher risk of developing depressive episodes than patients with other neurological disorders[26].

SYMPTOMS OF DEPRESSION AND DIAGNOSTIC CRITERIA

DSM (Diagnostic and Statistical Manual of Mental Disorders) is the manual of international standards that documents the knowledge about mental disorders by experts in the mental health and associated professional fields, for the benefit of those dealing with mental disorders inclusive of patients, doctors, research professionals, administrating officers, insurance agencies and others. American psychiatrists Dr. Jeffrey Liebermann and Dr. Thomas Insel credit DSM as the best information brochure along with ICD, presently providing all necessary details for the clinical diagnosis of mental disorders[28].

According to DSM V, major depressive disorder is characterized by nine symptoms namely,

1. Depressed mood;
2. Markedly diminished interest or pleasure;
3. Feelings of worthlessness or inappropriate guilt;
4. Insomnia or hypersomnia;
5. Psychomotor agitation or retardation;
6. Fatigue or loss of energy;
7. Increase or decrease in either weight or appetite;
8. Diminished ability to think or concentrate, or indecisiveness;
9. Recurrent thoughts of death or recurrent suicidal ideation.

To declare a patient to be depressed he or she must have any 5 of the above symptoms inclusive of anhedonia or depressed mood. Except for the first symptom, all the other symptoms contain sub symptoms. Among them, symptoms of sleep problems, appetite /weight problems, psyhomotor problems include both the extremes of the symptom spectrum. That is, insomnia/hypersomnia, loss/gain of weight and appetite, psychomotor retardation/agitation. These symptomatology ultimately gives 1000 symptom combinations that are unique to be given the diagnosis of depression which explains the heterogeneity of depression presentation[29].

Suicidality in Depression

One major and severe complication of depression is suicide. According to estimates of Indian Union Health ministry, there are about 120,000 suicides

reported every year. And there are about 400,000 suicide attempts per year. Of these people committing suicide, 37.8% are less than 30 years of age and 50% of them were diagnosed of depression primarily[9]. Out of ten individuals who die by suicide, nine of them have been found to be affected by psychiatric illness, of which depression is implicated as the most common cause. Among patients who die while on treatment for depression, 1 out of 6 deaths is due to suicide[30].

Depression and somatic symptoms

80% of patients diagnosed with depression, present with somatic symptoms including pain besides symptoms of affect. Somatic symptoms include disruption of sleep, tiredness, pain, body discomfort, altered appetite. According to Jackson et al, five or more physical symptoms are important predictors for the diagnosis of depression among the outpatients of medicine. Painful symptoms show increased occurrence in depressed patients. Moreover, depression is of greater severity if physical symptoms consist of chest pain or back pain. These physical symptoms are substantiated by perception of disrupted sensory inputs as painful symptoms in these patients, resulting from defective neurotransmission and inhibition in descending pathways[31].

Remission Relapse and Recovery

Many patients diagnosed with depression have previous history of similar episodes. Even among patients who have recovered, subsequent recurrences do occur, with each recurrent episode increasing the risk of chronicity and non remitting nature of the disease. 60% of depressed cases after first episode, have the chance of developing the second one. There is 70% of chance of recurrence after two episodes and 90% of developing 4th episode after the 3rd one. Sixteen years follow up study showed 50% of diagnosed depressive cases to be chronic of nature. In various clinical trials, remission is fixed as attainment of HAM-D score of ≤7 and maintenance for 2 consequetive weeks. Relapse is defined as reappearance of depression symptoms after attaining remission[27]. Hence complete therapy for complete remission based on severity, number and chronic nature of previous episodes is recommended which varies for every individual, since partial response may not give symptom free remission in between episodes[31]. Recovery is remission sustained for 6 consequetive months[32] .

SCALES FOR ASSESSMENT OF SEVERITY OF DEPRESSION

Various standard recommended scales that are available currently for assessment of severity of depression includes :

1) HAM-D (Hamilton Depression rating scale)(HAM-D17, HAM-D21, HAM-D24)

2) MADRS (montgomery-Asberg Depression Rating Scale)

3) CGI scale (Clinical Global Impression)

4) QIDS (The 16-item Quick Inventory of Depressive Symptomatology)

5) IDS (The 30-item Inventory of Depressive Symptomatology)

HAM-D (Hamilton Depression rating scale) gives either HAM-D17, HAM-D21, and HAM-D24 based on the number of items forming the questionnaire. QIDS is a new scale to measure the severity of depression that is derived from the 30-item Inventory of Depressive Symptomatology (IDS). This scale is available in two formats. ie) both self-report ($QIDS\text{-}SR_{16}$) and clinician-rated ($QIDS\text{-}C_{16}$) formats. Various studies are being conducted to compare and assess the validity of these available scales of depression. One study compared internal validity of QIDS with HAM-D depression rating scale using IRT(Item Response Theory)[33]. Currently available guidelines for treating MDD lays emphasis on the assessment of severity of symptoms and disease before deciding upon patient's initial therapy. On the basis of recommendations made by results of large clinical trials in the patients with depression, it is recommended to follow the severity ranges given below for HAM-D scale[34].

- HAM –D Score 0-7 - No depression
- HAM –D Score 8-16 - Mild depression
- HAM –D Score 17-23 - Moderate depression
- HAM –D Score ≥24 - Severe depression.

Apart from these scoring, severity can be labelled based on the need for hospitalisation depressive subtypes, functional capacity, level of suicidal thoughts. Response to the instituted therapy can be assessed based on following validated terminologies.

- **HDRS/HAM-D -17 Responders** are defined as patients who show ≥50% reduction in score from baseline.
- **HDRS/ HAM-D -17 Remitters** are defined as patients with a HDRS score of ≤7 points on a post-baseline assessment[35]

Depression induced -comorbidities

Co-morbidity can be explained as the presence of one disorder or disease in a patient, increasing the risk or prevalence of another disease in the same patient. This simultaneous occurrence of two diseases together can affect the course of both diseases[36]. In patients with major depressive disorder, several medical conditions show higher risk of occurrence, of which increased prevalence of coronary events and stroke in depression are proven by number of studies. Risk of developing stroke in patients with depression or with a history of depressive illness is found to be two to three times higher than among those without depression. This risk prediction is obtained after ruling out the influence of confounding factors of diabetes, hypertension, tobacco use[37]. According to a quantitative review, depression is a proven independent risk factor that can contribute for a significant increase in the incidence of coronary heart disease. This risk is greater than that contributed

by passive smoking for the development of coronary events[38]. Apart from the higher risk of occurrence of these co-morbidities, depression is also found to increase the risk of death, especially more by cardiovascular diseases and unnatural causes[39].

MANAGEMENT OF DEPRESSION

Guidelines of Management of Major Depressive Disorders outline that in patients with severe depression pharmacotherapy is the first choice of treatment, while psychotherapy has limited role in acute phase. In cases of mild to moderate depression both pharmacotherapy and psychotherapy are recommended options[34].

Psychotherapy for depression : Psycho therapeutic interventions for managing depression include the following.

Behavioral Therapy (BT) by means of activity scheduling, social skills training and problem solving

Cognitive Behavioural Therapy(CBT) featured by identifying problems, identifying cognitive distortions/errors, generating alternative thoughts, problem solving, mastery and pleasure rating, activity scheduling, anxiety management strategies relaxation exercises.

Interpersonal Therapy (IPT) deals with losses, role disputes and transitions, deficits in social skills, , social isolation and other interpersonal factors that may play role in the development of depression.

Supportive psychotherapy enables patient to ventilate, it guides and provides emotional support, helps to increase patient's self esteem, accepting feelings at face value, enhancing hope, enhancing adaptive coping.

Marital Therapy (MT) is the treatment which includes behavioral exchange, communication training, problem solving, and resolution of conflict around issues such as financial, sex, affection, parenting, and intimacy between both members involved in marital relationship. **Family Therapy** is similar to marital therapy but here it involves all the members in the family when pathological family dynamics are responsible for depression.

Brief Psychodynamic Psychotherapy (BPD) involves training the individual to learn new ways and methods to cope with inner conflicts[27].

PHARMACOTHERAPY FOR DEPRESSION

Anti depressant drugs available till date can be classified as follows.

- MAO inhibitors

  Non-Selective ; Tranylcypromine

  Selective MAO-A inhibitor: Moclobemide

- Drugs which block NE and 5-HT reuptake

  Tricyclic Antidepressants (TCAs): Imipramine, Clomipramine, Amitriptyline,

  Doxepin

- Drugs that mainly block NE reuptake(NRI)

Desipramine, Nortriptyline, Protriptyline, Maprotiline, Amoxapine, Reboxetine.

- Serotonin-Norepinephrine reuptake inhibitors (SNRIs)

Duloxetine, Venlafaxine, Desvenlafaxine, Milnacipran, Levomilnacipran

- Selective Serotonin Reuptake Inhibitors (SSRIs)

Sertraline, Fluoxetine, Fluoxamine, Paroxetine, vortioxetine, Citalopram, Escitalopram

- Atypical anti-depressants

  5-HT receptor modulators : Trazodone, Nefazodone, Vortioxetine
  Tetracyclic & Unicyclic agents: Bupropion, Mianserin.

- Norepinephrine Serotonin Reuptake Enhancer (NSRE) - Tianeptine.
- Noradrenaline and Specific Serotonin Antidepressant (NaSSA) Mirtazepine
- Serotonin partial agonist reuptake inhibitor (SPARI) - Vilazodone
- Anti depressant of natural origin - St. John's wort[27), (40),(41).]

ANTI-DEPRESSANTS - Features.

- Noradrenergic nerve terminal and serotonergic nerve terminal are the chief sites of action. SSRIs, SNRIs, and TCAs block NET, SERT (Norepinephrine or Serotonergic transporter), thereby increasing post

synaptic noradrenergic or serotonergic neurotransmission contributing to the anti-depressant action

- MAO is the enzyme responsible for metabolising norepinephrine and serotonin. MAOIs inhibit the catabolism of norepinephrine and serotonin thereby increasing their concentration at the synapse.
- Other atypical antidepressants such as trazadone produce clinical effects by acting directly on serotonergic receptors.
- Presynaptic autoreceptors and heteroreceptors are desensitized by chronic treatment with a number of antidepressants, thus producing long-lasting changes in monoaminergic neurotransmission. Long-term effects of antidepressant drugs are mediated by their post-receptor effects, that includes modulation of GPCR signaling and activation of protein kinases and ion channels[(42)].
- Common feature for all antidepressant drugs, is the biological lag of two to three weeks to produce desirable clinical antidepressant effect. Though inhibition of mono amine reuptake is immediate, complete therapeutic benefit is evident only with down regulation of post synaptic beta 1, beta 2, 5-HT2 receptors, along with desensitization of pre synaptic alpha2 and 5-HT1 autoreceptors[(40).]
- **Antidepressants and Suicidality:** Relationship between antidepressants use and suicidal tendency is controversial, since sufficient evidence based data to support the causal relation is lacking.

In general, patients with suicidal tendency are excluded from participating in any clinical trials for the reasons of safety. But due to the possibility of their association, a "black box" warning, is issued by the FDA, on the use of SSRIs and other antidepressants, during early phase of treatment in adolescents and children, However, recent studies suggest decrease in incidence of suicides since introduction of SSRIs, as evidenced by analysis of over 65,000 health records of patients on pharmacotherapy for depression. Hence, risk of suicide without medication for depression is greater than the risk of suicide while on antidepressants. Patients and their family members are advised to watch for worsening or occurrence of new symptoms especially in the initial phase of treatment for depression[42].

Advantages of SSRIs over TCAs

SSRIs have better tolerability, acceptability and better safety than first generation tricyclic antidepressants. SSRIs do not produce antihistaminic and anticholinergic side effects, they cause little or no sedation and do not interfere with psychomotor and cognitive functioning. SSRIs do not cause alpha adrenergic blockade and hence postural hypotension does not occur with SSRIs. This makes them drug of choice in elderly patients too. They do not precipitate seizures or produce cardiac arrhythmias even in overdose[43]. In a depressed individual there are less serotonin for neurotransmission and increased number of serotonin presynaptic auto receptors and post synaptic

serotonin receptors. SSRIs, increase 5-HT neurotransmission at the synaptic cleft by blocking SERT.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs)

Since 1984, many drugs were introduced in the group of SSRIs which includes fluvoxamine, fluoxetine, paroxetine, sertraline, citalopram, escitalopram. The drug Fluvoxamine is FDA approved for treatment of obsessive-compulsive disorder and generalised anxiety disorder, but not depression. Citalopram has labeled use in premenstrual dysphoric disorder. All drugs in the group of SSRIs are proven to have good safety profile, even in overdoses, as compared with TCAs. In terms of efficacy, these drugs cover a broad spectrum of applications on and off-label including many psychiatric, behavioral and medical conditions. Of these uses, SSRIs are known for their efficacy in managing patients with major depressive disorder. Many studies have proven the efficacy of SSRIs as antidepressants in terms of their effectiveness in producing remission. SSRIs also show significant reduction (50%) in depression symptoms in 6-8 weeks treatment trial. SSRI's antidepressant effect enables efficient execution of day to day activities and improves cognitive and motor functional capacity by its effect on neuronal plasticity[44].Selective Serotonin reuptake inhibitors block the Serotonin Transporter mediated reuptake of the neurotransmitter serotonin at the synaptic cleft and in somatodendritic area, thereby increasing serotonin concentration and consequent downregulation of autoreceptors, thereby

increased firing and increased concentration of serotonin at the synaptic cleft[40]. Selective serotonin reuptake inhibitors binds to serotonin transporter at a site different from that of serotonin to inhibit the transporter[45]. Treatment with SSRIs initially stimulates auto receptors and causes reduction in synthesis and release of serotonin. But with prolonged treatment, SSRIs cause down regulation and desensitization of these auto receptors gradually, contributing to anti depressant effects. In addition, down-regulation of postsynaptic 5-HT_{2A} receptors may contribute to antidepressant efficacy directly or by influencing the function of noradrenergic and other neurons via serotonergic heteroreceptors. Other postsynaptic 5-HT receptors respond to high concentration of serotonin in the synaptic cleft, producing the therapeutic effects of selective serotonin reuptake inhibitors[19][42].Apart from immediate effects produced by SSRIs, late effects are also essential to produce therapeutic results. Late effects are mediated by consistent rise in cyclic AMP signaling, leading to CREB (cAMP Response Element Binding Protein) nuclear transcription factor phosphorylation, increased expression of BDNF, its receptor TrkB and other trophic factors. Moreover, in the regions of dentate nucleus of hippocampus and subventricular zone, there is increased neurogenesis from progenitor cells during treatment with SSRIs. Increased neurogenesis dependent behavioral effects have been demonstrated in animal models of depression while on SSRIs. This proves the contributory role of this mechanism in the anti depressant action of SSRIs. Prolonged treatment with SSRIs also produces down regulation and reduced expression of

Serotonin transporters(SERT), thereby increasing serotonergic transmission by reducing their clearance at synaptic cleft. Evidences from animal models on SSRIs, also favour this later effect of reduced SERT expression, increased serotonergic neurotransmission and improved behavioral symptoms in them[42].

Other clinical applications of SSRIs

- Anxiety disorders – SSRIs have anxiolytic property with clinical role in managing PTSD, OCD, Social anxiety disorder, GAD, and pain disorder.
- Sertraline and Paroxetine in particular are approved for managing post-traumatic stress disorder (PTSD)
- Pain disorders – neuropathies
- Pre menstrual dysphoric disorder
- Prevention of vasovagal symptoms in post menopausal women.
- Eating disorders – bulimia
- Delayed orgasm produced by SSRIs is used to treat premature ejaculation[41],[42]

Adverse effects :

- SSRIs increase the serotonergic tone in all parts of the body including brain and spinal cord

- Enhanced serotonergic action on 5HT3 receptors in the gut produces nausea, diarrhoea , and associated GI symptoms. These symptoms are reported often during early therapy with SSRIs and show improvement after 1st week of treatment.

- Increased serotonergic action on 5HT2 receptors in spinal cord produces symptoms of sexual dysfunction that includes decreased or loss of libido, decreased sexual arousal and interest, delayed ejaculation, and delayed orgasm or anorgasmia. Sexual dysfunction is noted in one-third of patients on SSRIs.

- Laboratory animal studies show that increased serotonin in central nervous system decrease levels of dopamine, a neurotransmitter with role in normal sexual functioning[46]. These effects tend to be present till the patient is on SSRIs and may decrease with time.

- SSRIs do not affect weight of the patient adversely except Paroxetine, which causes weight gain.

- Insomnia, hypersomnia and headaches occur in SSRIs treatment due to raised serotonin levels acting on 5HT2 receptors in brain[41].

- SSRIs produce anxiety, agitation in certain patients and hence slow titration of their dose from lower levels are suggested[40].

- Pharmacodynamic drug interactions of SSRIs with Mono Amine Oxidase Inhibitors(MAOIs) produces serious adverse effect, namely Serotonin Syndrome[41].
- Studies suggest that SSRIs may be associated with the occurrence of drug-induced parkinsonism, dystonia, dyskinesia, and akathisia[47].
- Numerous case reports, observational studies, and case-controlled studies, as well as prospective clinical trial, have reported rare but potentially serious ADR, hyponatremia to be associated with the use of SSRIs. The incidence of hyponatremia varies from 0.5% to 32%. There are certain risk factors that are implicated in the development of hyponatremia with SSRIs which includes older age, female gender, concomitant use of diuretics, low body weight, and lower baseline serum sodium concentration. Based on the published studies, hyponatremia developed within the first few weeks of treatment and resolved within 2 weeks after the discontinuation of therapy[48]. The mechanism by which SSRIs cause hyponatremia is thought to be secondary to development of SIADH. The syndrome of inappropriate antidiuretic hormone secretion is characterized by a low serum sodium concentration (<135 mmol per liter), urinary osmolality exceeding 200 mOsm per kilogram, a urinary sodium concentration exceeding 20 mmol per liter, and serum osmolality of less than 280 mOsm per kilogram[49].

Treatment of isovolemic hypotonic hyponatremia associated with SSRI use includes water restriction and mild diuresis with a loop diuretic. More severe cases may be treated with higher doses of loop diuretics and hypertonic saline. There have been few studies that document about rechallenge with the same or another SSRI or substitution of another agent from a different therapeutic class, in which case, few of them but not all patients showed recurrence of hyponatremia[48]. Although SSRIs are the first line option even for elderly patients with depression, they should be prescribed cautiously in this population because of the risk of this potentially severe adverse effect hyponatremia. So such specifically vulnerable patients can be started with nonserotonergic antidepressants[50].

- SSRIs with shorter half life can produce "discontinuation syndrome" when withdrawn suddenly, after long duration of drug intake.

- Antidepressant Discontinuation Syndrome is due to abrupt stoppage of SSRI occurs in about 20% of patients, when discontinuation is done after at least 6 weeks of continuous treatment. When SSRIs are prescribed for a prolonged period of time, there is blockade of action SERT, subsequent increase in 5-HT in the synaptic cleft initially, hence over the long run, this produces down regulation of the serotonergic receptors. On sudden withdrawal of the anti depressants, there is less 5-HT at the synapse, in addition to the downregulated

receptors, still in their less active state, they affect other neurotransmitter systems (eg, norepinephrine, dopamine, and γ-aminobutyric acid) involved in the depressive and anxiety disorders adversely and culminate in ADS clinically[51]. Symptoms of Antidepressant discontinuation syndrome are mild and characterized by nausea, imbalance, insomnia, hyperarousal, flu like symptoms, and sensory disturbances last for about one to two weeks. Symptoms resolve by restarting the antidepressant medication[52].

STUDY DRUG - ESCITALOPRAM

Escitalopram belongs to Selective Serotonin Reuptake Inhibitors (SSRIs) class of anti-depressants. Escitalopram is the S-enantiomer of citalopram . It is twice potent than citalopram. Extensive in vivo and in vitro studies revealed that R-enantiomer is inactive, while S-enantiomer is active and produces the pharmacological effects of citalopram. Among the SSRIs Escitalopram is more selective for serotonin transporters than that of dopamine or norepinephrine .

Figure 2: Citalopram : contains both R and S enantiomers

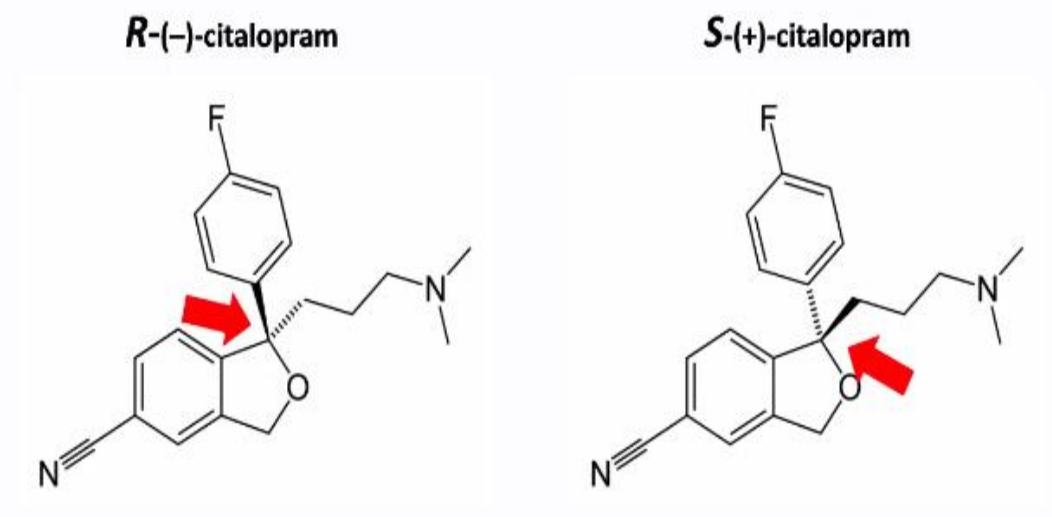
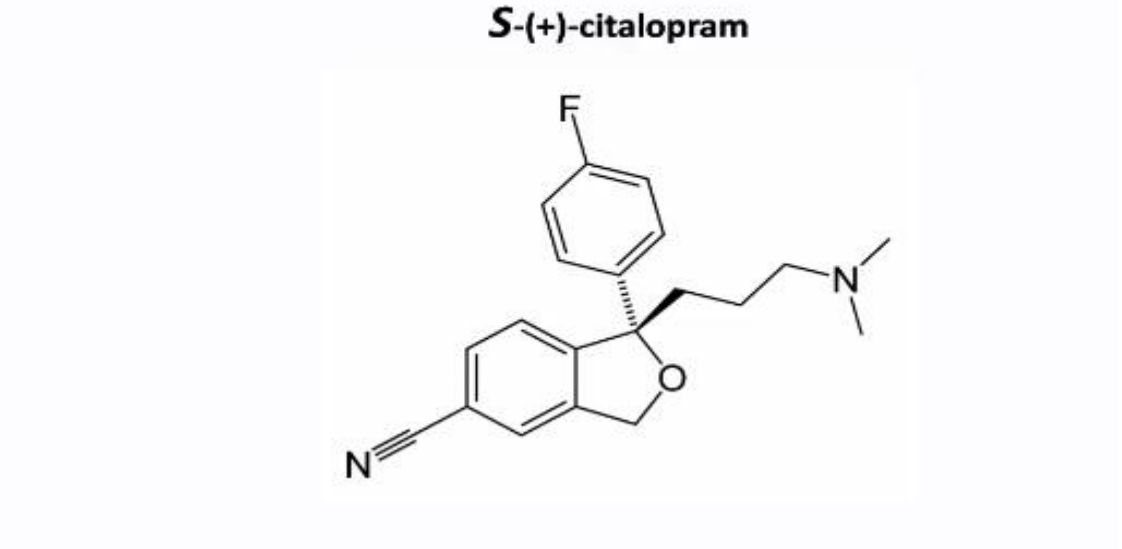


Figure 3: Escitalopram : contains only S- enantiomer



Citalopram is safe and better tolerated and has been used for over 35 million patients after its approval since 1989. Citalopram a racemic mixture of R ,S enantiomers requires higher dose to achieve therapeutic effects, while Escitalopram with pharmacologically active S enantiomer alone produces therapeutic effect at a lower dose. Development of Escitalopram has enabled

in halving the dose of the drug used in treatment of depression, preserving therapeutic efficacy. Hence a dose of 10mg was tried successfully in trials for treating depression. This dose is found to be effective and well tolerated for treating major depressive disorder in all levels of healthcare settings[53]. Escitalopram, is an effective first-line option in the management of patients with MDD[54].

