

DISSERTATION ON

**“A STUDY ON THE EFFECT OF PITAVASTATIN IN PATIENTS
WITH ACTIVE RHEUMATOID ARTHRITIS TREATED
AT A RURAL TERTIARY CARE HOSPITAL”**

Dissertation submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

In partial fulfilment of the regulations

For the award of the degree of

M.D. PHARMACOLOGY - BRANCH VI



**CHENNAI MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE,
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**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY,
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APRIL 2017

CERTIFICATE

This is to certify that the dissertation entitled **“A STUDY ON THE EFFECT OF PITAVASTATIN IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS TREATED AT A RURAL TERTIARY CARE HOSPITAL”** by **Dr. T.SUDHANANTHINI**, Postgraduate in Pharmacology (2014 – 2017), is a bonafide research work carried out under our direct supervision and guidance and is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai for M.D. Degree Examination in Pharmacology, Branch IV, to be held in **April 2017**. The period of study was from 2014 -2017.

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I, **Dr.T.SUDHANANTHINI** solemnly declare that the dissertation title **“A STUDY ON THE EFFECT OF PITAVASTATIN IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS TREATED AT A RURAL TERTIARY CARE HOSPITAL”** was done by me at Chennai Medical College Hospital and Research Centre, Irungalur ,Trichy, under the supervision and guidance of my Professor and Head of the Department, **Dr.S.Manickavasagam .M.D.,**

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University, towards the partial fulfilment of requirement for the award of M.D. Degree (Branch –VI) in Pharmacology.

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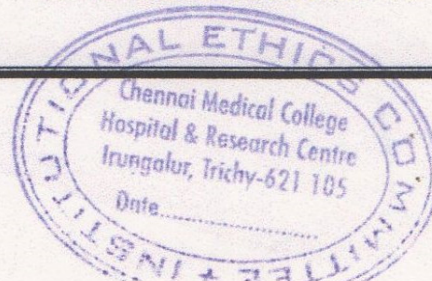
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INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder, autoimmune in nature that predominately affects synovial joints. "Being a crippling disease it is a leading cause of disability, that often reduces the quality of life and impairs patient's ability to work".¹

"The Worldwide prevalence of RA ranges between 2.0 to 10.7 per 1,000 based on the American College of Rheumatology (ACR) criteria. In Indian patients, the disease prevalence is approximately 0.75% and male: female ratio is 1:3. The peak incidence of RA occurs in individuals aged 40 – 60 years".²

"The clinical hallmark of RA is polyarticular synovial inflammation of peripheral joints - usually in the hands (metacarpophalangeal joints and proximal interphalangeal joints), manifest as pain, stiffness, and some degree of reversible joint damage that progresses to irreversible joint damage, deformity, and disability. The immunological mediators which precede the clinical manifestations of RA include Rheumatoid Factor (RF) and anti-citrullinated protein antibody (ACPA)".^{3,4}

"The primary goal of managing the patient with rheumatoid arthritis is to maximize long-term health-related quality of life and to achieve remission as soon as possible. Pharmacotherapy of RA involves Symptom-modifying

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INTRODUCTION

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ABBREVIATIONS

RA	-	Rhematoid Arthritis
DAS	-	Disease Activity Score
RF	-	Rheumatoid Factor
Anti-CCP	-	Antibodies to Cyclic Citrulinated Peptide
ESR	-	Erythrocyte Sedimentation Rate
CRP	-	C Reactive Protein the
ACR	-	American College of Rheumatology
EULAR	-	European League Against Rheumatism
ICAM	-	Intra Cellular Adhesion Molecule
TNF- α	-	Tumour Necrosis Factor-Alpha
IL	-	Interleukin
MMP	-	Matrix Metallo Proteinase
Cat K	-	Cathepsin K
RANKL	-	Receptor activator of NF- κ B ligand
DMARD	-	Disease Modifying Anti Rheumatoid Drugs
MTX	-	Methotrexate

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disorder, autoimmune in nature that predominately affects synovial joints. Being a crippling disease it is a leading cause of disability, that often reduces the quality of life and impairs patient's ability to work.¹

The Worldwide prevalence of RA ranges between 2.0 to 10.7 per 1,000 based on the American College of Rheumatology (ACR) criteria. In Indian patients, the disease prevalence is approximately 0.75% and male: female ratio is 1:3. The peak incidence of RA occurs in individuals aged 40 – 60 years.²

The clinical hallmark of RA is polyarticular synovial inflammation of peripheral joints - usually in the hands (metacarpophalangeal joints and proximal interphalangeal joints), manifest as pain, stiffness, and some degree of reversible joint damage that progresses to irreversible joint damage, deformity, and disability. The immunological mediators which precede the clinical manifestations of RA include Rheumatoid Factor (RF) and anti-citrullinated protein antibody (ACPA).^{3,4}

The primary goal of managing the patient with rheumatoid arthritis is to maximize long-term health-related quality of life and to achieve remission as soon as possible. Pharmacotherapy of RA involves Symptom-modifying antirheumatic drugs (SMARDs) like NSAIDs (Non Steroidal Anti Inflammatory Drugs), Disease modifying antirheumatic drugs (DMARDs) - small molecule non biological agents, biological agents