Pharmacological actions :

- Escitalopram is a highly selective potent, dose-dependent inhibition of the human serotonin transporter, inhibiting serotonin reuptake into presynaptic nerve terminals resulting in increased serotonergic activity in the CNS.
- Escitalopram causes minimal inhibition of Norepinephrine transporter (NET)
- Escitalopram induces alterations in neurotrophic activity and multiple signaling pathways[41].
- Unlike other SSRIs, escitalopram binds to a primary high-affinity site on the serotonin transporter protein and to a secondary, lower-affinity allosteric site resulting in stable prolonged drug binding. Radioligand binding assays support higher selectivity of escitalopram for the human serotonin transporter protein, than other SSRIs, including citalopram[55].

Pharmacokinetics - Escitalopram is available as 5/10/20 mg tablet and capsule formulation. It is also available as 5mg/5ml oral solution[56]. On multiple-dosing, it shows linear pharmacokinetic profile across a dose of 10–30 mg/day. 20 mg/day is the maximum approved dosage. On oral administration Tmax is achieved in 5 hours[51]. The bioavailability of escitalopram is about 80%. It is 55% plasma protein bound which is independent of its plasma concentrations. Food does not interfere absorption. Steady-state plasma concentration is achieved after 7–10 days of administration of escitalopram 10mg / day[55]. It is widely distributed throughout tissues with aVd of about 1100L, during the terminal phase[57]. Escitalopram is metabolized by CYP3A4 (34%) and CYP2C19 (36%) and to a lesser extent by CYP2D6 (30%). The elimination half-life of escitalopram is 27 to 33 hours., permitting once daily dosing. $T_{1/2}$ is longer than that of paroxetine but shorter than that of fluoxetine[51]. In plasma, major amount of escitalopram is found in unmetabolised form. Its principle metabolite S-demethylcitalopram (S-DCT), is present in amounts below quantifiable concentrations than the unmetabolised drug($1/3^{rd}$ of escitalopram only). Thus S-DCT a weak inhibitor of serotonin transporter does not contribute to the therapeutic activity of escitalopram. Escitalopram and its metabolite S-DCT, exhibit linear and dose-proportional pharmacokinetics following single or multiple doses in the 10-30 mg/day dose range. Adolescents, elderly individuals and patients with hepatic impairment do not show clinically significant differences in pharmacokinetics profile when compared with

healthy young adults, implying that dosage adjustment is not needed in these group of patients[57]. However, study suggests that in patients with mild and moderate hepatic impairment, AUC curve for escitalopram showed increase by 51% and 69% respectively. Plasma concentrations of escitalopram are significantly higher in poor CYP2C19 metabolizers versus extensive CYP2C19 metabolizers[51]. So in patients with hepatic impairment and poor metabolisers with respect to the cytochrome P450 isoenzyme CYP2C19, it would be ideal to start escitalopram with an oral dose of 5mg daily, increased to 10mg daily after 2 weeks depending on their response[58]. Antiviral drug, Ritonavir, though a potent inhibitor of CYP3A4, does not alter serum levels of Escitalopram, on coadministration. Escitalopram 20mg, when administered with cimetidine and omeprazole produced increased levels of these 2 drugs by 72% and 51% respectively. Escitalopram has negligible inhibitory effects on CYP isoenzymes and P-glycoprotein, as evidenced by various in-vitro studies, there is least clinically significant drug-drug interactions. This favourable pharmacokinetic profile of escitalopram with least drug interactions, renders high clinical utility to the drug, in a wide range of patients[57].Other SSRIs such as fluoxetine, fluvoxamine, and paroxetine cause moderate-to-strong inhibition of several CYP enzymes and have increased potential for drug interactions unlike escitalopram.

Escitalopram is equally effective as other SSRIs, but with added advantage of rapid onset of action and being cost effective .Its efficacy in

relapse prevention was better than placebo, maintenance therapy is required to prevent relapse & recurrence[55].

Uses Of Escitalopram

- Depression
- Anxiety disorders including panic disorder
- Obsessive compulsive disorder and
- Social anxiety disorder[58].

Adverse Effects: Escitalopram has less adverse drug reactions compared to other SSRIs, highest therapeutic efficacy when compared with citalopram, fluoxetine, generic paroxetine, paroxetine CR, sertraline, venlafaxine and venlafaxine XR[59].

Patients treated with escitalopram had nausea, ejaculation disorder, insomnia, diarrhoea, somnolence, dry mouth and dizziness. A large meta-analysis of data from placebo controlled studies that used escitalopram, revealed that no suicides with the drug occurred within the first 2 weeks or throughout up to 24 weeks of therapy[55]. Higher doses in low clearance states is associated with increased prevalence of ADS. It is found that high steady-state concentration of escitalopram is a risk factor for developing ADS.. Tapering of doses over an extended period of time is recommended for all patients to prevent ADS[51]. Though escitalopram has least propensity to cause hyponatremia, there are about 8 cases reported till date that are implicating

escitalopram as the agent responsible for inducing hyponatremia[60]. Further studies are required to confirm the association of occurrence of hyponatremia in patients treated with escitalopram.

Escitalopram has a predictable tolerability profile with transient adverse events of mild to moderate severity and a low propensity to produce drug interactions. Sexual dysfunction with escitalopram treatment occurs to a similar or lower extent as compared with paroxetine, to a similar or greater extent as compared with the SNRI duloxetine and bupropion. Escitalopram is well tolerated in treatment for moderate to severe MDD[54].

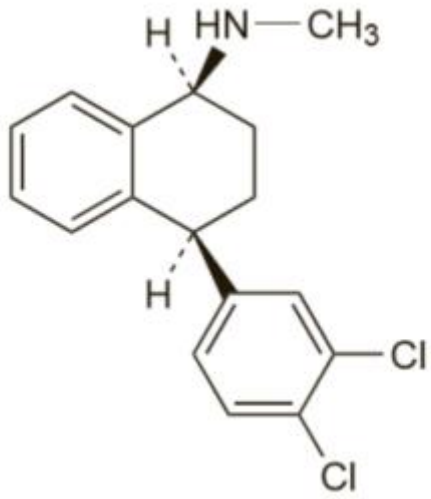
Drug-drug interactions of Escitalopram

As Escitalopram is metabolized by three cytochrome P450 (CYP) hepatic enzymes in humans, each enzyme offers relatively comparable contributions to intrinsic clearance of the drug in the body. With 3 parallel routes of biotransformation, a drug interaction that interferes with any one of these enzyme isoforms is least likely to affect overall drug clearance rates. Moreover, escitalopram and its 2 metabolites have only weak-to-negligible inhibitory effects on CYP enzymes, hence they are least likely to be producing clinically significant drug interactions mediated through these metabolic pathways. High protein binding nature increases the possibility of displacement of other protein bound drugs. Escitalopram is only 55% bound to human plasma proteins, further reducing its potential for producing drug-drug interactions[61].

ACTIVE CONTROL - SERTRALINE

Sertraline is an anti depressant belonging to the class of Selective Serotonin Reuptake Inhibitors (SSRIs). Sertraline (1 S,4S-N-methyl-4-[3,4-dichlorophenyl]- 1,2,3,4-tetrahedro-l-napthylamine) is a naphthylamine derivative with unique antidepressant chemical structure. It exerts its effect by inhibiting reuptake of serotonin into brain synaptosomes, with weak effects on dopamine and norepinephrine reuptake[62] [63].

Figure 4: Chemical structure of Sertraline[64]



Sertraline is an antidepressant and antipanic agent that is a potent and selective inhibitor of serotonin reuptake into the presynaptic terminal. Selective serotonin reuptake inhibitors (SSRIs) depress the firing of neurons in the raphe nucleus, which in turn may affect norepinephrine neurons of the locus coeruleus. Increased firing of locus coeruleus neurons leads to desensitization of the postsynaptic and presynaptic receptors, and it has been demonstrated that sertraline leads to subsensitivity of adrenoceptors in rat

brain. This blunted adrenoceptor responsivity of the noradrenergic receptor-coupled adenylate cyclase system occurs after repeated doses of many antidepressants and the same has been evidenced after electroconvulsive therapy also. This effect may also partially account for the effectiveness of sertraline as an antipanic agent, as noradrenergic neurons of the locus coeruleus as well as the serotonergic system have been implicated in anxiety.

Sertraline also exert its antidepressant effects through activation of the cAMP pathway, which in turn leads to regulation of cAMP-dependent protein kinase and subsequently to activation of the cAMP response element binding protein (CREB). CREB may mediate its effect by inducing increased expression of neuroprotective neurotrophins such as brain-derived neurotrophic factor which, along with CREB, has been shown to be elevated following chronic antidepressant and electroconvulsive therapy. The effect of increased neurotrophins is to mitigate hippocampal changes associated with exposure to stress. This model of antidepressant action provides the best current hypothesis regarding the mechanism of action of Sertraline[65].

Pharmacokinetics: Sertraline is available as tablets in doses of 25, 50, and 100mg. It is also available as oral concentrate of 60ml/ bottle in dose of 20mg/ml. Sertraline has a linear pharmacokinetic profile in therapeutic dose range of 50 to 200 mg/day. Sertraline is slowly and completely absorbed from gastro intestinal tract and has a bioavailability of 45%. The maximum plasma concentration is achieved at 4–8 h after oral administration. The

bioavailability of sertraline hydrochloride is increased by least 28% in the presence of food and hence it is advised to be taken with meals which also increases C_{max} by 25 % [65].

Sertraline accumulates more rapidly to reach steady-state plasma concentration at approximately 1 week of daily administration compared with fluoxetine and hence has faster onset of therapeutic action. Volume of distribution is 20 L/kg. It is 98% plasma protein bound and this highly protein bound nature influences the blood levels of other highly protein bound agents[41].

Sertraline undergoes extensive first pass metabolism. It is metabolised by CYP450 enzymes, monoamine oxidases and glucuronyl transferases. 5 isoforms of CYP 450 enzymes (2B6, 2C9, 2C19, 2D6, and 3A4) cause N-demethylation of sertraline. Since the contribution of any individual isoform of CYP450 does not exceed 40% of the overall metabolism, concurrent administration of a drug that inhibits one of these isoforms is unlikely to cause a marked increase in the plasma concentration of sertraline. Also any single drug-metabolizing enzyme genetic polymorphism (e.g., CYP2D6, CYP2C19, CYP2C9, UGT1A1) will not significantly impact the pharmacokinetics of sertraline. Purified human monoamine oxidases A and B also catalyzed sertraline deamination with comparable K(m) values (230-270 microM). Monoamine oxidase B catalyzed the reaction approximately 3-fold faster than did monoamine oxidase A[66].

Sertraline mildly inhibits the CYP2D6 isoenzyme, at a dose of 50mg/day resulting in 10%–50% elevation in plasma levels of a concomitantly administered CYP2D6 substrate (e.g., dextromethorphan). Sertraline has little effect on CYP1A2, CYP3A4, CYP2C9, or CYP2C19 enzymes. Drug interactions of Sertraline is due to its high plasma protein binding nature and may interact with other highly protein bound drugs. Cytochrome P450 3A isoenzyme activity may be greater in young and postmenopausal women and there are data describing sex- and age-related differences in plasma concentrations of sertraline. Studies have reported that the coadministration of sertraline with TCAs can increase the plasma concentrations of desipramine, imipramine, and nortriptyline[65].

The half-life of sertraline is 26 hrs enabling once daily dosing. The long t1/2 (62 to 104 hrs)of Desmethylsertraline, the major inactive metabolite of Sertraline has minimal significance since it is 10 times less potent as a serotonin reuptake inhibitor[67]. N-desmethylsertraline is oxidatively deaminated to desmethylsertraline ketone which, in turn, undergoes hydroxylation to an alpha-hydroxyketone and alcohol; these metabolites are then conjugated and excreted in equal amounts in the urine and faeces. Only a small amount of less than 0.2 % of unchanged drug is excreted in the urine[68].

There are few data about the excretion of sertraline and its metabolites in breast milk. Infants of breast feeding mothers taking Sertraline showed

detectable sertraline levels in their serum but they did not develop any adverse effects[69].

Half-life of Sertraline was prolonged by 42 to 92 h in patients with end-stage renal disease and in individuals with severe hepatic impairment. Its preferred in elderly patients since ageing does not affect its elimination[41].

Adverse drug reactions – sertraline is well tolerated in the dose of 50-200 mg/day. Mild to moderate adverse reactions reported in various studies include sexual dysfunction[70], diarrhoea, vomiting, anorexia, agitation[71], nausea, anxiety, abdominal pain, asthenia, palpitation, influenza, and tremor[72].

Other FDA approved uses of Sertraline

- Juvenile depression
- Premenstrual dysphoric disorder
- Social anxiety disorder
- Panic disorder
- Post traumatic stress disorder[43]
- Obsessive compulsive disorder[73].

Selection of antidepressant drug

Selecting an antidepressant for a particular patient is dependent on Patient specific factors like patients preference, previous history of

response/tolerability to medication in the patient or family member, past side effects with medication, other medication being taken concomitantly and drug interactions to be considered. Also patient's age since it is known that with increasing age the pharmacokinetic and pharmacodynamic changes can lead to significant alterations in drug disposition. Comorbid medical illness (e.g., glaucoma, cardiac conditions), Comorbid psychiatric disorder / symptoms, Gender issues (like sexual dysfunction), intellectual and psychological capacities are taken into account before deciding on a particular antidepressant. Choice of antidepressant is also determined by several drug specific factors like side effects, cost, dosing strategy, type of formulation (ie, tablet, capsules, syrup) and safety of the drug in its overdose (Relative Toxicity). Fatal overdose is significantly lower with SSRIs than with tricyclic antidepressants.

MANAGEMENT OF DEPRESSION

Acute phase treatment is for atleast 6-12 weeks which is aimed at producing remission. Apart from psycho education, acute phase management of depression should start with comprehensive psychiatric, medical and psychosocial assessment, followed by the decision on the goals of treatment regarding remission besides ensuring patient safety. Appropriate treatment modality of psychotherapy or pharmacotherapy or both is chosen based on patient's clinical assessment. Need for adjunctive medications or electro convulsive therapy are considered based on individual patient needs. Mild and

moderate depression are treated as a single entity while severe depression is treated as separate entity. Basic steps of evaluation is common in both which comprises evaluation of type & severity of depression, past history of depression, its treatment & response to treatment, aggravating psycho social stressors, presence of family history of depression, physical & psychiatric co-morbidities and concomitant drugs taken by the patient[27].

In mild to moderate depression, where there is no past history of depression, or there was a past history of depression with good response to combination of psycho and pharmacotherapy , or there is detectable psycoh social stressors that can be altered, or there is high risk of drug interaction due to concomitant drug intake by the patient, psychotherapy is preferred. If remission is not attained by psychotherapy in such cases, treatment should include antidepressants.

In cases of moderate depression, where there is history of good response to treatment in previous episodes, and when there is low risk of drug interactions, pharmacotherapy is preferred. In some patients who do not respond to one anti depresssant, change of antidepressant or adding psychotherapy to the existing anti depressant is to be considered. During the course of treatment with psychotherapy or pharmacotherapy, when there is partial response, there is need for optimising the treatment, in terms of increasing the frequency of psychotherapy and increasing the dose of antidepressants to maximum tolerable dose. Some patients may need

augmentation of treatment with second antidepressant, in which case, tolerability and safety is to be considered.

In severe depression, with past/family history of good response to treatment and with low risk of drug interactions, pharmacotherapy is the preferred modality of management. Electro convulsive therapy for acute phase management is considered in severely depressed patients with suicidal intentions, catatonic symptoms, poor oral intake and in those patients who do not respond to pharmacotherapy. In cases with severe depression who show partial response to pharmacotherapy, optimising treatment with increased dose of antidepressant, adding ECT/second antidepressant to be considered.

Treatment in continuation phase is for a period of 16-24 weeks which aims at maintaining the optimum response achieved in acute phase and to prevent relapses.

In patients treated with anti depressants during acute phase, same antidepressant at same dose is to be continued for 6-9 months after achieving remission.

In patients treated with psychotherapy alone , continue it in same or reduced frequency for 6-9 months after achieving remission.

In patients treated with combination of psychotherapy and pharmacotherapy, same antidepressant at same dose and psychotherapy in

same or reduced frequency is to be continued for 6-9 months after achieving remission.

For patients managed with antidepressants and ECT/antipsychotics during acute phase, treatment should be continued with antidepressants and antipsychotics at same dose for 6-9 months after achieving remission.

Maintenance phase treatment of continuing antidepressant drug therapy for a prolonged duration is given for patients who had previous history of depression and the duration of maintenance treatment is individualised based on the individual's treatment response in present and past episodes and their previous rate of relapses. Dose of antidepressants in maintenance therapy is the same as that in acute and continuation phase. Frequency of visits for cognitive behavioural therapy and inter personal therapy can be reduced to once every month during maintenance phase.

Discontinuation of treatment is considered in patients with no previous history of depression, and patients who remain stable after continuation phase. Discontinuation of pharmacotherapy with anti depressants must be in form of tapering over weeks to months, which avoids emergence of discontinuation syndrome. It also enables detection of recurring symptoms and intensity of therapy can be increased to previous doses, while the patient is still in partial therapy. Discontinuation of psychotherapy is dependent on patient's needs. All patients should be monitored for relapses after discontinuation of treatment.

Depression resistant to treatment is diagnosis of exclusion of incorrect diagnosis, inadequate treatment (duration/dose), non adherence, organic etiology and other comorbidities. Patients classified as treatment-resistant when they are Non responsive to treatment for 6-8 weeks with two successive trials of medications of different categories for adequate duration[74), (75)].

Management of Treatment resistant depression includes the following:

- Augmentation of therapy with lithium, thyroid supplement or buspirone as adjuncts. or
- Combination of antidepressants (TCA & SSRI) / (Bupropion & SSRI)
- Electro Convulsive Therapy / repetitive TranscranialMagnetic Stimulation (rTMS)
- Alternative drug is planned based on rationality eg. Lamotrigine, Fluvoxamine, Mirtazapine+ Bupropion, Olanzapine[(27)].

DEPRESSION - VARIED PRESENTATION:

Major depressive disorder with psychosis has increased risk of suicidality than with depression alone. These patients are treated with combination of anti depressants and antipsychotics. Clomipramine and the selective serotonin reuptake blockers have demonstrated efficacy in the management of obsessive-compulsive symptoms in addition to their antidepressants efficacy[(76)].

Panic disorder complicates depression in 15%-30% of cases. Individual with both disorders manifest greater impairment than isolated major depression. Tricyclic antidepressants though effective, selective serotonin reuptake inhibitors can initially worsen anxiety and panic symptoms; hence introduced at a low dose and gradually titrated. Alprazolam or Clonazepam either singly or in combination with antidepressants can be used with benefit for anxiety, with or without panic, coupled to milder forms of depression[77].

Depression with cognitive dysfunction synonym : pseudo dementia, treatment of depression often reverses the symptoms and signs of cognitive dysfunction. Pseudo demented patients have reduced capacity to process information and exert less effort but report more incapacity than do demented patients. The demented group in more advanced stage, typically neither recognize nor complain of their cognitive failure. It is vital that patients with major depression with cognitive disturbance should not be misdiagnosed and thereby denied the antidepressant medication or ECT. Depression related cognitive dysfunction is a reversible condition that resolves with treatment of the underlying depression.

Depression in elderly is similar to young adults in the "core" features, but differ by a less dysphoric mood, somatic symptoms, poor outcome and increased mortality. Antidepressants are effective yet high rate of adverse effects limits its use in the elderly. SSRIs are acceptable. However,

notriptyline has a role in severe depression in the elderly. Electroconvulsive therapy (ECT) is effective in old age depression with rapid response in the severely ill.

Depression in children, with moderate severity can be treated with CBT, IPT and other non pharmacological modalities. SSRIs are first line drugs to treat depression in children and adolescents.

Depression with atypical features include severe anxiety, vegetative symptoms of reserved polarity like increased rather than decreased sleep, appetite, and weight, marked mood reactivity, sensitivity to emotional rejection, phobic symptoms, and a sense of severe fatigue that creates a sensation of "leaden paralysis" or extreme heaviness of the arms or legs. There is often overlap between patients with atypical depression and patient with anergic bipolar depression. Tricyclic antidepressants yield response rates of only 35%-50%. MAO inhibitors response rates of 55%-75% in patients with atypical depression. If it is determined that the patient does not wish to, cannot, or is unlikely to adhere to the dietary and drug precautions associated with MAO inhibitor treatment, the use of an alternative antidepressant is indicated. The results of several studies suggest that SSRIs, MAOIs, and possibly bupropion maybe more effective treatment for Atypical depression. SSRI & Bupropion are preferred drugs for treatment of Atypical Depression[78].

Substance abuse / dependence and Depression : depression and alcoholism often coexist which makes a detailed history of substance use mandatory in patients diagnosed with depression. Major depression with comorbid addiction is more likely to attempt suicide with decreased compliance to therapy. In such cases a program to secure abstinence is regarded as a principle priority in the treatment plan. It is advisable, to detoxify such patient before initiating antidepressant therapy.

Benzodiazepines and other sedative hypnotics carry the potential for abuse or dependence and should be used cautiously except as part of a detoxification regimen. Hepatic dysfunction and hepatic enzyme induction frequently complicate pharmacotherapy of patients with alcoholism and other substance abuse. these conditions require careful monitoring of blood levels.

Seasonal depression : Annual episode of depression occur in some individuals usually at the same time (winter onset) each year. It is characterised by atypical features like hypersomnia and overeating. Seasonal affective disorder is treated either with light therapy alone or in combination with antidepressants.

Management of depression associated with other systemic diseases:

- MAOIs interact with sympathomimetic bronchodilators used in Bronchial Asthma. Other antidepressant like SSRIs, TCAs, etc may be used in such group of patients

- Cardiac conditions like Ventricular Arryhythmia, Subclinical Sinus node dysfunction, Conduction defects, prolong QT intervals or history of recent Ml preclude use of tricyclics. The SSRIs, Bupropion, newer antidepressant and ECT appears to be safer for patients with preexisting cardiac disease.
- Patients with glaucoma may be treated with antidepressants lacking anticholinerigic activity like Bupropion, SSRIs and Trazodone.
- Antihypertensive agents and TCAs may interact to either intensify or counteract the effect of antihypertensive therapy. TCA may antagonize the therapeutic actions of many antihypertensives like guanethidine, clonidine and alpha methyldopa. Concurrent antihypertensive treatment especially with trazodone or MAOIs will induced symptomatic orthostatic hypotension. Dose dependent elevation in blood pressure with venlafaxine makes this agent less preferable in patients with hypertension[79].

AIM:

To compare the efficacy and safety of two anti depressants, escitalopram and sertraline in patients diagnosed with major depressive disorder in outpatient department of psychiatry in a tertiary care hospital in Chengalpattu.

OBJECTIVE:

- **Primary objective :** To compare the efficacy of escitalopram versus sertraline in treating major depressive disorder
- **Secondary objective :** To assess the safety of escitalopram and sertraline in treating major depressive disorder

METHODOLOGY:

Study Design Prospective, randomized, open labelled, comparative study.

Study Duration 3 months

Study Period March 2016 to March 2017 (12 months)

Study Centre Department of Psychiatry, Chengalpattu Medical College and Hospital, Chengalpattu.

Study population Newly diagnosed Drug naive patients with major depressive disorder attending the outpatient department of psychiatry

Sample size 120 patients

SELECTION CRITERIA:

Inclusion criteria:

- Drug naive patients diagnosed with major depression and started with antidepressants in out patient clinic of department of psychiatry.
- Age: 18- 60 years, both male and female patients
- Patients who are willing to give informed consent.

Exclusion criteria:

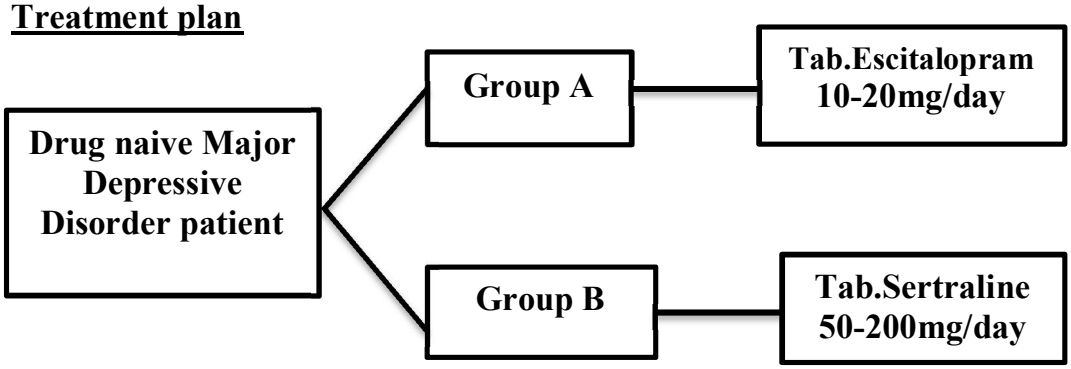
- Age: <18yrs & >60yrs
- Patients with Bipolar depression
- Patients who are not willing to give informed consent.
- Uncooperative patients

STUDY PROCEDURE

The study was conducted after Institutional Ethical Committee approval. Patients who fulfilled the selection criteria were recruited for the study. The study was conducted according to good clinical practice guidelines. Written informed consent was obtained from all patients, in regional language in the prescribed format and explained about the study purpose and procedures prior to their enrollment in study. In patients who were illiterate, the study procedure and their right to withdraw or contact the principal investigator in case of any side effects was explained and left thumb impression was obtained.

Randomisation was done by lots method . Among the 132 patients recruited and screened, 120 were enrolled in the study. Patients were assigned either to group A to receive study drug Tab. Escitalopram 10mg to 20 mg or to group B to receive Tab. Sertraline. 50 - 200mg .Dose of study drug and active control was titrated in the dose range mentioned above based on response after 4 weeks of continuous therapy.

Treatment plan



Demographic details and complete history were recorded during enrolment. Clinical examination, screening with Hamilton depression rating scale and lab investigations were done at baseline.

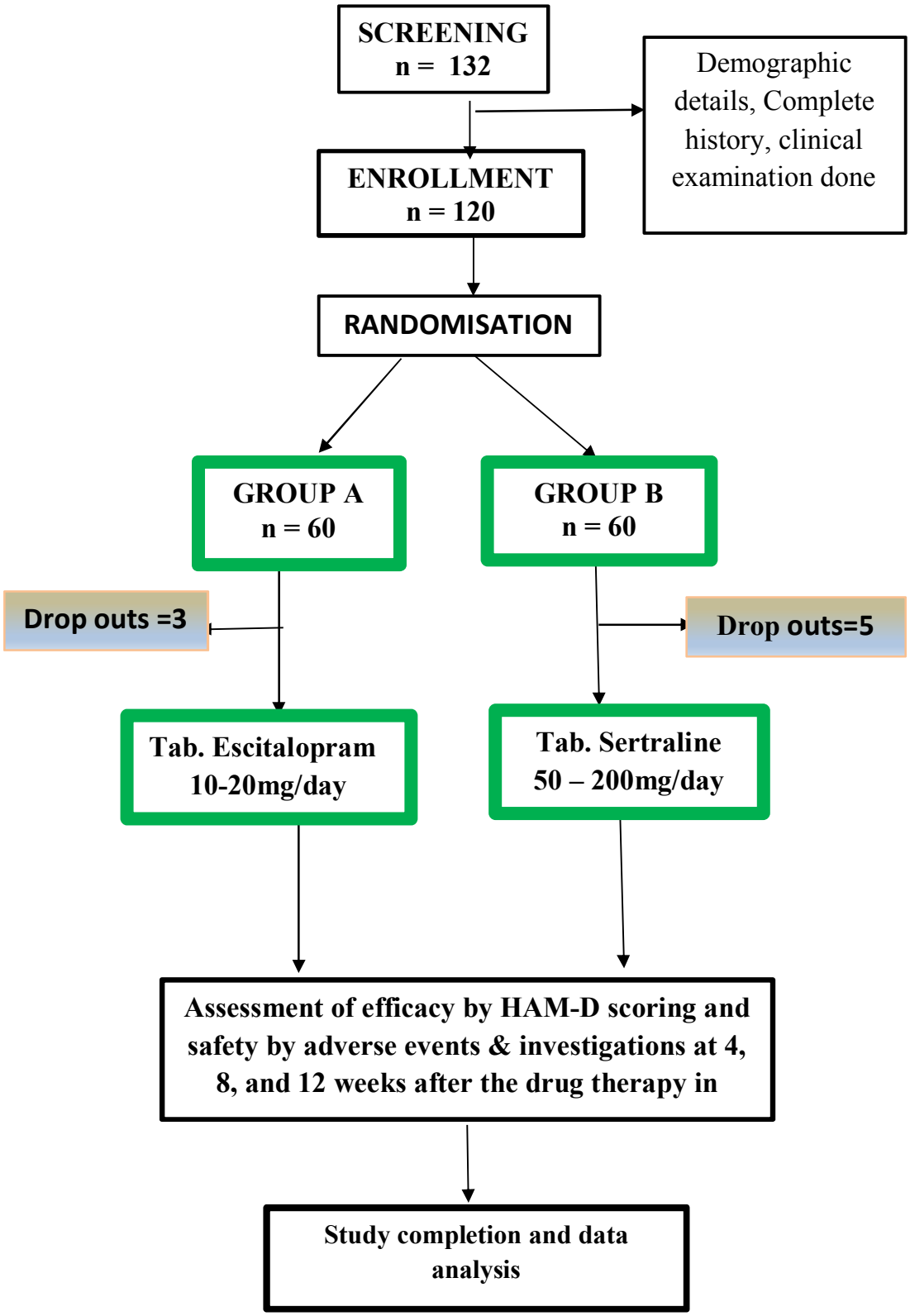
- Group A received Tab. Escitalopram 10mg OD or BD orally after food.
- Group B received Tab. Sertraline 50mg titrated from 1Tab to 4 Tab per day(50 -200mg) orally after food.

ASSESSMENT OF EFFICACY AND SAFETY

- **Efficacy** is measured by response in terms of improvement of symptoms assessed by scoring with Hamilton Depression Rating Scale at baseline, at 4, 8, and 12 weeks.

- **Safety** is ensured by recording Vitals of the patients and laboratory parameters at baseline, 4, 8, 12 weeks of study period .Safety is assessed by recording adverse drug reactions reported voluntarily or observed clinically or changes reported in lab investigation during follow up. Causality assessment of adverse drug reactions were done using WHO scale.
- Both the study and control groups were followed up for efficacy and safety.

Figure 5: Study Flow Chart



RESULTS

The data collected from the study were statistically analysed using SPSS software 21 version according to per protocol analysis. Hence the data of 112 patients who completed the 12 week study was included for analysis.

- Percentage distribution of age was analysed by chi-square test and mean age distribution among groups were analysed by student independent t'- test.
- Analysis of sex distribution between group A and B was done by chi-square test
- The change in mean HAM-D score from 0, 4, 8 and 12 weeks within the same group was analysed using Analysis of variance(ANOVA)
- Difference in HAM-D scoring between two groups A and B was assessed by student independent – t' test.
- The blood investigations were done at 0 (baseline), 4, 8 and 12 weeks. The difference in blood investigations within the groups before and after treatment was analysed using students paired t-test.
- The variations in the blood investigations between group A and group B were analysed by student independent t-test.
- Percentage of incidence of adverse effects among the study groups were analysed using chi-square test.

Probability of < 0.05 was considered to be statistically significant.

*$P \leq 0.05$ significant, **$P \leq 0.01$ highly significant, ***$P \leq .001$very highly significant

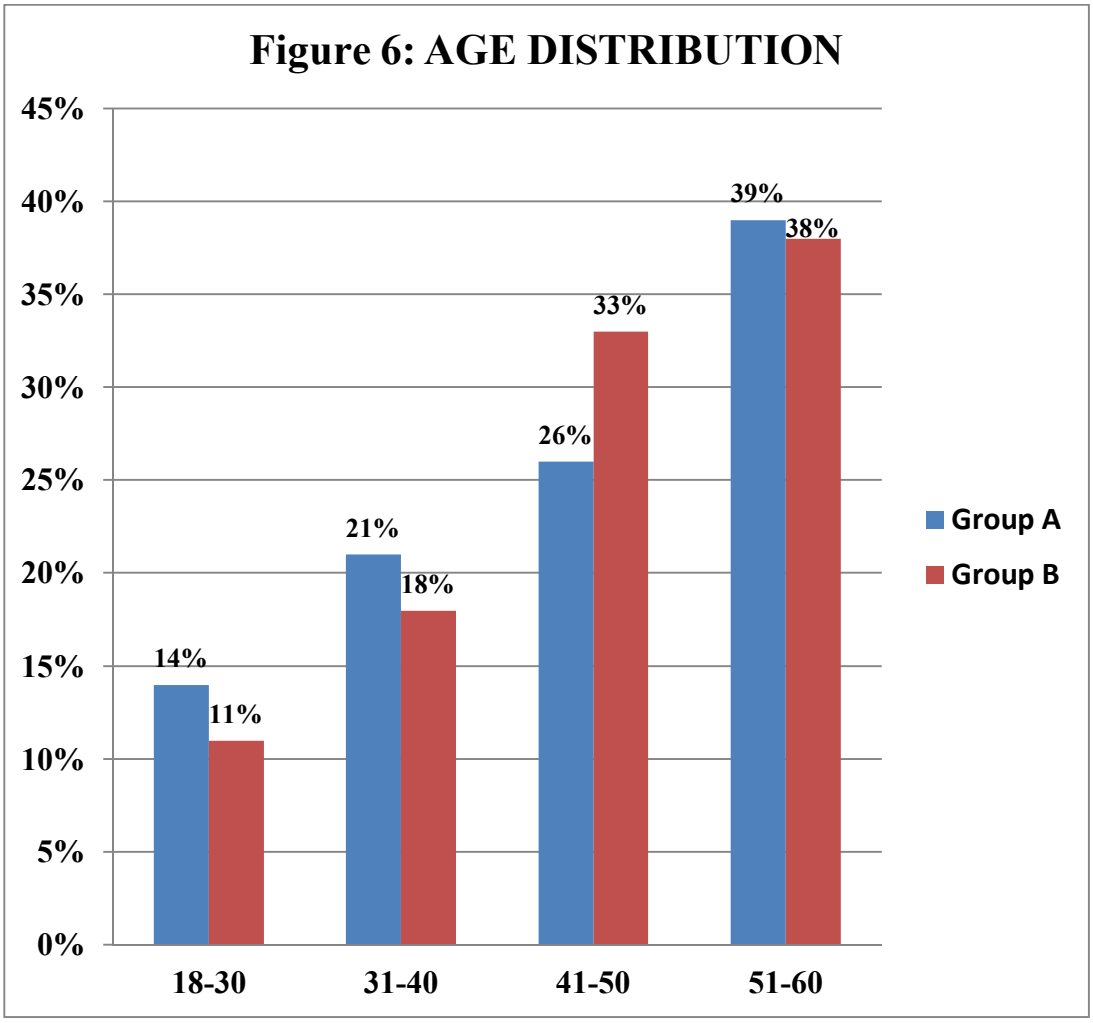
In this study, 120 patients diagnosed with depresssion, were screened, randomised and included to participate in the study. Of them 112 patients, i.e, 95% of group A and 91% of group B successfully completed the 12 weeks study.

TABLE 1: AGE DISTRIBUTION

AGE	GROUP A	%	GROUP B	%	CHI SQ	P VALUE
18 - 30	8	14%	6	11%	0.728	0.866
31-40	12	21%	10	18%		
41-50	15	26%	18	33%		
51-60	22	39%	21	38%		
Total	57	100%	55	100%		

Table 1 depicts the age distribution of 112 patients in the study groups.

- Highest number of patients were observed in the range of 51- 60 years
- Using Chi-square test, it was found that p=0.8 and hence there exists no significant statistical difference in the percentage age distribution between the groups.



- Figure 6 is the diagrammatic representation of the age distribution among the study groups

TABLE 2: MEAN AGE DISTRIBUTION

Groups	N	Mean	SD	Student independent t test	P Value
Group A	57	45.05	11.46	0.335	0.738
Group B	55	45.74	10.28		

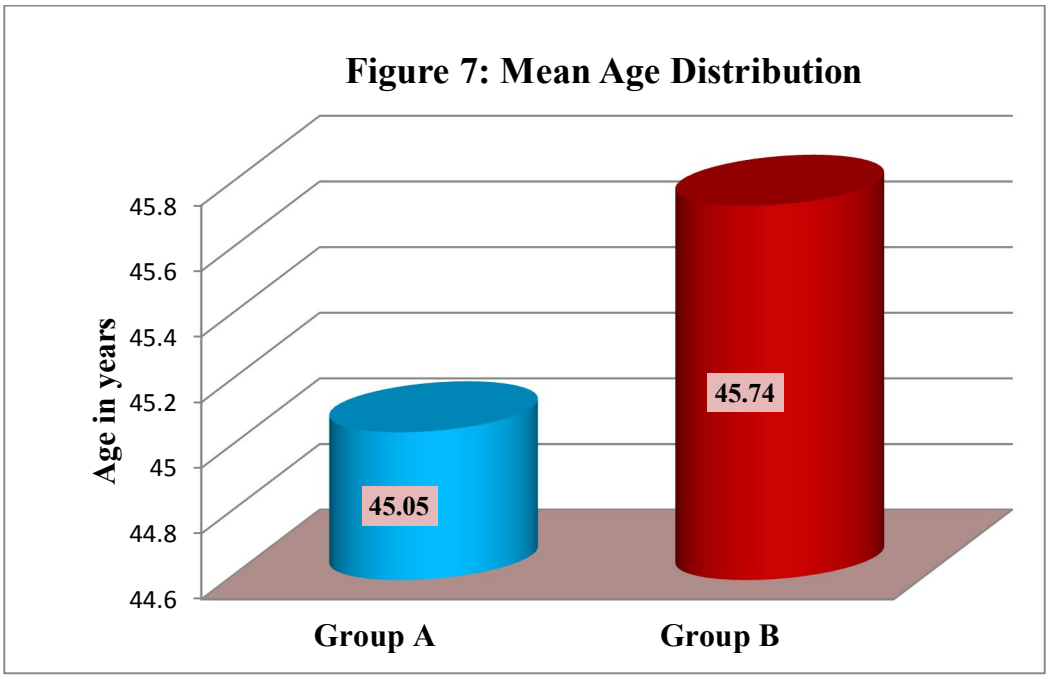
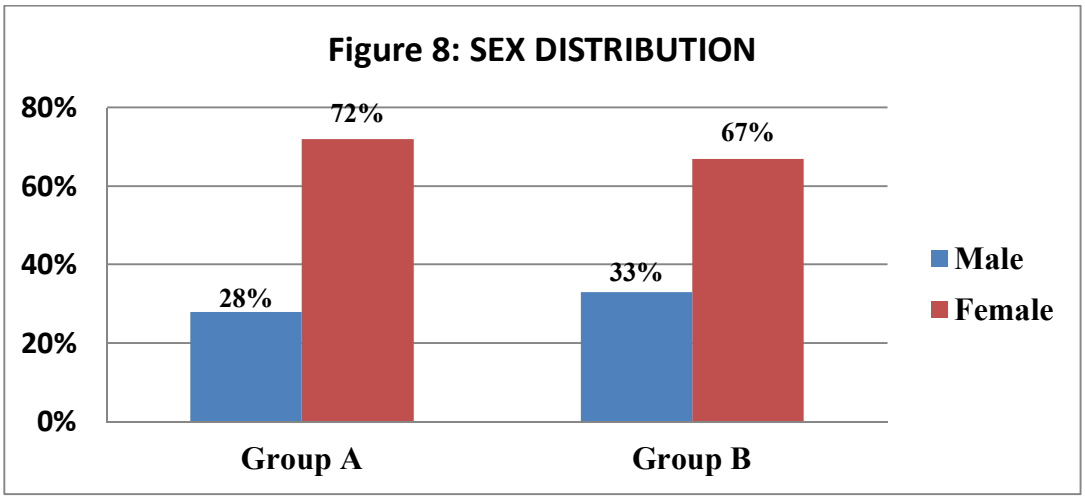


Table 2 and figure 7: shows mean age distribution to be even in both groups. There is no significant difference in age distribution among the study groups.

TABLE 3: SEX DISTRIBUTION

GENDER	GROUP A	%	GROUP B	%	CHI SQ	P VALUE
Male	16	28%	18	33%	0.287	0.592
Female	41	72%	37	67%		
Total	57	100%	55	100%		

- Table 3 shows sex distribution in the study groups.
- The prevalence of depression was twice more common in females than males Statistical analysis was done by Chi square test .There was no statistically significant difference between groups regarding sex distribution



- Figure 8 shows sex distribution among study groups, which shows predominance of females in both the groups.

TABLE 4: DISTRIBUTION OF SEVERITY OF DEPRESSION AT BASELINE IN GROUPS A & B

Baseline HAM-D Score	Escitalopram (Group A) n (%)	Sertraline (Group B) n(%)
Mild	14(25%)	16(29%)
Moderate	24(42%)	21(38%)
Severe	19 (33%)	18(33%)

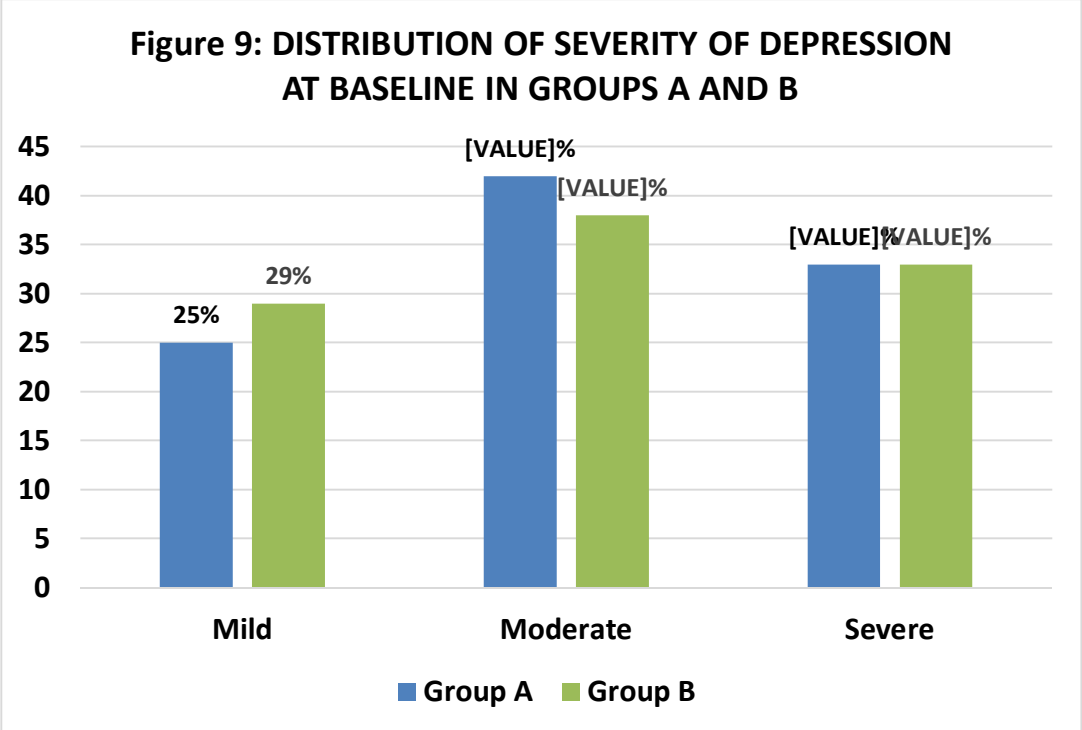


Table 4 & Figure 9 shows Baseline Severity assessment of depression - similarly distributed and comparable between groups A and B.

TABLE 5 : BASELINE & 4TH WEEKLY HAM-D SCORE FOR GROUP A

GROUP A					
HAM-D SCORE	NO OF PARTICIPANTS	MEAN	SD	T TEST	P VALUE
Baseline	57	20.77	6.72	658.35	< 0.001
Week 4	57	16.89	6.18		
Baseline	57	20.77	6.72	7.521	< 0.001
Week 8	57	12.35	5.13		
Baseline	57	20.77	6.72	11.35	< 0.001
Week 12	57	8.75	4.33		

- Table 5 shows Significant statistical difference between the baseline HAM-D score and at the end of week 4, 8, and 12 follow-up score in group A patients.
- Statistical analysis was done by student paired t-test between the baseline and 4week, 8 week, 12 week in HAM-D score.

TABLE 6 : BASELINE & 4TH WEEKLY HAM-D SCORE FOR GROUP B

GROUP B					
HAM-D SCORE	NO OF PARTICIPANTS	MEAN	SD	T TEST	P VALUE
Baseline	55	20.96	7.61	12.8	< 0.001
Week 4	55	15.45	6.04		
Baseline	55	20.96	7.61	14.7	< 0.001
Week 8	55	11.6	4.96		
Baseline	55	20.96	7.61	10.9	< 0.001
Week 12	55	8.65	4.18		

- Table 6 shows Significant statistical difference between the baseline HAM-D score and at the end of week 4, 8, and 12 follow-up score in group B patients.
- Statistical analysis was done by student paired t-test between the baseline and 4week, 8 week, 12 week in HAM-D score.

TABLE 7: 4TH WEEKLY HAM-D SCORE IN GROUP A

TEST OF SIGNIFICANCE BY ANOVA

GROUP A	STUDY PARTICIPANTS	MEAN	SD	F VALUE (ANOVA)	P VALUE
Baseline	57	20.77	6.72	48.86	< .001
4 week	57	16.89	6.18		
8 week	57	12.35	5.13		
12 week	57	8.75	4.33		
TOTAL	228	58.76	22.36		

Table 7 shows statistical analysis of mean HAM-D by ANOVA in group A over 3 months which shows significant difference every week within the group

TABLE 8: 4TH WEEKLY HAM-D SCORE IN GROUP B

TEST OF SIGNIFICANCE BY ANOVA

GROUP B	STUDY PARTICIPANTS	MEAN	SD	F VALUE (ANOVA)	P VALUE
Baseline	55	20.96	7.61	45.57	<0.0001
4 week	55	15.45	6.04		
8 week	55	11.6	4.96		
12 week	55	8.65	4.18		
TOTAL	220	56.66	22.79		

Table 8 shows statistical analysis of mean HAM-D by ANOVA in group B over 3 months shows significant difference every week within the group

TABLE 9 : MEAN HAM-D SCORE IN GROUPS A & B AT THE END OF 12 WEEKS

	GROUP A	GROUP B	INDEPENDENT T TEST	P VALUE
Sample size	57	55	0.124	0.901
Mean	8.75	8.65		
SD	4.33	4.18		
SE	0.574	0.564		
95% CI	7.601 to 9.899	7.52 to 9.79		
DF	56	54		

Table 9 shows mean HAM-D score at the end of 12th week in groups A and B, there is no significant difference by student independent t-test between the groups.

TABLE 10: BASELINE AND 4TH WEEKLY MEAN HAM-D SCORE IN GROUPS A AND B

HAM-D SCORE	GROUP A		GROUP B		T TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	20.77	6.72	20.96	7.61	0.140	0.888
Week 4	16.89	6.18	15.45	6.04	1.246	0.215
Week 8	12.35	5.13	11.6	4.96	0.786	0.433
Week 12	8.75	4.33	8.65	4.18	0.124	0.901

Table 10 depicts no statistically significant difference in mean HAM-D score reduction from baseline to 4th, 8th and 12th week as tested by independent t-test between group A & B.

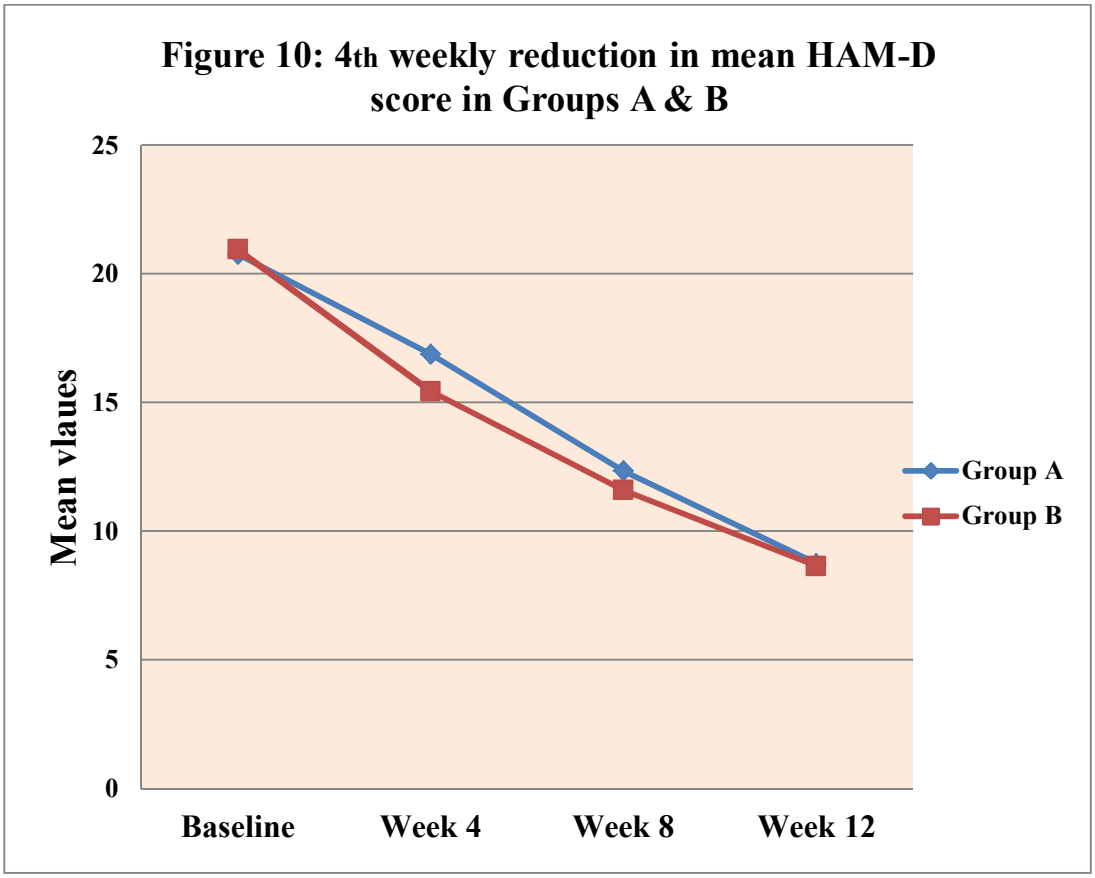


Figure 10 depicts the mean reduction in HAM-D score from baseline at 4 week intervals in group A & B.

TABLE 11: RESPONDERS BY HAM-D SCORE IN 4, 8 AND 12 WEEKS IN GROUPS A & B

Responders by HAM-D Score	Escitalopram (Group A) n (%)	Sertraline (Group B) n (%)
Week 4	13(23%)	11(20%)
Week 8	9(16%)	12(22%)
Week 12	24 (42%)	19(34%)
Total	46 (81%)	42 (76%)

Figure 11: Total responders in groups A and B

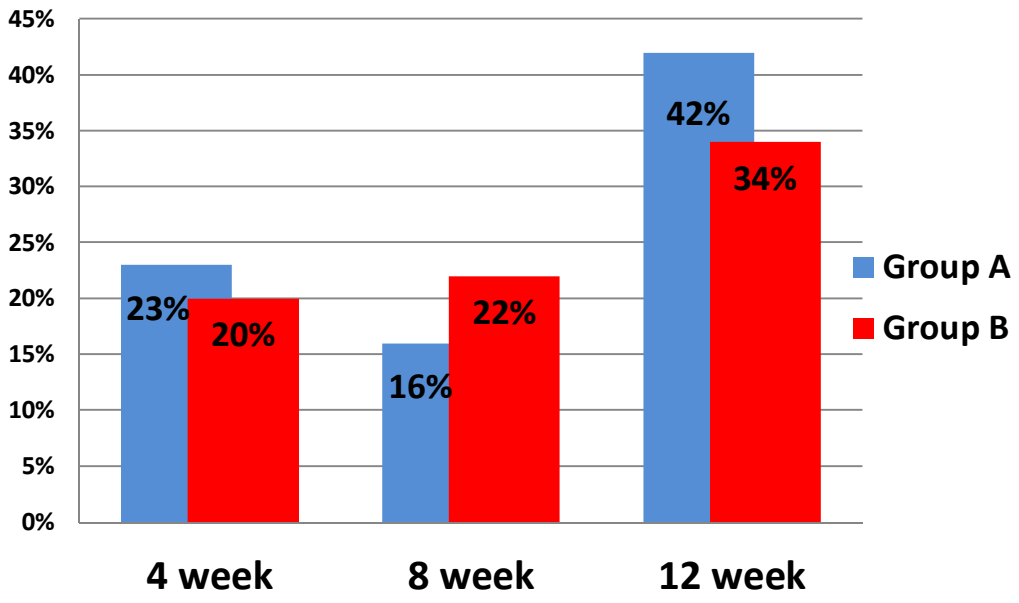


Table 11 and figure 11 shows percentage of responders by HAM-D score at the end of 4th, 8th and 12th week of therapy in both groups.

TABLE 12: REMITTERS BY HAM-D SCORE IN 4, 8 AND 12 WEEKS IN GROUPS A & B

Remitters by HAM-D Score	Escitalopram (Group A) n (%)	Sertraline (Group B) n (%)
Week 4	7(12%)	8(15%)
Week 8	9(16%)	8(15%)
Week 12	16 (28%)	13(24%)
Total	32 (56%)	29 (54%)

Table 12 shows percentage of remitters in both groups at 4 weeky intervals.

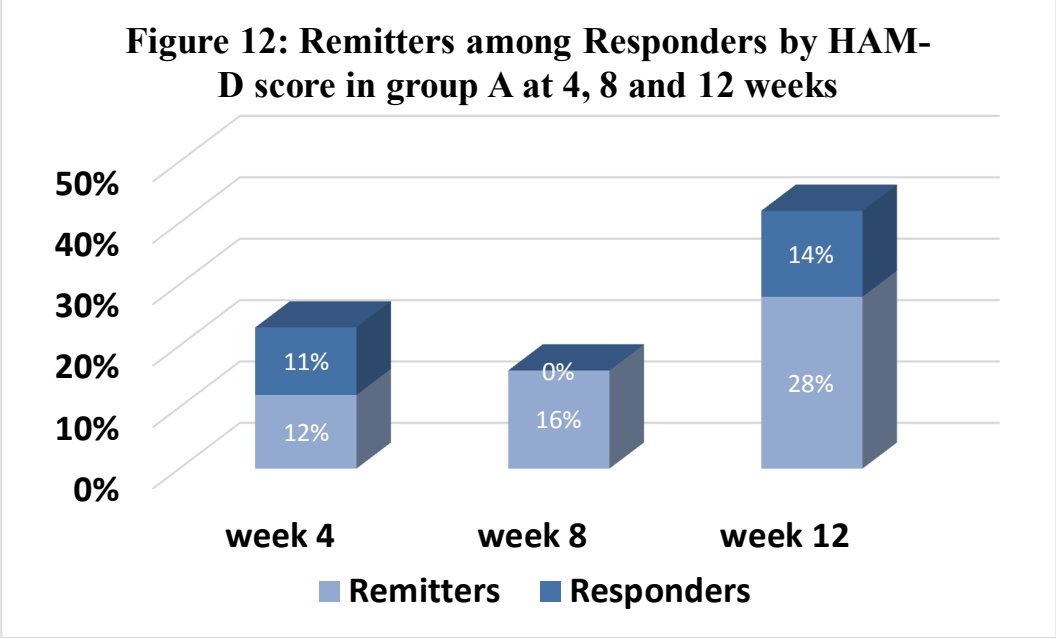


Figure 13: Remitters among Responders by HAM-D score in group B at 4, 8 and 12 weeks

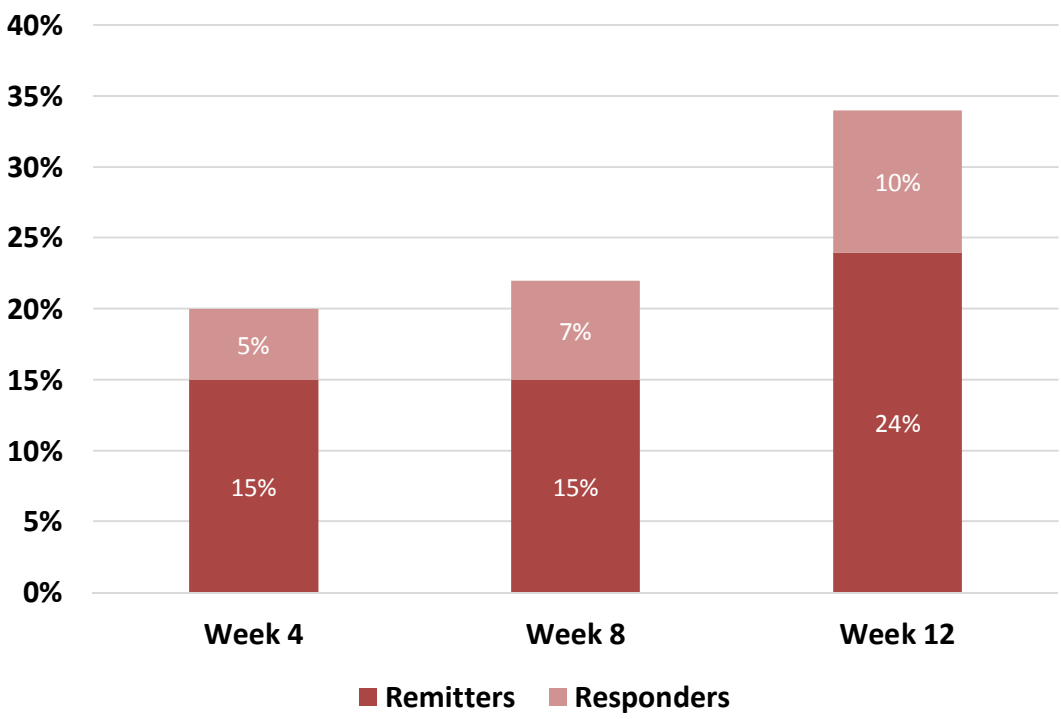


Figure 12 and 13 shows the percentage of remitters among responders in group A &B at the end of 4th, 8th and 12th week respectively.

TABLE 13a: INCIDENCE OF ADVERSE EVENTS IN GROUP A & B

ADVERSE EVENTS	ESCITALOPRAM (N=57)	%	SERTRALINE (N= 55)	%
HEADACHE	2	3.5	5	9
NAUSEA	2	3.5	4	7.3
DIARRHOEA	0	0	2	3.6
LOSS OF APPETITE	0	0	1	1.8
INSOMNIA	1	1.8	3	5.5
SEXUAL DYSFUNCTION	1	1.8	2	3.6
TOTAL	6	10.6	17	30.8

Table 13a shows the incidence of adverse events reported in two groups.

TABLE 13 b:ADVERSE DRUG REACTIONS IN GROUPS A AND B

Groups	Adverse events		Total	Chi-square value	P value
	Present	Absent			
Group A	6	51	57	7.126	0.007
Group B	17	38	55		

Table 13b shows statistically significant difference in the reported adverse events between group A & B as assessed by chi-sq test.

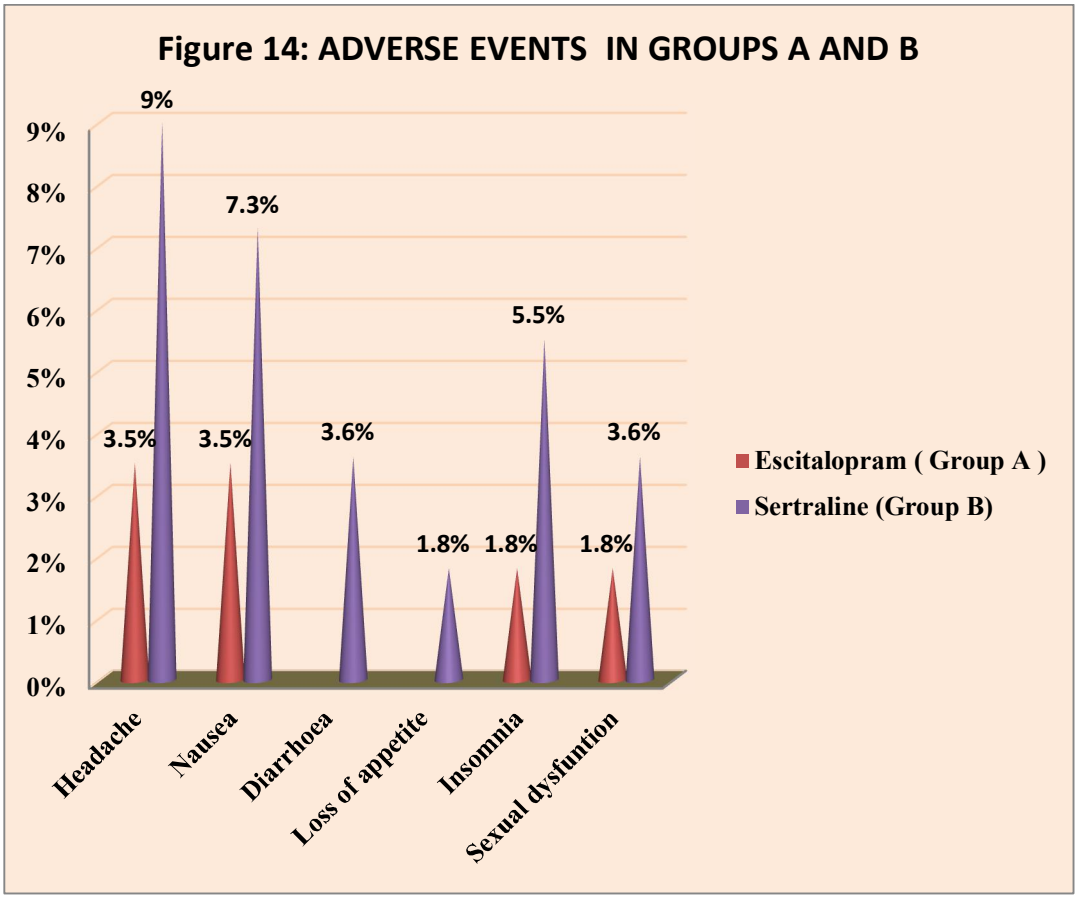


Figure 14 shows occurrence of ADR in test and control groups. They were mild and no serious adverse effects were reported. Among adverse events reported, headache was the most common followed by nausea, insomnia, diarrhoea and sexual dysfunction in sertraline group.

Among escitalopram patients, reported adverse effects of headache and nausea had equal incidence followed by insomnia and sexual dysfunction

TABLE 14a: MEAN SCORE OF DEPRESSIVE MOOD AT 0, 4, 8 AND 12 WEEKS BETWEEN GROUPS A AND B

Depressed mood score	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	n= 57		n=55			
	MEAN	SD	MEAN	SD		
Baseline	2.824	0.840	2.672	0.935	0.905	0.367
Week 4	1.684	0.861	1.581	0.966	0.596	0.552
week 8	1.052	0.711	0.890	0.845	1.099	0.274
week 12	0.614	0.585	0.618	0.646	0.035	0.972

TABLE 14b: MEAN SCORE OF DEPRESSIVE MOOD AT 0, 4, 8 AND 12 WEEKS WITHIN GROUPS A AND B

Depressed mood score	GROUP A						GROUP B					
	0 week	4 week	0 week	8 week	0 week	12 week	0 week	4 week	0 week	8 week	0 Week	12 week
Mean	2.824	1.684	2.824	1.052	2.824	0.614	2.672	1.581	2.672	0.890	2.672	0.618
SD	0.840	0.861	0.840	0.711	0.840	0.585	0.935	0.966	0.935	0.845	0.935	0.646
Student Paired t-test	t = 16.70 p = 0.0001		t= 23.57 p= 0.0001		t= 28.30 p=0.0001		t=11.54 p= 0.0001		t= 17.91 p= 0.0001		t= 20.85 p=0.0001	

Table 14 a & b shows difference in individual mean score of depressed mood before and after therapy in both groups. The difference was significant within groups by paired t-test and not significant between groups as tested by Independent t-test.

TABLE 15a: BASELINE AND 4TH WEEKLY MEAN SUICIDE SCORE BETWEEN GROUPS A AND B

suicide score	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	n= 57		n=55			
	MEAN	SD	MEAN	SD		
Baseline	1.368	1.237	1.527	1.059	0.729	0.467
Week 4	0.684	0.881	0.763	0.830	0.488	0.626
week 8	0.403	0.671	0.472	0.628	0.561	0.575
week 12	0.210	0.407	0.254	0.435	0.553	0.581

TABLE 15b : BASELINE AND 4TH WEEKLY MEAN SUICIDE SCORE WITHIN GROUPS A AND B

suicide score	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 Week	12th week
Mean	1.368	0.684	1.368	0.403	1.368	0.210	1.527	0.763	1.527	0.472	1.527	0.254
SD	1.237	0.881	1.237	0.671	1.237	0.407	1.059	0.830	1.059	0.628	1.059	0.435
Student Paired t-test	t = 8.18 p = 0.0001		t= 8.85 p= 0.0001		t=8.47 p=0.0001		t=9.82 p=0.0001		t=10.70 p=0.0001		t= 10.844 p=0.0001	

Table 14 a & b shows reduction in individual mean score of suicide before and after therapy in both groups. The difference was significant within groups by paired t-test and not significant between groups as tested by Independent t-test.

Figure 15: Mean score of Depressive mood in groups A and B at 0, 4, 8 and 12 weeks

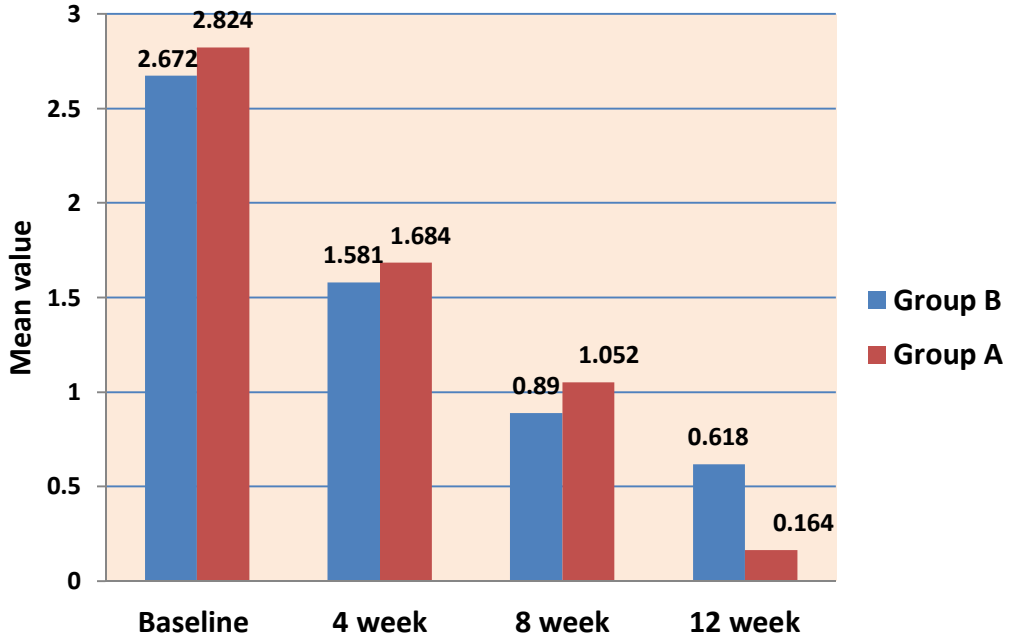


Figure 16: Mean suicide score in groups A and B at 0, 4, 8 and 12 weeks

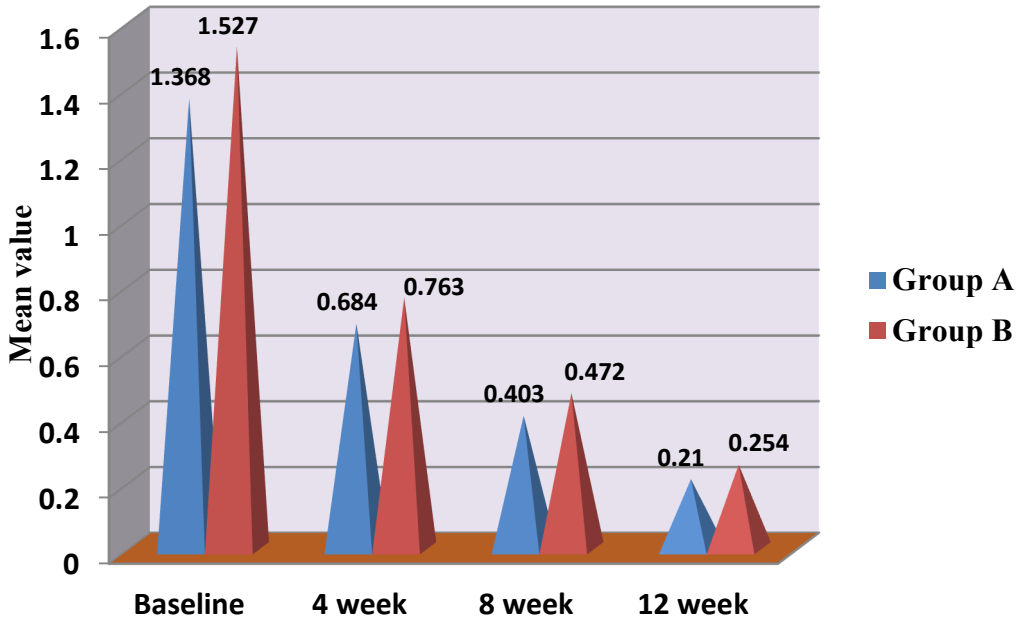


Figure15 & 16 show individual mean (depressed mood & suicide)score reduction in both groups after drug therapy

TABLE 16a: BASELINE AND 4TH WEEKLY MEAN ANXIETY-(PSYCHIC)SCORE BETWEEN GROUPS A AND B

Anxiety (Psychic) score	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	n= 57		n=55			
	MEAN	SD	MEAN	SD		
Baseline	2.561	0.858	2.309	1.126	1.335	0.184
Week 4	1.649	0.826	1.472	0.849	1.118	0.265
week 8	1.087	0.755	0.945	0.724	1.015	0.312
week 12	0.701	0.724	0.545	0.627	1.217	0.226

TABLE 16b: BASELINE AND 4TH WEEKLY MEAN ANXIETY-(PSYCHIC) SCORE WITHIN GROUPS A AND B

Anxiety (Psychic) score	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	2.561	1.649	2.561	1.087	2.561	0.701	2.309	1.472	2.309	0.945	2.309	0.545
SD	0.858	0.826	0.858	0.755	0.858	0.724	1.126	0.849	1.126	0.724	1.126	0.627
Student Paired t-test	t = 13.50 p = 0.0001		t= 18.52 p= 0.0001		t= 18.90 p=0.0001		t=12.39 p=0.0001		t=13.40 p=0.0001		t= 14.18 p=0.0001	

Table 14 a & b shows reduction in individual mean score of anxiety before and after therapy in both groups. The difference was significant within groups by paired t-test and not significant between groups as tested by Independent t-test.

Figure 17: Mean Anxiety (psychic) score in groups A & B at 0, 4, 8 and 12 weeks

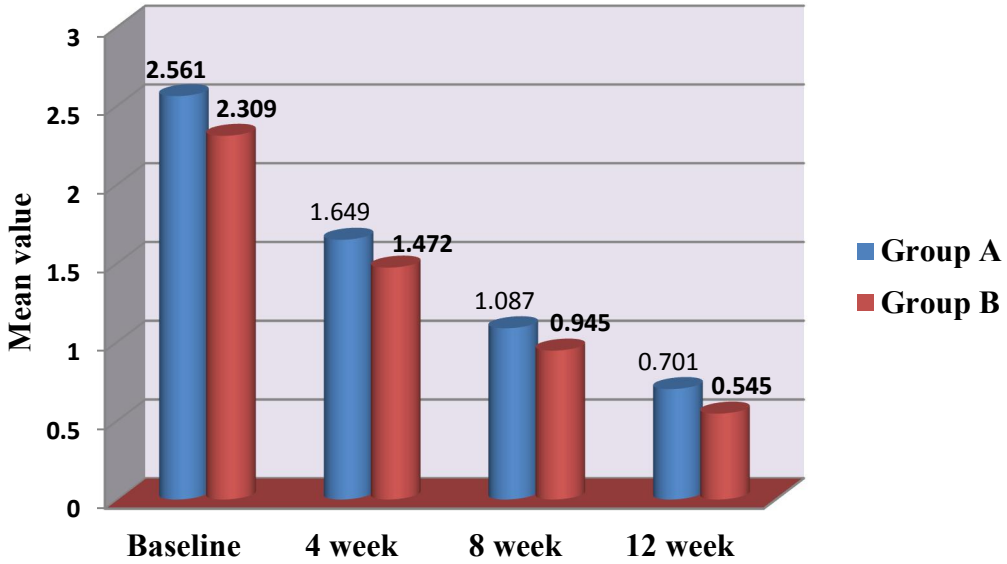


Figure 18: Mean Somatic (general) score in groups A & B at 0, 4, 8 and 12 weeks

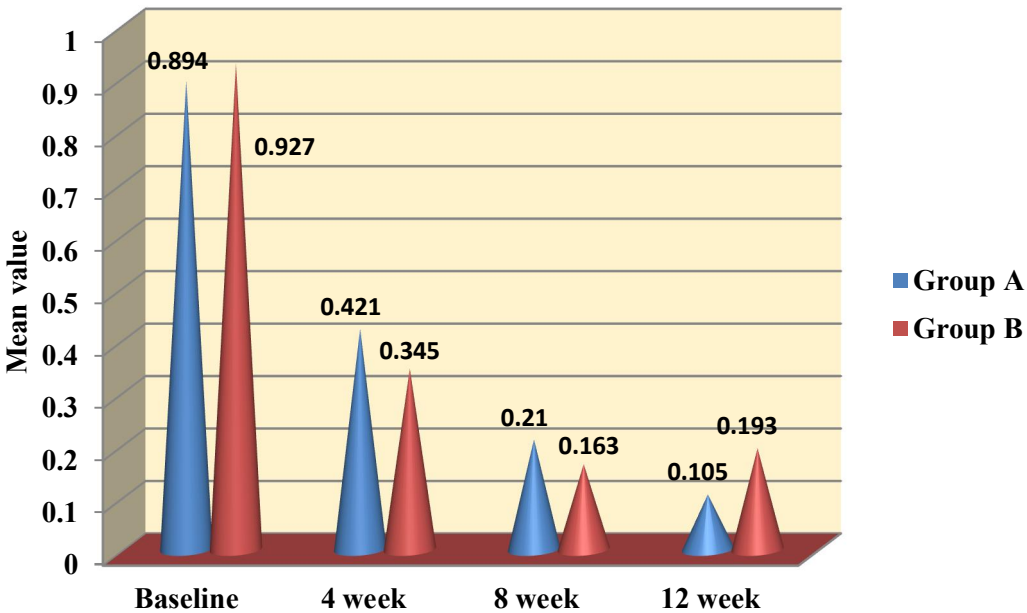


Figure17 & 18 show individual mean (anxiety & somatic symptom) score reduction in both groups after drug therapy

TABLE 17A: SOMATIC (GENERAL) SCORE

Somatic (general) score	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	n= 57		n=55			
	MEAN	SD	MEAN	SD		
Baseline	0.894	0.741	0.927	0.805	0.225	0.821
Week 4	0.421	0.493	0.345	0.475	0.830	0.408
week 8	0.210	0.407	0.163	0.369	0.639	0.523
week 12	0.105	0.306	0.193	0.395	1.320	0.189

TABLE 17B: SOMATIC (GENERAL) SCORE

Somatic (general) Score	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12 week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	0.894	0.421	0.894	0.210	0.894	0.105	0.927	0.345	0.927	0.163	0.927	0.193
SD	0.741	0.493	0.741	0.407	0.741	0.306	0.805	0.475	0.805	0.369	0.805	0.395
Student Paired t-test	t = 5.95 p = 0.0001		t= 7.83 p= 0.0001		t= 7.95 p=0.0001		t= 7.60 p=0.0001		t= 8.17 p=0.0001		t= 6.80 p=0.0001	

Table 17 a & b shows reduction in individual mean score of somatic symptom before and after therapy in both groups. The difference was significant within groups by paired t-test and not significant between groups as tested by Independent t-test.

TABLE 18a: HAEMOGLOBIN

Hemoglobin	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	10.53	1.463	10.59	1.516	0.213	0.83
Week 4	10.39	1.427	10.52	1.341	0.496	0.620
week 8	10.65	1.524	10.35	1.427	1.074	0.285
week 12	10.56	1.454	10.68	1.047	0.499	0.618

Table 18a depicts the hemoglobin level at baseline, end of week 4, 8 and 12 in groups A and B. There is **no statistically significant** difference in the levels of hemoglobin between the groups as analysed by student independent t-test

TABLE 18b:HAEMOGLOBIN

HB	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	10.53	10.39	10.53	10.65	10.53	10.56	10.59	10.51	10.59	10.35	10.59	10.67
SD	1.463	1.427	1.463	1.524	1.463	1.453	1.516	1.340	1.516	1.426	1.516	1.04
Student Paired t-test	t = 0.702 p = 0.485		t= 0.529 p= 0.598		t= 0.177 p=0.859		t=0.272 p=0.782		t=0.416 p=0.819		t= 0.316 p=0.753	

Table 18b depicts the difference in hemoglobin levels measured in 4 weeks interval, before and after therapy with study or control drug. Using student paired t-test, there was **no significant difference** between baseline, 4, 8 and 12 week hemoglobin values in both the groups.

TABLE 19a: TOTAL LEUCOCYTE COUNT

Total leucocyte count	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	6912	906.09	6786.72	902.32	0.733	0.46
week 4	6809	965.17	6682.78	664.92	0.803	0.42
week 8	6739.42	892.50	6777.09	881.85	0.224	0.82
week 12	6625.43	926.10	6613.76	775.15	0.072	0.94

Table 19 a depicts the total leucocyte count at baseline, end of week 4, 8 and 12 in groups A and B. There is **no statistically significant** difference in the total leucocyte count between the groups as analysed by student independent t-test

TABLE 19b:TOTAL LEUCOCYTE COUNT

TLC	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th Week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	6912	6809	6912	6739.4	6912	6625	6786.7	6682.7	6786.7	6777	6786.7	6613.7
SD	906.0	965.1	906.0	892.5	906.0	926.1	902.3	664.9	902.3	881.5	902.3	775.5
Student Paired t-test	t= 1.245 p = 0.218		t= 1.072 p= 0.288		t=1.901 p=0.062		t=1.728 p=0.089		t=0.053 p=0.957		t= 1.005 p=0.319	

Table 19b depicts the difference in the total leucocyte count measured before and 4th weekly after therapy with study or control drug. Using student paired t-test, there was **no significant difference** between baseline, 4, 8 and 12 week total leucocyte count in both the groups

TABLE 20a: ERYTHROCYTE SEDIMENTATION RATE

ESR	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	11	1.69	10.79	1.44	0.706	0.481
week 4	11	1.38	10.55	1.51	1.647	0.102
week 8	10.68	1.51	10.48	1.63	0.707	0.480
week 12	10.58	1.55	10.46	1.45	0.422	0.673

Table 20a depicts the erythrocyte sedimentation rate at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the erythrocyte sedimentation rate between the groups as analysed by student independent t-test.

TABLE 20b: ERYTHROCYTE SEDIMENTATION RATE

ESR	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 Week	12th week
Mean	1 1	11	11	10.68	11	10.58	10.79	10.55	10.79	10.48	10.79	10.46
SD	1.69	1.38	1.69	1.51	1.69	1.55	1.44	1.51	1.44	1.63	1.44	1.45
Student Paired t-test	t = 1.384 p = 0.717		t=0.251 p= 0.802		t=0.610 p=0.544		t=0.803 p=0.425		t=1.031 p=0.307		t=1.148 p=0.256	

Table 20b depicts the difference in erythrocyte sedimentation rate before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week total leucocyte count in both the groups

TABLE 21a: PLATELET COUNT

PLATELET COUNT	GROUP A		GROUP B		STUDENT INDEPENDENT T-TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	2.51	0.28	2.417	0.39	1.563	0.12
Week 4	2.48	0.31	2.412	0.37	1.087	0.28
Week 8	2.5	0.28	2.514	0.39	0.216	0.82
Week 12	2.57	0.4	2.53	0.43	0.509	0.61

Table 21a depicts the platelet count at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the platelet count between the groups as analysed by student independent t-test

TABLE 21b:PLATELET COUNT

Platelet Count	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	2.513	2.486	2.513	2.505	2.513	2.578	2.417	2.412	2.417	2.514	2.417	2.532
SD	0.286	0.31	0.286	0.288	0.286	0.4	0.39	0.373	0.39	0.39	0.39	0.432
Student paired t - Test	t=0.503 p=0.616		t=0.153 p=0.878		t=1.071 p=0.313		t=0.105 p=0.916		t=1.492 p=0.141		t=1.906 p=0.061	

Table 21b depicts the difference in platelet count before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week platelet count in both the groups

TABLE 22a: BLOOD SUGAR

Blood Sugar	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	124.49	26.73	120.34	13.83	1.026	0.3
week 4	123.01	21.42	121.74	11.9	0.385	0.7
week 8	123.38	20.34	121.7	13.46	0.514	0.6
week 12	123.8	17.84	120.6	14.04	1.052	0.3

Table 22a depicts the blood sugar at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the blood sugar values between the groups as analysed by student independent t-test

TABLE 22b: BLOOD SUGAR

Blood Sugar	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	124.4	123	124.5	123.4	124.4	123.8	120.3	121.7	120.3	121.7	120.3	120.6
SD	26.73	21.42	26.73	20.34	26.73	17.84	13.83	11.9	13.83	13.46	13.83	14.04
Student Paired t-test	t = 0.743 p =0.460		t= 0.562 p= 0.576		t=0.314 p=0.754		t=1.020 p= 0.312		t=1.069 p=0.289		t= 0.173 p=0.862	

Table 22b depicts the difference in blood sugar before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week blood sugar values in both the groups

TABLE 23a: SERUM CREATININE

Serum Creatinine	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	0.735	0.046	0.731	0.048	0.45	0.65
Week 4	0.731	0.052	0.738	0.043	0.774	0.44
Week 8	0.723	0.06	0.728	0.054	0.463	0.64
Week 12	0.719	0.046	0.733	0.053	1.494	0.13

Table 23a depicts the serum creatinine at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the serum creatinine values between the groups as analysed by student independent t-test

TABLE 23b: SERUM CREATININE

Serum Creatinine	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	0.735	0.731	0.735	0.723	0.735	0.719	0.731	0.738	0.731	0.728	0.731	0.733
SD	0.046	0.052	0.046	0.06	0.046	0.046	0.048	0.043	0.048	0.054	0.048	0.053
Student Paired t-test	t = 0.493 p = 0.623		t= 1.151 p= 0.254		t=1.920 p=0.059		t=0.700 p=0.486		t= 0.389 p=0.698		t= 0.175 p=0.861	

Table23b depicts the difference in serum creatinine before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week serum creatinine values in both the groups

TABLE 24a: BLOOD UREA

BLOOD UREA	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	22.00	1.61	21.81	1.47	0.651	0.516
Week 4	22.00	1.46	21.92	1.69	0.268	0.788
Week 8	21.89	1.60	21.87	1.60	0.066	0.947
Week 12	21.94	1.61	21.96	1.65	0.308	0.948

Table 24a depicts the blood urea at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the blood urea values between the groups as analysed by student independent t-test

TABLE 24b: BLOOD UREA

Blood urea	GROUP A						GROUP B					
	0 week	4 week	0 week	8 week	0 week	12 week	0 week	4 week	0 week	8 week	0 week	12 week
Mean	22.0	22.0	22.0	21.89	22.0	21.94	21.81	21.92	21.81	21.87	21.81	21.96
SD	1.61	1.46	1.61	1.60	1.61	1.61	1.47	1.69	1.47	1.60	1.47	1.65
Student Paired t-test	t = 0.442 p =0.660		t= 0.184 p= 0.854		t=0.322 p=0.748		t=1.360 p= 0.719		t=0.221 p=0.825		t= 0.498 p=0.620	

Table 24b depicts the difference in blood urea before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week blood urea values in both the groups

TABLE 25a : SGOT

SGOT	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	14	2.527	14.6	2.122	1.358	0.177
week 4	14.29	2.286	14.96	2.496	1.482	0.141
Week 8	15.12	2.822	15.38	2.204	0.542	0.588
Week 12	15	1.932	14.4	2.137	1.557	0.217

Table 25a depicts the SGOT values at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the SGOT values between the groups as analysed by student independent t-test

TABLE 25b : SGOT

SGOT	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	14	14.29	14	15.12	14	15	14.6	14.96	14.6	15.3	14.6	14.4
SD	2.52	2.28	2.52	2.82	2.52	1.93	2.12	2.49	2.12	2.20	2.12	2.13
Student Paired t-test	t = 0.289 p = 0.773		t= 1.304 p= 0.197		t= 0.895 p= 0.374		t= 1.097 p= 0.277		t= 0.044 p= 0.964		t= 0.452 p= 0.652	

Table 25b depicts the difference in the SGOT values before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week the SGOT values in both the groups

TABLE 26a: SGPT

SGPT	GROUP A		GROUP B		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	16.87	3.83	15.83	2.81	1.633	0.105
week 4	16.26	2.85	15.85	3.05	0.735	0.463
Week 8	17.17	2.51	16.27	2.69	1.831	0.069
Week 12	17.61	2.68	16.89	2.85	1.377	0.171

Table 26a depicts the SGPT values at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the SGPT values between the groups as analysed by student independent t-test

TABLE 26b: SGPT

SGPT	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	16.87	16.26	16.87	17.17	16.87	17.61	15.83	15.85	15.83	16.27	15.83	16.89
SD	3.83	2.85	3.83	2.51	3.83	2.68	2.81	3.05	2.81	2.69	2.81	2.85
Student Paired t-test	t =1.007 p=0.318		t=0.558 p=0.579		t =1.260 p=0.212		t= 0.003 p=0.979		t=0.723 p=0.472		t=1.802 p=0.077	

Table 26b depicts the difference in the SGPT values before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week the SGPT values in both the groups

TABLE 27a : SERUM ELECTROLYTES (SODIUM)

SERUM ELECTROLYTES (SODIUM)	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	138.75	3.56	138.61	2.99	0.218	0.82
Week 4	139.19	3.35	139.27	3.10	0.129	0.89
week 8	137.66	2.70	138.49	3.11	1.496	0.13
week 12	139.33	3.36	138.58	2.87	1.268	0.20

Table 27a depicts the serum electrolyte(Na) values at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the serum electrolyte(Na) values between the groups as analysed by student independent t-test

TABLE 27b: SERUM ELECTROLYTES (SODIUM)

Serum Electrolyte (sodium)	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th week	0 week	4th week	0 week	8th week	0 week	12th week
Mean	138.7	139.1	138.7	137.6	138.7	139.3	138.6	139.2	138.6	138.4	138.6	138.5
SD	3.56	3.35	3.56	2.70	3.56	3.36	2.99	3.10	2.99	3.11	2.99	2.87
Student Paired t-test	t=0.654 p = 0.515		t= 1.697 p= 0.095		t=0.914 p=0.364		t=1.116 p=0.269		t=0.214 p=0.831		t= 0.062 p=0.950	

Table 27b depicts the difference in the serum electrolyte(Na) values before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week the serum electrolyte(Na) values in both the groups

TABLE 28a: SERUM ELECTROLYTES (POTASSIUM)

SERUM ELECTROLYTES (POTASSIUM)	GROUP A		GROUPB		STUDENT INDEPENDENT t- TEST	P VALUE
	MEAN	SD	MEAN	SD		
Baseline	4.038	0.399	4.081	0.357	0.60	0.54
Week 4	4.084	0.382	3.987	0.316	1.36	0.17
Week 8	4.094	0.409	3.974	0.370	1.10	1.62
Week 12	4.115	0.387	4.116	0.369	0.01	0.98

Table 28a depicts the serum electrolyte(K) values at baseline, end of week 4, 8 and 12 in groups A and B. There is no statistically significant difference in the serum electrolyte(K) values between the groups as analysed by student independent t-test

TABLE 28b: SERUM ELECTROLYTES (POTASSIUM)

Serum Electrolyte (Potassium)	GROUP A						GROUP B					
	0 week	4th week	0 week	8th week	0 week	12th wk	0 wk	4th week	0 week	8th week	0 week	12th week
Mean	4.038	4.084	4.038	4.094	4.038	4.115	4.081	3.987	4.081	3.974	4.081	4.116
SD	0.39	0.38	0.39	0.40	0.39	0.38	0.35	0.31	0.35	0.37	0.35	0.36
Student Paired t-test	t = 0.693 p = 0.490		t= 0.924 p= 0.359		t= 1.123 P= 0.265		t-1.604 p-0.114		t=1.560 p=0.124		t= 0.507 p=0.613	

Table 28b depicts the difference in the serum electrolyte(K) values before and 4th weekly after drug therapy in both the groups. Using student paired t-test, there was no significant difference between baseline, 4, 8 and 12 week the serum electrolyte(K) values in both the groups

DISCUSSION

Of the 120 patients enrolled in the study, 112 patients i.e, 93% of participants completed the study. Attrition due to drop out was 5 % in test group and 8% in control group. Study groups A and B were comparable and did not show statistically significant difference in Baseline Demographic characteristics.

Study participants were divided as per standard recommendation into four age class intervals for analysis of prevalance of depression. Data tabulated showed increase in prevalance of depression with increase in age. Highest prevalence was observed in 51-60 years with 39% and 38% in group A and B respectively. In the age class intervals spaning from 31 to 50 years showed a simlar percent of prevalance in depression ranging from 21 to 33 % . The 18 -30 yrs group showed the least. Mean $\pm$ SD baseline age for group A is 45.05 $\pm$11.46 years and in group B is 45.75 $\pm$10.28 years. The trend in the prevalence of depression which increases with age was identical to the observations by Wild et al[80]. Females represented 72% in group A and 67% in group B among the overall study population, which shows depression to be twice more common in females than males in both treatment groups. The female preponderance was similar to the prevalence of depression studied by Maier et al[81].There was no significant difference in gender distribution between the study groups.

Escitalopram was given in dose of 10-20mg/day orally to patients in test group A. Sertraline was given in a dose of 50-200mg/day orally to patients in control group B. Dose of escitalopram and sertraline was optimised by increasing after 4 weeks treatment in the respective groups. Hamilton Depression rating scale was used to assess the severity of depression at baseline and treatment response at monthly intervals. Hamilton depression rating score of 0-7 indicates no depression, score between 8-16 denotes mild depression, 17-23 denotes moderate depression and a score more than or equal to 24 indicates severe depression[35]. On the basis of HAM-D scoring at baseline, distribution of severity of depression observed in test group was mild in 25% , moderate in 42% and severe in 33%. Similar scoring based severity assessment in control group turned to be mild in 29% , moderate in 38% and severe in 33%. Distribution of patients with different grades of severity in both the study groups were comparable. Assessment of response by HAM-D Scoring at 4 and 8 weeks necessitated dose hike in 30% and 38% of patients in group A and B respectively. The mean baseline HAM-D score was 20.77 in group A and 20.96 in group B. There was no significant difference in mean baseline HAM–D score between the two treatment groups.

- **Responders are** patients who showed $\geq$50% reduction of HAM-D score from baseline value.

- **Remitters** are those with $\leq$ 7 in HAM-D scoring after initiation of drug therapy[35].
- **Non responders** are patients who did not show 50% reduction in HAM-D score from baseline till completion of 12 weeks of therapy.

Rate of response within and between the treatment groups were assessed in terms of improvement in mean scores at subsequent visits at 4, 8, and 12 weeks.

At the end of 4 weeks of treatment, the mean HAM-D score of participants in group A reduced from 20.77 to 16.89, while in group B from 20.96 to 15.45.

Within the group analysis by paired t'test showed statistically significant ($P<0.0001$) reduction in mean HAM-D score after 4 weeks of treatment in both the study groups. Since depression imparts significant disability, early achievement of improvement in symptoms is a treatment advantage and improves compliance in patients, thereby prevents progression of disease to chronic form[53].

At the end of 4 weeks, 23% were responders including 7 remitters in Escitalopram (test) group, and 20% were responders including 8 remitters in sertraline (control) group. Comparison of reduction of mean HAM-D scores

between two treatment groups at week 4 did not show statistical significance (P=0.215).

At the end of 8 weeks, 16% of in test group were responders including 9 remitters while 22% responded in control group including 8 remitters. Mean HAM-D score Reduction from 20.77 at baseline to 12.35 at the end of 8 weeks of drug therapy within group A was statistically significant ($p<0.001$). Mean HAM-D score reduction from 20.96 at baseline to 11.6 at the end of 8 weeks therapy showed statistical significance in group B too. The above result indicates that the percent of responders and remitters increases with the increase in duration of treatment from 4 to 8 weeks proportionately to the concept that antidepressants take time to produce clinical response by the mechanism of pharmacological action. .

Comparison between 8^{th} week mean HAM-D score of group A (12.35) and B (11.6) were not statistically significant. Analysis of score inbetween groups does not differ in the overall score reduction infering equivalent therapeutic efficacy of drugs used in study and active control groups .

In the last visit **at the end of 12 weeks**, 42% in escitalopram group and 34% in sertraline group were responders. Aggregate total of responders at the end of 12 weeks of continuous drug therapy was 81% and 76% in escitalopram and sertraline groups respectively.

Mean HAM-D score reduction from 20.77 to 8.75 in test group A and 20.96 at baseline to 8.65 after 12 weeks therapy in group B is statistically significant. Hence, in both the treatment groups there is significant reduction in mean HAM-D score as assessed every 4 weeks in patients after the drug therapy was instituted, which implies that both escitalopram and sertraline are equally efficacious in reducing the symptoms of depression as early as 4 weeks of treatment. There was no statistical significant difference in response rates between two treatment groups as determined by tests of significance with the mean HAM-D score.

Remitters as estimated at the end of 12 weeks were 56% in escitalopram group as compared to 54% in sertraline group. Number of remitters assessed during the course of therapy showed increasing trend with duration of therapy.

Non responders or resistant to treatment were measured by HAM–D score. 19% in escitalopram group versus 24% in sertraline group turned out to be non responders . As per guidelines prescribed in American Psychiatric Association, patient can be termed as non responders only after continous therapy period not less than 6 months. But clinical trials done in antidepressant treatment suggest that three months therapy is adequate to ascertain efficacy .

Adverse events were reported by 23 patients (6 in group A and 17 in group B)out of 112 patients who participated in the study. 10.5% reported

adverse drug reactions in group A which includes nausea(3.5%), headache(3.5%), insomnia(1.8%) and sexual dysfunction of delayed orgasm(1.8%) during 12 weeks of drug intake. Adverse events reported by 17(30.9%) patients among group B were nausea(7.3%), insomnia(5.5%), headache(9%), diarrhoea(3.6%), decreased libido(1.8%), delayed ejaculation(1.8%), during the study period. The occurrence of adverse effects in sertraline group was numerically higher than escitalopram group and this difference was also found to be statistically significant (P=0.007). There were no treatment emergent suicides in this study. There were no other treatment related adverse events in both groups. No serious adverse events occurred during the course of study. None of the study participants in either groups withdrew due to adverse effect, drop out were due other reasons.

There was significant improvement in the symptoms like depressed mood, suicide, anxiety and somatic symptoms with treatment, in both groups during and at the end of therapy and symptomatic improvement showed a gradual rise with longer duration of therapy.

- Patients who have attempted suicide were given a score of 4. At baseline 5.3% of patients enrolled in test group and 1.8 % in control group scored high in the measure of suicidal tendency. 15.7 % of test group and 14.5 % of control had suicidal ideations at baseline. A statistically significant reduction in corresponding HAM-D item III score in subsequent visits, was achieved with both escitalopram and

sertraline. While absolute change in HAM-D item I, X and XIII with respect to depressed mood, psychic anxiety and general somatic symptoms respectively showed statistically significant difference within the group before and after treatment ,but there was no statistically significant difference between two treatment groups. Early response in terms of improvement in somatic symptoms of HAM-D, is predictive of achieving remission with active treatment but were not done due to limited study period.

Limitations

- The study involves smaller number of patients and conducted for short duration of 12 weeks. Though 12 weeks of open labelled therapy is adequate to establish the effectiveness of the treatment drugs. Current guidelines to treat depression recommends a duration of 6-9 months of anti depressant therapy after achieving remission. Hence a study period and follow up upto 6 to 9 months after achieving remission is needed to compare efficacy of these drugs in preventing relapses requiring further studies.
- There was no placebo group for comparing absolute effectiveness of escitalopram and sertraline treatment. But good clinical practice does not recommend deprivation of therapy in patients .
- Effect of treatment on quality of life need to be analysed by further studies .

- Health care costs impacted by these drugs need to be analysed through pharmaco economic studies.

Drop outs 3 drop outs in escitalopram group of which 2 patients did not turn up and one patient wished to receive treatment from the hospital nearby. There were 5 drop outs in sertraline group. Of which 3 patients lost follow up after 4 weeks of treatment, and one patient was not willing to continue in study and one patient was not compliant.

CONCLUSION

- The study confirms that both Escitalopram and Sertraline are appropriate as first line drugs in treatment for depression.
- Efficacy profile was identical for both Escitalopram and sertraline as seen in the statistically significant difference in the values observed.
- The Primary endpoint, Efficacy of Escitalopram, the test drug is found to be Non inferior to the control Sertraline as measured by response (81% vs 76%) and remission rates (56% vs 54%) and the significant improvement in baseline mean HAM-D score at 12^{th} week of therapy .
- Secondary endpoint is assessment of safety, which was done by clinical and laboratory parameters showed that Escitalopram was better tolerated with statistically significantly less number of reported adverse events than sertraline.

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ANNEXURE – I

Patient Name:_____ **Date:**_____

Hamilton Rating Scale for Depression (17-items)

Instructions: For each item select the "cue" which best characterizes the patient during the past week.

1. **Depressed Mood**
   (sadness, hopeless, helpless, worthless)
   0 Absent
   1 These feeling states indicated only on questioning
   2 These feeling states spontaneously reported verbally
   3 Communicates feeling states nonverbally, i.e., through facial expression, posture, voice and tendency to weep
   4 Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and nonverbal communication

2. **Feelings of Guilt**
   0 Absent
   1 Self-reproach, feels he has let people down
   2 Ideas of guilt or rumination over past errors or sinful deeds
   3 Present illness is a punishment. Delusions of guilt
   4 Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

3. **Suicide**
   0 Absent
   1 Feels life is not worth living
   2 Wishes he were dead or any thoughts of possible death to self
   3 Suicide ideas or gesture
   4 Attempts at suicide (any serious attempt rates 4)

4. **Insomnia - Early**
   0 No difficulty falling asleep
   1 Complains of occasional difficulty falling asleep i.e., more than ½ hour
   2 Complains of nightly difficulty falling asleep

5. **Insomnia - Middle**
   0 No difficulty
   1 Patient complains of being restless and disturbed during the night
   2 Waking during the night – any getting out of bed rates 2 (except for purposes of voiding)

6. **Insomnia - Late**
   0 No difficulty
   1 Waking in early hours of the morning but goes back to sleep
   2 Unable to fall asleep again if gets out of bed

7. **Work and Activities**
   0 No difficulty
   1 Thoughts and feelings of incapacity, fatigue or weakness related to activities; work or hobbies
   2 Loss of interest in activity; hobbies or work – either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities)
   3 Decrease in actual time spent in activities or decrease in productivity. In hospital, rate 3 if patient does not spend at least three hours a day in activities (hospital job or hobbies) exclusive of ward chores.
   4 Stopped working because of present illness. In hospital, rate 4 if patient engages in no activities except ward chores, or if patient fails to perform ward chores unassisted.

8. **Retardation**
   (slowness of thought and speech; impaired ability to concentrate; decreased motor activity)
   0 Normal speech and thought
   1 Slight retardation at interview
   2 Obvious retardation at interview
   3 Interview difficult
   4 Complete stupor

9. **Agitation**
   0 None
   1 "Playing with" hand, hair, etc.
   2 Hand-wringing, nail-biting, biting of lips

10. **Anxiety - Psychic**
    0 No difficulty
    1 Subjective tension and irritability
    2 Worrying about minor matters
    3 Apprehensive attitude apparent in face or speech
    4 Fears expressed without questioning

11. **Anxiety - Somatic**
    0 Absent
    1 Mild
    2 Moderate
    3 Severe
    4 Incapacitating
    Physiological concomitants of anxiety such as:
    Gastrointestinal - dry mouth, wind, indigestion, diarrhea, cramps, belching
    Cardiovascular – palpitations, headaches
    Respiratory - hyperventilation, sighing
    Urinary frequency
    Sweating

12. **Somatic Symptoms - Gastrointestinal**
    0 None
    1 Loss of appetite but eating without staff encouragement. Heavy feelings in abdomen.
    2 Difficulty eating without staff urging. Requests or requires laxatives or medications for bowels or medication for G.I. symptoms.

13. **Somatic Symptoms - General**
    0 None
    1 Heaviness in limbs, back or head, backaches, headache, muscle aches, loss of energy and fatigability
    2 Any clear-cut symptom rates 2

14. **Genital Symptoms**
    0 Absent
    1 Mild
    2 Severe
    0 Not ascertained
    Symptoms such as: loss of libido, menstrual disturbances

15. **Hypochondriasis**
    0 Not present
    1 Self-absorption (bodily)
    2 Preoccupation with health
    3 Frequent complaints, requests for help, etc.
    4 Hypochondriacal delusions

16. **Loss of Weight**
    A. When Rating by History:
    0 No weight loss
    1 Probable weight loss associated with present illness
    2 Definite (according to patient) weight loss

    B. On Weekly Ratings by Ward Psychiatrist, When Actual Changes are Measured:
    0 Less than 1 lb. weight loss in week
    1 Greater than 1 lb. weight loss in week
    2 Greater than 2 lb. weight loss in week

17. **Insight**
    0 Acknowledges being depressed and ill
    1 Acknowledges illness but attributes cause to bad food, climate, overwork, virus, need for rest, etc.
    2 Denies being ill at all

Total Score:_____

ANNEXURE – II

PROFORMA

Serial No: **Hospital No:**

1.Name:

2. Age: **3. Sex: a: male b: female**

4.Marital status:

5.Occupation:

6.Educational status

7. Socio economic class: L/ M/ H

8. Informant – Name, Age, Relationship, Intimacy, Length of acquaintance with patient

9. History of presenting illness

Time of onset of illness/symptoms:

Frequency:

Duration:

10. Past history : psychiatric, medical, surgical, accidents, injuries, thyroid diseases,hypertension, diabetes

11. History of use of any other drugs / drug allergies

12. Family history of depresssion

General Examination:

Heart rate :

Blood Pressure :

Respiratory Rate :

Systemic Examination

- CVS :
- RS :
- Abdomen :
- CNS :

Lab investigations

Investigations	**Baseline**	**At the end of 4th week**	**8th week**	**12th week**
Hb%				
Total leucocyte count				
ESR				
Platelet count				
RBS				
Blood urea				
Serum creatinine				
S. electrolytes(Na)				
S. electrolytes(K)				
SGOT				
SGPT				

ANNEXURE - III

INFORMATION SHEET

We are conducting a study on **"A prospective randomised open label comparative study of efficacy and safety of Escitalopram versus Sertraline in major depressive disorder in a tertiary care hospital.**" in our Institution, Chengalpattu Medical College Hospital, Chengalpattu.

- Your participation may be of immense value for the study.
- We are selecting patients who satisfy our inclusion criteria and they are included in the study.
- The privacy of the patients will be maintained throughout the study, in the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.
- Participation depends on patients own voluntary decision. Their decision will not result in any loss of benefits to which you are otherwise entitled.
- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of the Participant

Dr V.J.Sharmi

Date :

Place :

ANNEXURE - IV

INFORMED CONSENT FORM

Title of the study : **"A prospective randomised open label comparative study of efficacy and safety of Escitalopram versus Sertraline in major depressive disorder in a tertiary care hospital.**"

Name of the participant :

Name of the Investigator : Dr.V.J.Sharmi

Name of the Institution : Chengalpattu Medical College Hospital

Documentation of the informed consent.

I _____have read the information in this form (or it has been read to me).I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in "**A prospective randomised open label comparative study of efficacy and safety of Escitalopram versus Sertraline in major depressive disorder in a tertiary care hospital.**"

1. I have read and understand this consent form and the information provided to me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.
4. I have been explained about my rights and responsibilities by the investigator.
5. I have been informed the investigator of all the treatments I am taking or have taken in the past _____including any native (alternative) treatment.
6. I have been advised about the risks associated with my participation in this study.
7. I agree to cooperate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.
8. I have not participated in any research study within the past_____.

9. I have not donated blood within the past_____- Add if the study involves extensive blood sampling.
10. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.
11. I am also aware that the investigator may treatment my participated in the study at any time for any reason, without my consent.
12. I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the sponsors, regulatory authorities, Govt.Agencies, and IEC. I understand that they are publicly presented.
13. I have understood that my identity will be kept confidential if my data are publicly presented.
14. I have had my questions answered to my satisfaction.
15. I have decided to be in the research study.

I am aware that if I have any question during this study, I should contact the Investigator. By signing this consent form I attest that the information given in this document has been clearly explained to me and understood by me, I will be given a copy of this consent document.

For adult participants:

Name and signature/thumb impression of the participant (or legal representative if participant incompetent)

Name_____signature_____Date_____

Name and signature of impartial witness (require for illiterate patients)

Name_____signature_____Date_____

Address and contact number of the impartial witness:

_____

Name and signature of the investigator or his representative obtaining consent:

Name_____signature_____Date_____

Name and signature of the investigator or his representative obtaining consent:

Name_____signature_____Date_____

ANNEXURE – V

தகவல் படிவம்

செங்கல்பட்டு அரசு பொது மருத்துவமனை மனநல மருத்துவ புறநோயாளிகள் சிகிச்சைப்பிரிவில் மன அழுத்தத்திற்கு சிகிச்சை பெறுவோர்களுக்கு வழங்கப்படும் 'எஸ்சிட்டலோபிராம்' மற்றும் 'செர்ட்டிராலின்' எனப்படும் இரு வேறு மன அழுத்த சிகிச்சை மருந்துகளின், பயன்பாடு மற்றும் பாதுக்காப்பு குறித்ததான ஒப்பீட்டு ஆய்வு மேற்கொள்ளப்படுகிறது.

- இந்த ஆய்வு அனுபவம் வாய்ந்த மருத்துவர்களின் உதவியோடு நடத்தப்படுகிறது.
- இம்மருந்துகள் அனுதின பயன்பாட்டில் உள்ள மருந்துகளே. இம்மருந்துகளினால் மிகப் பெரிய அளவில் பக்க விளைவுகள் ஏற்பட வாய்ப்புகள் இல்லை.
- ஆராய்ச்சியின் போது ஒரு பிரிவினருக்கு 'எஸ்சிட்டலோபிராம்' மாத்திரையும் மற்றொரு பிரிவினருக்கு 'செர்ட்டிராலின்' மாத்திரை வழங்கப்படும்.
- நோயாளிகள் இம்மருந்துகளை பயன்படுத்தியபின் நோயின் தன்மையை குறித்து 4, 8, 12 வாரங்களில் தரமதிப்பீடு செய்யப்படுவர்.
- ஆராய்ச்சியின் தொடக்கத்திலும், 4, 8, 12 வாரங்களின் முடிவிலும் இரத்தப் பரிசோதனை செய்யப்படும்.
- நோயின் தன்மைகளை வெளியிடும்போது தங்களது பெயரையோ அடையாளங்களையோ வெளியிட மாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.
- இந்த ஆராய்ச்சியில் பங்கேற்பது உங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின் வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.
- இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

நாள்:

இடம்: கையொப்பம்

ANNEXURE - VI

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு: செங்கல்பட்டு அரசு பொது மருத்துவமனை மனநல மருத்துவ புறநோயாளிகள் சிகிச்சைப்பிரிவில் மன அழுத்தத்திற்கு சிகிச்சை பெறுவோர்களுக்கு வழங்கப்படும் 'எஸ்சிட்டலோபிராம்' மற்றும் 'செர்ட்டிராலின்' எனப்படும் இரு வேறு மன அழுத்த சிகிச்சை மருந்துகளின், பயன்பாடு மற்றும் பாதுக்காப்பு குறித்ததான ஒப்பீட்டு ஆய்வு மேற்கொள்ளப்படுகிறது.

திரு/திருமதி _____

என்ற விலாசத்தில் வசிக்கும் நான், எனக்கு அளிக்கப்பட்ட தகவல் படிவத்தில் உள்ள விஷயங்களைப் படித்தும் கேட்டும் புரிந்து கொண்டேன்.

இந்த ஆய்விற்குத் தேவையான இரத்தப் பரிசோதனைகளுக்கு உட்பட சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் பிறரின் நிர்ப்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகிறேன்.

ஆய்வில் தொடர்ந்து பங்குபெற விருப்பம் இல்லை என்றால் விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

ஆய்வின் முடிவினை சொந்த அடையாளங்களை வெளியிடாமல் மருத்துவ ஆராய்ச்சிக்காக பயன்படுத்திக் கொள்ள சம்மதிக்கிறேன்.

நாள்:

இடம்: **கையொப்பம்**

INSTITUTIONAL ETHICAL COMMITTEE

CHENGALPATTU MEDICAL COLLEGE, CHENGALPATTU

Title of Work	:	A prospective randomized open label comparative study of efficacy and safety of Escitalopram versus Sertraline in major depressive disorder in a tertiary care hospital
Principal Investigator	:	Dr.Sharmi.V.J.,
Designation	:	Final Year Post Graduate
Co-Investigators	:	Dr.K.Vijayarani, MD., Associate Professor and HOD Department of Pharmacology, Chengalpattu Medical College, Chengalpattu.
Department	:	Pharmacology

The request for an approval From the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 29.02.2016 at the Medical Education Unit, Government Chengalpattu Medical College, Chengalpattu at 11.00 AM.

The Members of the committee, the Secretary and the Chairman are pleased to inform you that your proposed project mentioned above is approved.

You should inform the IEC in case of any changes in study procedure, site, investigator investigation or guide or any other changes.

1. You should not deviate from the area of work for which you applied for ethical clearance.
2. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
3. You should abide to the rules and regulations of the institution(s).
4. You should complete the work within the specific period and if any extension is required, you should apply for permission again and do the work.
5. You should submit the summary of the work to the ethical committee on complete of work.

28/8/17

MEMBER SECRETARY,
IEC, CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU.

31/8/17

DEAN
CHENGALPATTU MEDICAL COLLEGE
CHENGALPATTU.

S.No	Age	Sex	Rx group	0w HAMD	4w HAM D	8w HAM D	12w HAM D	Depressed mood(0-4)				Suicide(0-4)				Anxiety(Psychic)(0-4)				somatic(general)(0-2)			
								0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12
1	45	F	A	16	8	8	5	2	1	0	0	1	1	0	0	2	1	0	0	0	0	0	0
2	41	F	A	17	7	6	3	1	0	0	0	0	0	0	0	2	1	1	1	0	0	0	0
3	53	M	A	20	20	14	7	4	3	2	1	1	0	0	0	1	1	0	0	0	0	0	0
4	35	M	A	17	15	7	6	3	2	1	1	0	0	0	0	2	1	1	0	1	1	0	0
5	21	F	A	18	7	8	7	2	2	1	0	1	0	0	0	2	0	0	0	0	0	0	0
6	59	M	A	20	20	18	12	3	2	1	1	2	1	0	0	3	2	1	1	1	1	1	1
7	24	F	A	24	22	16	11	3	2	1	1	0	0	0	0	3	2	1	0	1	1	0	0
8	57	F	A	24	21	15	11	2	1	1	0	1	0	0	0	4	3	2	1	1	0	0	0
9	38	F	A	33	27	20	19	4	3	2	2	3	2	1	1	4	3	3	3	2	1	1	0
10	52	F	A	28	23	21	20	4	2	2	1	4	3	2	1	4	3	3	2	2	1	1	1
11	45	F	A	9	6	6	4	2	1	1	0	0	0	0	0	2	1	0	0	0	0	0	0
12	54	F	A	12	12	7	6	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
13	27	F	A	18	18	7	6	3	2	1	0	1	1	0	0	1	1	1	1	0	0	0	0
14	32	F	A	28	14	12	6	4	2	2	1	1	0	0	0	2	0	0	0	1	1	0	0
15	55	F	A	20	20	16	13	4	3	2	1	3	2	2	1	4	4	3	3	1	1	0	0
16	50	M	A	27	26	18	7	3	2	1	1	2	1	0	0	3	2	1	1	1	1	1	0
17	48	F	A	12	10	7	6	2	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0
18	56	F	A	26	21	14	7	4	3	2	1	2	1	0	0	4	2	2	1	2	1	1	0
19	58	F	A	32	26	22	19	4	3	3	2	4	3	2	1	2	2	1	1	1	1	1	1
20	29	F	A	13	12	10	7	2	2	1	0	0	0	0	0	2	2	1	1	2	1	1	0
21	38	M	A	18	18	12	11	2	1	1	1	2	2	1	0	3	2	1	1	1	1	0	0
22	44	M	A	22	21	16	10	3	2	1	1	2	1	1	0	2	1	1	0	0	0	0	0
23	47	F	A	21	18	7	7	3	0	0	0	3	0	0	0	3	2	1	1	1	1	1	1
24	55	F	A	21	18	13	6	3	2	0	0	0	0	0	0	2	1	1	1	1	0	0	0
25	59	F	A	9	7	7	5	2	1	1	0	0	0	0	0	1	1	0	0	0	0	0	0
26	39	F	A	34	17	12	10	4	3	2	1	3	2	1	1	3	2	2	2	2	0	0	0
27	21	M	A	31	26	18	7	2	1	1	0	1	0	0	0	4	3	1	1	1	1	0	0
28	52	M	A	14	12	11	7	2	0	0	0	0	0	0	0	2	1	1	1	2	0	0	0
29	55	M	A	22	20	19	16	3	2	2	1	3	2	2	1	3	2	2	1	2	1	1	0
30	25	F	A	20	18	11	6	4	3	2	1	2	1	0	0	2	1	1	0	1	0	0	0
31	50	F	A	17	16	12	7	3	2	1	1	1	0	0	0	3	2	1	1	2	1	1	0
32	40	F	A	21	20	14	10	3	2	1	1	2	1	1	1	3	2	2	1	2	1	1	1
33	60	M	A	32	30	27	22	4	2	2	1	3	2	1	1	3	3	2	2	1	0	0	0
34	43	F	A	26	21	17	7	2	1	1	0	0	0	0	0	3	2	1	1	0	0	0	0
35	50	F	A	16	15	12	7	3	2	1	1	2	1	0	0	3	2	1	0	0	0	0	0
36	23	F	A	9	7	7	6	2	1	0	0	1	0	0	0	2	1	1	0	0	0	0	0
37	35	M	A	16	13	10	8	2	1	1	0	0	0	0	0	3	2	1	1	1	0	0	0
38	60	M	A	11	7	5	5	2	0	0	0	0	0	0	0	1	1	0	0	1	1	0	0
39	48	M	A	30	26	19	14	3	2	1	1	2	1	1	0	2	1	1	1	1	1	1	1
40	50	M	A	17	15	10	7	2	1	1	1	1	0	0	0	2	1	1	0	1	0	0	0
41	35	F	A	22	11	8	6	3	2	1	1	2	0	0	0	3	2	1	0	0	0	0	0
42	60	F	A	31	28	19	7	4	3	2	1	2	1	1	0	3	3	2	1	1	0	0	0
43	57	F	A	10	10	6	6	2	1	0	0	0	0	0	0	2	1	0	0	0	0	0	0
44	53	F	A	21	18	12	7	3	2	1	0	1	0	0	0	3	2	1	1	0	0	0	0
45	27	M	A	24	20	16	13	3	2	1	1	3	2	2	1	3	2	1	0	2	1	0	0
46	37	F	A	23	22	15	10	3	2	1	1	2	1	1	0	3	2	2	1	0	0	0	0
47	49	F	A	19	18	7	6	3	2	1	0	1	0	0	0	2	1	0	0	0	0	0	0
48	60	F	A	14	12	12	10	3	2	2	1	3	2	1	1	3	1	1	0	1	0	0	0
49	51	F	A	12	12	10	7	1	0	0	0	0	0	0	0	2	1	1	1	1	1	0	0
50	45	F	A	23	20	16	11	4	1	1	1	2	1	0	0	3	2	1	1	2	0	0	0
51	34	F	A	27	13	8	6	3	2	1	1	1	0	0	0	3	2	1	0	2	1	0	0

S.No	Age	Sex	Rx group	0w HAMD	4w HAM D	8w HAM D	12w HAM D	Depressed mood(0-4)				Suicide(0-4)				Anxiety(Psychic)(0-4)				somatic(general)(0-2)			
								0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12
52	54	F	A	18	16	6	6	3	2	1	1	0	0	0	0	4	2	1	1	1	1	0	0
53	60	F	A	31	28	22	20	4	3	2	2	4	2	2	1	3	2	2	1	2	1	0	0
54	55	F	A	32	14	9	7	3	2	1	1	3	2	1	0	4	3	2	1	1	0	0	0
55	31	F	A	17	7	6	5	2	1	0	0	0	0	0	0	2	1	1	0	1	0	0	0
56	47	M	A	19	18	14	7	3	2	1	0	0	0	0	0	2	1	1	0	1	0	0	0
57	40	F	A	20	16	7	5	3	1	0	0	0	0	0	0	2	1	1	1	0	0	0	0
58	27	F	B	15	13	12	9	3	2	2	1	2	2	1	0	2	2	1	1	1	0	0	0
59	25	F	B	18	7	7	6	3	2	1	0	2	1	1	1	2	1	0	0	0	0	0	0
60	38	M	B	24	20	15	14	4	2	2	2	2	1	1	1	3	1	1	1	0	0	0	0
61	41	F	B	10	7	7	5	2	1	1	1	0	0	0	0	2	1	1	0	1	0	0	0
62	45	F	B	21	12	7	5	3	0	0	0	2	0	0	0	4	2	1	1	1	1	1	0
63	29	F	B	28	22	18	12	3	2	1	1	3	2	1	0	3	2	2	1	2	1	0	0
64	51	M	B	10	7	5	5	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
65	54	F	B	11	10	9	5	2	1	1	0	0	0	0	0	1	1	0	0	1	0	0	0
66	56	F	B	22	20	16	13	3	2	2	1	2	1	1	0	2	1	1	0	1	0	0	0
67	52	M	B	19	12	9	8	3	3	1	1	2	1	0	0	2	1	1	1	2	0	0	0
68	44	F	B	32	25	20	18	4	3	2	2	3	2	1	1	3	2	1	1	2	1	0	0
69	34	F	B	31	26	14	7	4	3	1	1	4	3	2	1	3	2	1	0	0	0	0	0
70	39	M	B	15	14	11	7	3	2	1	1	2	0	0	0	3	2	1	0	1	0	0	0
71	47	F	B	20	13	10	7	2	1	1	1	2	1	0	0	2	1	0	0	2	1	1	1
72	50	F	B	27	20	12	6	2	1	1	1	1	0	0	0	2	2	1	1	0	0	0	0
73	48	M	B	11	11	7	5	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
74	53	F	B	13	14	12	10	4	3	2	1	3	2	2	1	2	2	1	1	0	0	0	0
75	57	M	B	14	12	11	9	2	2	1	1	2	1	1	0	2	1	1	0	1	0	0	0
76	55	F	B	22	18	16	15	4	3	3	2	2	2	1	0	2	1	0	0	0	0	0	0
77	45	M	B	21	16	10	7	2	0	0	0	1	0	0	0	2	1	1	0	2	1	1	1
78	47	M	B	24	18	12	9	3	0	0	0	2	1	1	1	3	2	1	0	0	0	0	0
79	35	M	B	30	17	16	14	3	2	2	1	3	2	1	1	4	3	1	1	2	1	0	0
80	50	F	B	33	24	22	17	3	2	2	1	2	1	1	1	4	3	2	2	1	1	0	0
81	43	M	B	10	6	6	4	1	1	0	0	0	0	0	0	2	1	0	0	0	0	0	
82	37	F	B	23	15	6	6	4	3	2	1	0	0	0	0	3	2	1	1	2	1	0	0
83	50	M	B	19	18	15	11	3	2	1	1	0	0	0	0	2	1	1	0	1	0	0	0
84	45	M	B	34	19	7	6	2	2	1	1	2	1	1	0	3	2	1	0	1	0	0	0
85	50	M	B	38	26	13	7	4	2	2	1	2	1	0	0	3	2	1	1	2	1	1	1
86	46	F	B	16	8	7	3	2	0	0	0	2	2	1	1	1	0	0	0	0	0	0	0
87	31	F	B	22	11	10	9	3	2	1	1	3	2	2	1	3	2	2	1	0	0	0	0
88	42	F	B	17	12	10	8	2	1	0	0	1	0	0	0	2	1	0	0	1	0	0	0
89	45	M	B	21	16	10	8	1	1	0	0	0	0	0	0	3	2	1	0	0	0	0	0
90	59	M	B	37	26	25	22	4	3	2	2	3	2	1	1	4	3	2	2	2	1	1	1
91	40	F	B	14	10	6	5	3	2	0	0	0	0	0	0	0	0	0	0	1	0	0	0
92	52	F	B	20	10	9	8	1	0	0	0	1	0	0	0	3	2	1	1	1	1	0	0
93	55	F	B	28	20	13	11	3	2	0	0	1	0	0	0	3	2	2	1	2	1	1	1
94	58	F	B	9	9	8	7	1	1	0	0	0	0	0	0	2	1	1	0	1	0	0	0
95	59	M	B	12	10	9	6	1	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0
96	55	F	B	23	21	17	14	3	2	2	1	2	1	1	1	3	2	2	1	0	0	0	0
97	35	F	B	21	16	7	3	3	0	0	0	2	0	0	0	2	1	0	0	0	0	0	0
98	57	F	B	18	6	5	5	2	1	0	0	2	1	1	0	2	2	1	0	0	0	0	0
99	54	F	B	26	22	18	13	2	1	0	0	2	1	1	0	4	3	2	1	2	1	1	1
100	51	F	B	12	11	5	4	2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
101	40	F	B	17	7	6	5	3	2	0	0	1	0	0	0	2	1	1	1	2	0	0	0
102	60	F	B	19	15	10	7	2	1	1	0	1	1	0	0	4	3	3	1	0	0	0	0
103	55	F	B	32	27	16	7	3	2	1	1	1	0	0	0	3	2	1	0	2	1	0	0
104	23	M	B	27	18	12	6	4	2	0	0	2	0	0	0	2	1	1	1	1	0	0	0
105	27	F	B	9	6	5	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
106	49	F	B	20	18	16	12	2	2	1	0	3	2	1	1	2	1	1	0	1	1	0	0
107	60	M	B	20	15	12	9	2	1	1	1	1	0	0	0	2	1	1	1	2	1	0	0
108	52	F	B	29	22	21	17	4	3	2	2	3	2	2	1	3	2	2	2	2	1	1	1
109	48	F	B	32	24	19	14	4	3	2	1	2	1	0	0	4	3	2	2	2	1	1	1
110	21	M	B	9	7	4	4	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
111	35	F	B	23	20	18	11	3	2	1	1	2	1	0	0	4	2	2	1	1	0	0	0
112	60	F	B	25	21	15	7	4	3	2	1	2	1	0	0	2	1	0	0	1	1	0	0

S.No	Age	Sex	Rx group	Hemoglobin(g/dl)				Total leukocyte count(cells/cumm)				ESR(mm/hour)				Platelet count (lakhs/cumm)				Blood sugar(mg/dl)			
				0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12
1	45	F	A																				
2	41	F	A	11.8	10.5	9.5	10.8	7734	7700	5680	9020	12	12	8.5	9	2.6	2.85	2.4	2.5	90	112	97	106
3	53	M	A	9.4	8.9	10.2	9	8800	9000	5420	7522	13	11.5	11	10	2.65	2.8	2.9	2.3	124	115	120	122
4	35	M	A	15.8	14.2	14.8	13.9	8750	7700	6250	6800	11	11.5	10	12	2.5	2.3	3.12	2.5	225	175	186	190
5	21	F	A	13	11.9	12.3	12.4	7805	7580	6500	5750	13	12	10	8.8	2.8	2.56	2.35	2.8	96	110	105	102
6	59	M	A	10.4	11.1	12.4	12.5	7830	7568	6280	6700	12	12.5	12.5	11	2.5	2.4	2.46	2.4	94	120	114	126
7	24	F	A	10.2	10.6	11	10.5	6786	6950	8400	7600	10	10	11	9.5	2.65	2.35	2.55	2.6	125	135	122	136
8	57	F	A	8.3	9.2	12	11.5	6500	6450	6300	8900	9	9.5	9.5	9	2.8	2.5	2.34	2.2	85	91	96	98
9	38	F	A	10.5	10.5	9.5	9.4	6600	6300	9020	6450	10	8	13	12	2.3	3.24	2.15	2.45	140	128	138	140
10	52	F	A	9.8	9.6	9.3	9.2	8562	9020	7522	6500	9.5	9	9.5	11.5	2.55	2.6	2.6	2.35	102	114	120	116
11	45	F	A	8.2	9.1	12	10.2	7753	7522	6800	6960	9.5	10	12.5	9.5	2.14	2.15	2.4	2.5	142	132	136	116
12	54	F	A	7	8.1	11.3	10.5	6862	6800	5750	6540	12.5	12	11.5	9.5	2.56	2.67	3.5	2.5	145	140	146	136
13	27	F	A	8.9	10	10.6	9.5	5845	5750	6700	7950	8.5	8.8	10	13	2.5	2.4	2.75	2.45	120	124	122	124
14	32	F	A	9.8	10.1	10.7	10.3	6623	6700	7600	6021	11	11	8	8.4	2.8	2.14	2.14	2.3	86	102	94	88
15	55	F	A	11	10.6	8.9	9.6	7862	7600	6845	6750	10	9.5	9.5	14	2.56	2.4	2.99	3.5	110	98	106	120
16	50	M	A	11.6	11.8	9.2	10.4	8739	8900	8780	6860	10	9	11	11	2.5	2	2.68	3	140	136	144	128
17	48	F	A	13.8	12.5	13	13.5	6845	6450	6430	5682	12.5	12	12	9.6	2.8	2.5	2.34	2.4	134	143	136	140
18	56	F	A	9.5	8.2	8.8	8.3	6955	6500	4200	6952	11	11.5	11	9	1.7	1.9	2.5	2.35	158	164	140	144
19	58	F	A	12.8	11.8	11.2	12.1	7652	6960	6540	6320	10	10	11	10	2.2	2.5	2.25	2.5	124	121	112	118
20	29	F	A	9.8	9.6	11.6	10	6862	6540	9250	9862	10	9	11.4	12	2.65	2.35	2.55	2.5	126	132	122	118
21	38	M	A	9.6	9.5	8.9	8.6	7798	7950	8400	8020	9.5	10	10.2	8.8	2.56	2.45	2.01	2.65	97	94	81	99
22	44	M	A	13	12.6	10.6	11.7	5791	6021	7040	6860	9.5	9.5	10.5	11	3.45	2.12	2.09	2.15	136	110	102	96
23	47	F	A	10	12	10	11	6700	6750	5430	5400	13	13	9.5	9.5	2	2.84	2.35	2.45	143	120	126	138
24	55	F	A	9.7	9.5	8.2	9.2	6587	6860	6630	6500	8.4	9.5	9	9	2.09	2	2.15	2.25	164	135	136	120
25	59	F	A	9.2	9.3	7	8	5865	5682	7652	4320	14	12.5	9	12	2.3	2.56	2.02	1.75	121	91	98	136
26	39	F	A	10	9.4	8.9	8.5	6860	6952	6862	6800	11	11.5	10.6	10.8	2.65	2.25	2.3	2.45	136	134	136	126
27	21	M	A	9.5	10.4	9.8	8.9	6800	6320	7798	6796	9.6	10	10.8	13.5	2.45	2.64	2.55	2.55	88	80	95	86
28	52	M	A	8.6	10.6	10.2	10	6796	9862	5791	5867	8.6	8	13.5	9	2.45	2.65	2.14	2.75	85	91	96	98
29	55	M	A	11.3	13.5	12.5	12.6	5867	5462	6700	5863	9	9.5	9	9.8	2.42	3	2.3	2.01	117	124	116	118
30	25	F	A	11.4	10.5	11.5	10.2	5863	4963	6587	6752	12	11	9.8	8	2.65	3.22	2.45	1.95	145	133	132	140
31	50	F	A	11.4	8	9	9	6752	5652	5865	7766	13.5	12	8	12.5	2.65	2.66	2.35	2.55	105	95	110	112
32	40	F	A	10	10.2	9.6	9.5	7766	7568	6860	6800	11.4	11	12.5	12	2.45	2.56	2.56	2.75	150	140	135	142
33	60	M	A	11.1	8.8	8.5	8.6	6893	6954	6950	6450	11	11	12	15	2.54	2.5	2.35	2.35	120	124	122	127
34	43	F	A	10.2	13.5	14	12.5	5807	5623	5620	6250	10.5	11.5	15	11	2.45	2.56	2.5	2.75	123	86	132	124
35	50	F	A	10.5	7.5	8.5	9	5769	5821	5820	6200	9.5	9	11	8.5	2.45	2.75	2.8	2.45	146	136	147	144
36	23	F	A	11	12.6	9.6	10.5	6651	6620	6620	6045	9	9.5	9	11	3.12	2.14	2.56	3	99	105	104	112
37	35	M	A	10	10.4	11.3	11.5	5862	6600	6600	6796	9	9	10	10	2.35	2.99	2.5	3.5	140	142	150	135
38	60	M	A	11.4	9.6	9.9	10.4	5459	6320	6320	5867	10.6	10	9.5	10	2.46	2.68	2.8	3.75	124	127	120	122
39	48	M	A	9.3	12	10	9.8	6596	6564	6560	5863	11.2	11	13	12.5	2.25	2.3	2.4	2.5	86	124	123	132
40	50	M	A	10.4	9.5	8.2	8.1	6359	6500	6950	6752	13.5	12	9.5	11	2.5	2.45	2.13	1.95	136	144	146	147
41	35	F	A	10.5	9.3	9.8	8.5	7755	7452	6560	7766	9	9.5	12.5	9.5	2.29	2.35	2.68	2.75	105	112	99	104
42	60	F	A	8.3	11.3	11.6	11	6869	7420	6800	6893	9.8	10	11.5	13	2.54	2.56	2.34	2.15	110	98	106	120
43	57	F	A	11.3	10.4	11	10.7	6878	5620	6450	5807	8	9.5	10	9.5	2.23	2.35	3.01	3.5	140	136	144	128
44	53	F	A	10.4	10	12	12.5	5792	6200	6250	5690	12.5	11	8	9.5	2.55	2.34	2.3	2.65	214	202	164	160
45	27	M	A	10.4	11.6	9.8	10.5	6700	6045	6500	5420	12	10	9.5	11	3.05	3.4	2.55	2.85	91	98	85	96
46	37	F	A	10.6	8.9	12.6	12.4	6635	6235	6245	6235	15	14	11	12	2.09	2.45	2.66	2.5	124	118	117	116
47	49	F	A	12.3	11.4	10.4	10.3	6805	6240	6860	5950	11	12	12	11	2.35	2.49	2.56	2.54	133	140	145	132
48	60	F	A	12.4	9.5	11.6	12.1	5813	5800	6100	6025	10	11.5	11	11	2.98	2	2.5	3.1	95	112	105	110
49	51	F	A	10.4	11.5	12	12.2	7440	6980	6560	5890	9.5	9.5	11	11.5	2.15	2.56	2.65	2.35	140	142	150	135
50	45	F	A	9.6	10.2	11.5	11	6965	7503	7500	6010	7.5	8	11.5	9	2.86	2.58	2.65	2.95	124	127	120	122
51	34	F	A	11.5	9.5	9.6	9.5	5698	5632	6450	6235	12	11.5	9	9.5	2.15	2.06	2.45	2.5	120	118	112	119
52	54	F	A	9	8.3	11	10.2	6835	6855	6250	6240	9.5	9.5	9.5	10.5	2.3	2.12	2.54	2.65	124	127	121	117
53	60	F	A	11.6	11.3	11.6	11	6685	7000	6500	5800	13	12.5	9	9.5	2.65	2.14	2.25	2.25	125	130	135	126
54	55	F	A	10.8	10.4	11	11.3	5866	6020	7500	6980	8.4	9	11	9	2.65	2.8	2.9	3.5	128	120	129	121
55	31	F	A	9.6	10	12	11.5	6854	6505	6500	7503	12	11	10	9	2.5	2.3	3.12	2.75	126	132	140	144
56	47	M	A	11.3	11.4	10.6	10.4	9786	8450	6850	6780	13.5	12	13.5	10.6	2.8	2.56	2.35	2.15	121	113	116	120
57	40	F	A	9.9	9.3	12.3	12.9	6635	6245	7500	6500	11.4	12	12.5	10.8	2.5	2.4	2.46	2.5	125	134	143	128
58	27	F	B	10.8	10.4	12.4	12.8	7789	6865	7450	6820	11	12.5	12	13.5	2.65	2.35	2.55	2.75	124	126	139	137
59	25	F	B	9.5	9.5	11.1	10.2	5762	6100	6350	5470	10.5	9	11.5	9	3.5	3.45	3.55	3.25	122	106	128	123
60	38	M	B	10.2	8.6	10.2	11.5	6856	6560	7200	7450	9.5	10	11	9.5	1.75	1.95	1.9	1.95	112	123	126	127
61	41	F	B	14.8	11.3	10.5	10.5	8869	7500	5860	7580	9.6	12	10	10	2.15	2.56	2.65	2.45	114	127	132	118

S.No	Age	Sex	Rx group	Hemoglobin(g/dl)				Total leukocyte count(cells/cumm)				ESR(mm/hour)				Platelet count (lakhs/cumm)				Blood sugar(mg/dl)			
62	45	F	B	12.3	11.4	11	9.1	6860	6950	5690	7000	12	8.8	11.5	9.5	2.86	2.58	2.65	2.5	118	124	126	122
63	29	F	B	12.4	11.4	10	9	6758	6560	6760	5840	13	11	10.5	11	2.15	2.06	2.45	2.25	121	123	127	124
64	51	M	B	11	10	11.4	9.8	6790	6800	6720	6620	11	9.5	9.5	10	2.3	2.12	2.54	2.65	113	124	110	112
65	54	F	B	12	11.1	9.3	9.9	6000	6450	5965	6540	13	9	10	14	2.65	2.14	2.25	2.55	134	122	135	121
66	56	F	B	9.5	10.2	10.4	8.9	6025	6250	5600	7950	12	12	11	12	1.95	2.15	1.95	2	126	112	122	135
67	52	M	B	9.3	10.5	10.5	10.1	6680	6500	6680	6020	10	9.5	15	14	2.55	2.34	2.3	2.54	106	114	119	129
68	44	F	B	12	11	8.3	11.2	7850	7500	6420	6600	9	9.5	9.5	10	3.05	3.4	2.55	3	139	124	127	124
69	34	F	B	11.3	10	11.3	10.5	6568	6500	7600	8560	10	9.5	8	13	2.09	2.45	2.66	2.5	128	112	124	144
70	39	M	B	10.6	12.3	10.4	9.8	6803	6850	7590	7750	9.5	13	7.5	11	2.35	2.49	2.56	2.09	126	121	123	112
71	47	F	B	10.7	11.3	10.4	11.5	8960	7500	8450	5860	9.5	8.4	9.8	10	2.98	2	2.5	2.25	90	112	97	106
72	50	F	B	8.9	9.9	10.6	9.1	6862	6425	7650	5450	12.5	14	10	9.5	2.23	2.35	3.01	3.15	124	115	120	122
73	48	M	B	9.2	11.2	12.3	12	7861	7600	6450	5860	8.5	11	15	12	2.09	2	2.15	2.25	110	102	105	96
74	53	F	B	13	8.6	12.4	9.2	7798	7596	6250	5690	11	9.6	11	11	2.3	2.56	2.02	2	120	126	114	94
75	57	M	B	8.8	12	10.4	12.2	8960	8450	6500	5420	10	9	10	10.5	2.65	2.25	2.3	2.85	135	136	122	125
76	55	F	B	11.2	11.2	9.6	9.5	6790	6800	7500	7805	10	10	9.5	10	2.45	2.64	2.55	2.05	102	86	94	88
77	45	M	B	11.6	11.6	11.5	10	6000	6450	6500	7830	12.5	12	8.6	13.5	1.6	1.9	2	1.6	98	110	106	120
78	47	M	B	8.9	8.9	10.2	11	6025	6250	9000	7650	11	8.8	9	9.5	3.05	2.35	2.8	3.22	136	140	144	128
79	35	M	B	10.6	10.6	9.5	9.6	6680	6500	7700	6860	10	11	12	12	2.63	2.56	2.4	2.2	143	134	136	140
80	50	F	B	10	10	11.9	10.6	6522	6450	7580	7790	10	9.5	9	11	2.35	2.35	3.5	1.9	118	127	127	121
81	43	M	B	8.2	8.2	10.3	11.5	6545	6820	7560	5790	9.5	9	9	10.5	1.95	2.4	2.4	2.35	117	135	142	136
82	37	F	B	7	7	9.8	9.5	6021	6920	6950	6700	9.5	12	10.6	10	2.78	2.99	2.9	2.75	124	126	118	128
83	50	M	B	8.9	8.9	10.2	10	7102	6895	6300	5865	13	10.8	11.2	9	2.54	2	2.01	2.45	102	114	120	108
84	45	M	B	9.8	9.8	12.5	11.2	6720	6456	9020	5865	8.4	13.5	13.5	11	2.25	2.5	2.15	2.5	126	132	136	128
85	50	M	B	10.2	10.2	11.5	9.5	6800	6765	7520	6860	14	9	9.5	12	2.5	2.8	2.12	2.5	130	128	132	138
86	46	F	B	12.5	12.5	9	12.5	6750	6720	6800	6800	11	9.8	12	12	2.29	2.23	2.3	3.2	136	122	121	127
87	31	F	B	11.5	11.5	9.6	11.7	6400	5965	5750	6790	9.6	8	11	12.5	2.85	2.36	3.2	2.6	122	126	124	129
88	42	F	B	9	9	8.5	11.8	5862	5600	6540	6240	8.6	12.5	10.5	9.5	3	2.56	2.2	3.25	104	96	94	86
89	45	M	B	9.6	9.6	10.6	11.4	6586	6685	7950	5800	11	12	10	10	2.46	2.3	1.7	1.95	109	112	102	118
90	59	M	B	8.5	8.5	10.7	9.6	6542	6400	6020	6450	12	15	9	9	2.55	2.45	2.65	2.2	115	118	121	105
91	40	F	B	14	14	8.9	10.5	5478	5500	6750	6820	9	11	11	8	3.05	2.35	2.02	3	82	112	96	93
92	52	F	B	8.5	8.5	9.2	11.2	7452	7900	6860	6920	14	8.5	12	8.5	2.63	2.56	2.36	3.1	112	121	126	123
93	55	F	B	9.6	9.6	13	11.6	7582	7600	4960	6895	10	11	12	10.5	2.35	2.35	2.55	2.3	145	150	148	143
94	58	F	B	11.3	11.3	8.8	11.5	7003	6800	5650	6456	13	10	12.5	11	3	2.56	2.9	2.74	125	126	128	126
95	59	M	B	9.9	9.9	11.2	10.5	5021	5896	7560	6765	11	10	9.5	11	2.5	2.12	2.5	2.55	138	132	128	126
96	55	F	B	10	10	11.6	13	6245	6010	6950	6720	10	12.5	10	10	2.29	2.65	3.24	2.35	120	127	126	124
97	35	F	B	8.2	8.2	8.9	11.5	7520	7450	5620	5965	9.5	11	9	11.5	2.04	2.02	3.02	3.4	136	140	144	132
98	57	F	B	9.8	9.8	10.6	10.2	6520	6350	6500	5600	12	11	8	10.5	2.23	2.36	2.5	3	126	123	112	121
99	54	F	B	11.6	11.6	10	10.4	6950	7200	7450	6685	11	13	8.5	9.5	2.1	2.4	2.35	2.15	148	143	145	150
100	51	F	B	11	11	8.2	12	6032	5862	7420	6400	10.5	9.5	10.5	11	2.5	3.5	2.46	2.65	128	126	125	126
101	40	F	B	12	12	7	9.8	5965	5698	5620	5500	10	9.5	11	10	2.8	2.4	2.55	2.45	127	126	126	120
102	60	F	B	9.8	9.8	8.9	9.5	5810	5800	6200	7900	10.5	11	11.5	13.8	2.56	2.9	3.05	3	140	144	124	136
103	55	F	B	12.6	12.6	9.8	9.6	7440	6980	6045	7600	10	12	10	11.5	2.8	2.01	2.3	2.15	123	112	132	126
104	23	M	B	10.4	10.4	10.2	10.7	6965	7500	5800	6800	13.5	11	8	9	2.3	2.15	2.45	2.4	112	109	102	118
105	27	F	B	11.6	11.6	12.5	11.6	5690	5630	6980	5896	9.5	11	9.5	9	2.55	2.12	2.35	2.5	118	115	121	105
106	49	F	B	12	12	11.5	10.2	5860	6020	7500	6010	12	11.5	11	9	2.14	2.3	2.56	3	112	118	96	93
107	60	M	B	11.5	11.5	9	9.5	6850	6500	5630	7450	11	9	12	9	2.34	3.2	2.35	1.9	124	118	128	126
108	52	F	B	9.6	9.6	9.6	12.5	9780	8450	6020	6350	10.5	9.5	9.8	9.5	1.7	2.2	2.15	2	102	120	108	114
109	48	F	B	11	11.3	8.5	11	6630	6240	6500	7200	10	10.5	10	9	1.6	1.7	2.2	2.01	126	136	128	132
110	21	M	B	11.6	11.6	14	11	7450	6860	8450	5862	13.5	9.5	15	10	2.29	2.65	3.24	3.15	125	118	128	126
111	35	F	B	11	11	8.5	11.3	6350	6750	6240	5698	9.5	9	11	10	2.04	2.02	3.02	3	92	104	102	106
112	60	F	B	12	12	9.6	12.5	7200	6790	6860	6950	12	11	10	9	2.23	2.36	2.5	2.9	112	115	111	105
				10.6	11.3	14	11.7	5870	6000	6750	6560	11	11	9.5	8	2.09	2.55	2.8	2.65	126	132	136	128

S.No	Age	Sex	Rx group	Blood urea(mg)				serum creatinine				SGOT (U/L)				SGPT (U/L)				serum electrolytes(sodium)				serum electrolytes(potassium)			
1	45	F	A	0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12	0	4	8	12
2	41	F	A	21	20	23	24	0.69	0.8	0.79	0.76	12	15	12	16	25	16	20	17	136	135	136	130	3.5	3.5	3.6	3.8
3	53	M	A	20	22	20	22	0.73	0.82	0.65	0.65	15	13	13	13	25	15	18	17	136	139	144	142	3.8	4	4.2	3.9
4	35	M	A	21	23	22	22	0.62	0.73	0.63	0.71	13	16	14	16	26	18	23	22	138	140	142	138	3.7	3.8	4	3.5
5	21	F	A	21	20	22	20	0.63	0.69	0.8	0.72	18	18	18	16	22	19	16	18	130	136	136	139	3.5	4.1	4.3	4.2
6	59	M	A	22	24	23	20	0.7	0.78	0.76	0.73	20	15	11	14	21	14	18	20	140	143	141	138	3.6	3.5	3.9	3.7
7	24	F	A	21	22	21	22	0.76	0.64	0.74	0.69	12	16	18	15	27	15	22	21	142	143	138	136	4.4	4.2	4	4.4
8	57	F	A	20	22	24	21	0.65	0.77	0.76	0.78	13	12	16	18	16	19	18	15	144	136	135	144	3.7	3.6	4	3.8
9	38	F	A	24	20	20	22	0.71	0.79	0.76	0.64	13	11	12	12	19	14	23	20	135	136	142	140	5	3.6	4.5	4.3
10	52	F	A	21	20	23	23	0.72	0.62	0.71	0.77	15	12	14	15	28	15	13	20	141	144	136	139	4.8	4.7	4.3	4.2
11	45	F	A	25	22	25	20	0.73	0.69	0.79	0.79	14	13	11	10	17	16	19	19	139	138	135	141	4.6	4.9	4.2	4.4
12	54	F	A	23	21	21	21	0.69	0.73	0.77	0.69	10	13	18	19	16	13	15	17	136	142	135	136	4	3.8	3.9	4.1
13	27	F	A	25	22	23	20	0.78	0.81	0.72	0.73	12	10	19	20	24	18	17	19	143	144	136	141	4.2	4.1	5	3.8
14	32	F	A	21	23	22	23	0.64	0.73	0.73	0.62	11	14	16	16	18	20	15	16	144	135	136	144	3.7	4.4	4.1	4.2
15	55	F	A	22	20	24	27	0.77	0.75	0.69	0.63	18	14	13	13	16	18	16	18	142	135	141	138	4.4	3.7	3.5	3.8
16	50	M	A	21	23	21	21	0.79	0.69	0.78	0.7	10	15	12	16	15	19	16	15	137	136	138	142	3.9	4	4.2	3.7
17	48	F	A	20	22	20	22	0.62	0.75	0.64	0.76	13	21	18	12	13	15	15	19	142	138	136	144	3.5	4.5	3.8	5
18	56	F	A	25	23	23	20	0.69	0.8	0.79	0.65	12	20	19	14	13	14	19	15	136	139	144	144	4.2	4.3	3.9	4.8
19	58	F	A	20	22	27	21	0.73	0.82	0.65	0.71	12	13	13	14	19	19	19	16	135	138	138	138	4.3	4.2	3.6	3.8
20	29	F	A	21	21	22	24	0.79	0.72	0.78	0.77	14	12	12	17	15	20	18	14	143	138	136	142	3.9	3.9	4.5	4.1
21	38	M	A	22	20	20	21	0.7	0.62	0.73	0.72	16	15	15	16	14	16	15	12	135	141	140	139	4.1	4.2	3.5	4.4
22	44	M	A	21	23	20	24	0.66	0.63	0.82	0.73	17	13	14	14	20	16	16	13	143	136	135	136	4	4.3	3.6	3.7
23	47	F	A	22	21	22	20	0.74	0.7	0.71	0.69	10	14	15	16	19	19	17	17	142	143	137	136	3.5	4.2	3.8	4.8
24	55	F	A	20	20	21	21	0.73	0.76	0.76	0.78	14	12	18	17	13	18	15	19	141	144	138	138	4	3.8	4.3	4.6
25	59	F	A	22	24	22	22	0.79	0.62	0.74	0.64	15	15	12	18	15	19	13	12	140	145	139	137	3.8	4.3	4.2	4
26	39	F	A	20	25	20	23	0.81	0.69	0.76	0.79	13	15	13	16	17	20	21	21	144	135	138	142	4.1	3.9	4.4	4.2
27	21	M	A	21	23	24	20	0.73	0.73	0.62	0.65	13	16	20	15	15	21	15	13	138	137	141	141	4.1	4.5	4.1	3.7
28	52	M	A	22	20	21	20	0.75	0.79	0.73	0.74	12	18	13	10	17	16	16	15	136	138	136	140	4.4	4.3	4.4	4.4
29	55	M	A	24	20	20	22	0.69	0.7	0.75	0.75	16	10	11	12	15	13	17	16	144	135	135	143	3.7	4.2	3.7	3.9
30	25	F	A	21	24	21	21	0.75	0.66	0.69	0.72	15	13	14	14	21	16	15	17	138	136	143	144	4	3.9	4	3.5
31	50	F	A	22	22	22	22	0.8	0.74	0.75	0.76	21	11	12	15	15	13	13	19	136	139	135	145	3.9	3.5	3.9	4.2
32	40	F	A	24	20	21	22	0.82	0.62	0.63	0.74	20	14	16	15	15	16	20	15	140	141	143	135	3.5	3.6	4.1	3.8
33	60	M	A	21	22	20	20	0.72	0.69	0.82	0.76	18	13	10	14	16	14	16	22	135	140	139	136	3.6	3.8	4	4.3
34	43	F	A	20	23	24	23	0.76	0.73	0.72	0.73	13	12	18	16	14	13	15	18	137	144	136	143	3.8	3.6	3.5	3.9
35	50	F	A	23	25	21	22	0.74	0.79	0.76	0.73	19	15	19	14	19	15	18	16	138	138	136	144	3.9	4.2	4	4.4
36	23	F	A	27	24	25	22	0.76	0.7	0.71	0.69	16	13	20	12	16	12	19	17	139	136	138	145	3.5	4	3.8	4.5
37	35	M	A	21	20	23	24	0.73	0.66	0.79	0.73	13	18	11	14	15	11	14	23	135	139	137	135	4.2	4.3	4.1	3.5
38	60	M	A	22	23	25	23	0.73	0.74	0.62	0.62	15	15	12	15	13	15	15	20	136	144	137	142	3.8	4	3.6	3.7
39	48	M	A	20	22	21	20	0.79	0.76	0.63	0.63	13	16	13	16	17	18	19	16	138	138	142	135	4.3	4.5	3.6	5
40	50	M	A	21	22	22	22	0.74	0.74	0.81	0.7	16	15	19	16	15	18	14	21	137	136	136	137	4.2	4.3	4.7	4.8
41	35	F	A	24	22	21	21	0.76	0.78	0.76	0.76	15	16	13	15	16	21	15	19	136	140	135	138	4.4	4.2	4.9	4.6
42	60	F	A	20	23	20	24	0.74	0.72	0.75	0.65	15	18	14	13	13	19	16	18	141	144	136	139	4.7	4.1	5	4.5
43	57	F	A	20	21	21	22	0.76	0.77	0.69	0.71	16	16	16	14	13	18	13	17	135	138	138	138	4.9	3.5	4.8	4.3
44	53	F	A	23	24	21	24	0.82	0.76	0.75	0.72	18	15	18	15	16	17	18	21	136	136	130	137	3.8	3.7	3.8	4.3
45	27	M	A	22	20	22	23	0.77	0.72	0.8	0.66	12	16	15	13	19	21	20	16	136	143	140	142	4.1	4.1	4.1	3.9
46	37	F	A	23	21	21	20	0.74	0.71	0.64	0.74	17	11	14	14	13	16	18	18	144	135	137	136	5	4.5	4.8	4.6
47	49	F	A	20	22	20	22	0.75	0.81	0.72	0.75	13	14	16	14	13	18	19	21	142	143	135	135	4.1	4.2	3.5	3.6
48	60	F	A	23	22	20	21	0.72	0.74	0.62	0.72	16	12	18	13	15	20	15	19	138	139	139	144	3.5	3.8	3.8	4
49	51	F	A	24	24	21	24	0.76	0.77	0.69	0.76	15	13	19	14	17	22	14	18	136	135	136	138	3.5	3.9	4.2	4.3
50	45	F	A	23	23	22	23	0.74	0.73	0.64	0.74	16	16	20	15	12	13	19	17	143	136	136	136	4	3.6	3.8	3.5
51	34	F	A	20	20	21	27	0.76	0.71	0.77	0.76	15	15	11	16	14	16	20	21	144	136	138	143	4.5	3.6	4.3	4
52	54	F	A	22	22	22	21	0.73	0.77	0.79	0.73	14	11	15	13	15	14	16	16	145	144	137	135	4.3	4.7	4.2	3.8
53	60	F	A	22	21	20	22	0.73	0.76	0.62	0.73	11	14	16	16	12	13	16	18	135	136	138	143	4.2	4.9	4.4	4.1
54	55	F	A	23	24	23	21	0.79	0.74	0.63	0.79	14	12	18	15	14	14	19	20	136	143	140	139	4.1	5	4.7	3.6
55	31	F	A	21	24	22	22	0.74	0.76	0.64	0.74	12	14	15	16	15	11	18	22	138	144	135	138	3.5	4.8	4.9	4.3
56	47	M	A	24	22	23	24	0.76	0.72	0.76	0.76	13	16	16	18	16	15	19	13	130	145	137	135	4.1	3.8	3.5	3.9
57	40	F	A	20	22	25	21	0.74	0.77	0.71	0.74	15	15	18	16	18	13	20	16	140	135	138	141	3.9	4.1	4.2	4.4
58	27	F	B	21	20	22	20	0.76	0.74	0.79	0.76	14	15	16	16	15	10	21	14	143	142	136	136	4.5	4.1	3.7	4.1
59	25	F	B	25	20	22	22	0.82	0.75	0.71	0.69	16	14	13	13	12	19	17	18	135	136	143	143	4.3	4.4	4.4	4.4
60	38	M	B	20	23	20	23	0.77	0.72	0.68	0.75	16	13	15	17	13	18	21	20	143	135	144	137	4.2	3.7	3.9	3.7
61	41	F	B	22	27	20	20	0.74	0.76	0.69	0.73	13	12	13	12	14	19	11	21	139	135	145	142	3.5	3.5	4.2	3.9

S.No	Age	Sex	Rx group	Blood urea(mg)				serum creatinine				SGOT (U/L)				SGPT (U/L)				serum electrolytes(sodium)				serum electrolytes(potassium)			
62	45	F	B	23	21	22	24	0.72	0.73	0.78	0.79	16	17	16	14	10	19	19	15	135	136	135	136	3.6	3.5	3.8	4.1
63	29	F	B	20	22	21	22	0.7	0.73	0.64	0.74	15	13	15	13	12	15	20	16	139	140	143	135	3.8	3.6	4.3	4
64	51	M	B	24	20	24	25	0.72	0.79	0.77	0.76	12	16	12	14	14	18	18	12	136	136	135	140	3.6	3.8	4.6	3.5
65	54	F	B	22	21	23	21	0.77	0.74	0.79	0.74	14	16	13	16	18	17	15	17	138	143	144	144	4.2	3.9	4.4	4
66	56	F	B	22	24	20	22	0.76	0.76	0.62	0.76	16	13	16	12	15	19	16	16	137	144	139	138	4.3	4.2	4.7	4.8
67	52	M	B	20	20	22	21	0.72	0.74	0.63	0.82	15	16	15	13	16	15	12	13	142	145	143	136	4.2	4.4	4.9	4.6
68	44	F	B	20	22	21	20	0.71	0.71	0.72	0.77	13	12	14	14	13	17	13	19	136	135	135	139	3.9	4.1	3.8	4
69	34	F	B	22	24	20	25	0.73	0.72	0.77	0.7	14	17	13	18	13	16	19	15	135	137	143	136	5	4.4	4.1	4.2
70	39	M	B	21	23	21	20	0.78	0.73	0.76	0.66	12	14	17	11	12	15	19	19	139	141	140	141	4.2	3.7	3.6	3.6
71	47	F	B	22	20	22	22	0.73	0.69	0.72	0.74	17	16	12	12	17	20	17	17	136	136	135	140	3.9	3.9	4.5	4.5
72	50	F	B	22	22	21	21	0.82	0.78	0.71	0.62	13	14	16	12	15	21	21	21	140	141	137	144	4.2	4.1	3.5	3.5
73	48	M	B	20	21	20	22	0.71	0.64	0.81	0.69	16	12	16	13	11	10	16	16	138	144	138	138	4.3	4	3.6	3.6
74	53	F	B	23	24	24	20	0.76	0.77	0.74	0.73	15	17	21	16	19	16	14	14	137	138	135	136	4.2	3.5	3.8	3.8
75	57	M	B	22	20	23	23	0.77	0.79	0.77	0.79	15	14	13	15	20	20	20	20	142	136	139	137	3.5	4	3.5	4.2
76	55	F	B	23	20	21	22	0.72	0.62	0.73	0.7	14	13	12	14	18	21	21	21	144	138	136	142	3.5	4.8	3.6	3.8
77	45	M	B	22	23	25	23	0.73	0.7	0.71	0.74	13	17	15	16	12	14	18	18	138	139	136	136	3.6	4.6	3.8	4.3
78	47	M	B	21	22	23	25	0.69	0.75	0.64	0.76	17	18	18	17	16	12	17	17	136	138	141	136	3.8	4	3.7	4.5
79	35	M	B	20	23	25	23	0.78	0.72	0.77	0.73	12	17	16	16	12	17	19	19	135	138	136	141	3.7	3.6	3.9	4
80	50	F	B	23	23	21	20	0.64	0.77	0.79	0.73	14	10	13	17	13	15	18	18	142	143	136	140	4.1	3.8	4.4	4.5
81	43	M	B	20	24	22	22	0.77	0.76	0.62	0.79	16	14	14	16	17	11	11	11	136	135	143	144	4.2	3.6	4.5	4.3
82	37	F	B	21	23	21	22	0.72	0.72	0.72	0.74	14	16	15	14	16	19	14	14	135	143	144	140	3.9	4.2	4.4	4.6
83	50	M	B	22	20	20	23	0.76	0.71	0.77	0.76	15	21	17	18	15	20	16	16	135	139	145	137	4	4.1	3.5	4.3
84	45	M	B	24	21	25	21	0.63	0.73	0.74	0.74	12	20	15	11	20	18	15	15	136	141	135	135	4.9	4.5	3.6	4.4
85	50	M	B	21	20	20	24	0.7	0.74	0.75	0.76	17	13	12	12	21	12	15	15	141	140	135	144	4.1	3.8	4	3.9
86	46	F	B	22	21	21	20	0.76	0.73	0.62	0.82	14	12	17	15	15	16	17	17	136	144	139	137	3.8	4.1	4.2	5
87	31	F	B	23	22	22	21	0.65	0.78	0.69	0.79	15	15	17	16	16	12	12	12	141	138	136	142	4.3	3.6	3.6	4.2
88	42	F	B	20	21	21	20	0.71	0.73	0.73	0.62	16	15	14	12	17	13	13	13	144	136	142	136	3.9	4.5	4.5	3.9
89	45	M	B	22	20	22	23	0.72	0.82	0.79	0.63	18	16	16	13	18	11	17	17	138	135	143	135	4.1	3.5	3.5	4.2
90	59	M	B	20	24	23	27	0.73	0.71	0.7	0.72	17	18	14	17	17	18	16	16	138	144	138	136	3.8	3.6	4.1	3.5
91	40	F	B	22	21	20	22	0.69	0.76	0.66	0.77	10	12	15	16	19	11	11	11	135	140	139	140	4.3	3.8	4	3.6
92	52	F	B	23	25	22	20	0.78	0.77	0.74	0.76	14	16	13	17	15	14	16	16	137	144	136	144	4.5	3.7	3.5	3.8
93	55	F	B	20	23	22	20	0.64	0.76	0.73	0.72	15	21	13	16	17	16	15	15	138	138	136	138	4	3.9	3.6	3.7
94	58	F	B	24	25	23	21	0.77	0.73	0.79	0.8	13	13	12	13	16	15	16	16	139	136	138	136	4.5	4.4	3.8	4.1
95	59	M	B	22	21	21	20	0.79	0.73	0.81	0.64	12	12	16	15	15	15	17	17	138	140	137	141	3.6	3.6	3.9	4.1
96	55	F	B	22	22	24	21	0.62	0.79	0.72	0.72	16	15	16	10	20	17	18	18	145	143	136	136	4.5	3.8	4.1	3.8
97	35	F	B	20	21	20	21	0.69	0.74	0.73	0.62	21	15	21	12	16	12	20	20	135	138	138	141	3.5	4.2	4	4.3
98	57	F	B	20	20	23	22	0.82	0.76	0.69	0.69	20	16	16	14	13	13	21	21	143	139	139	144	4.1	3.8	3.5	3.9
99	54	F	B	22	21	20	21	0.79	0.76	0.78	0.64	18	13	12	15	19	17	12	12	143	141	138	138	3.8	3.5	3.7	4.5
100	51	F	B	21	23	21	20	0.72	0.71	0.64	0.77	13	16	17	13	15	16	16	16	138	144	137	142	3.7	3.6	3.9	4
101	40	F	B	22	20	22	24	0.81	0.79	0.77	0.73	12	11	18	14	18	11	12	12	139	138	142	136	4.1	3.8	4.4	4.5
102	60	F	B	22	22	22	21	0.73	0.78	0.82	0.69	15	12	18	16	12	10	17	21	141	141	136	135	4.1	3.9	3.6	3.6
103	55	F	B	24	20	21	23	0.73	0.64	0.71	0.82	15	13	18	13	22	18	17	16	136	136	135	135	4.4	4.2	3.8	3.9
104	23	M	B	21	22	20	20	0.79	0.77	0.76	0.79	16	18	20	17	18	20	13	18	138	141	135	136	3.5	3.7	4	4
105	27	F	B	20	23	24	22	0.74	0.79	0.77	0.72	13	20	17	16	16	21	15	21	139	144	139	138	4.7	4.8	4.5	4.6
106	49	F	B	23	25	21	22	0.76	0.62	0.76	0.81	16	18	17	13	16	15	17	19	138	138	136	139	4.2	4.3	4	4.5
107	60	M	B	27	24	25	23	0.74	0.63	0.73	0.73	11	13	10	19	13	16	14	18	140	141	136	138	4.5	4.4	3.8	4.1
108	52	F	B	21	20	23	21	0.71	0.72	0.73	0.73	12	12	16	12	15	12	18	17	137	140	135	136	4.3	4.5	3.6	4.2
109	48	F	B	22	23	25	24	0.72	0.77	0.79	0.76	13	15	17	13	16	17	15	21	136	144	137	139	4.6	4.4	4.2	3.9
110	21	M	B	21	23	21	20	0.65	0.78	0.69	0.79	18	13	17	14	14	16	18	16	143	138	138	136	4.3	3.5	4.1	4
111	35	F	B	22	20	20	23	0.71	0.73	0.73	0.62	11	18	20	16	18	13	16	18	144	136	139	136	4.4	3.6	4.5	4.9
112	60	F	B	24	21	25	23	0.64	0.77	0.79	0.73	14	14	20	18	20	19	17	20	145	135	138	138	4.3	4.4	3.7	3.9
				21	20	20	25	0.77	0.76	0.62	0.79	13	16	12	11	21	15	17	22	135	136	139	137	4	4.5	3.5	4.7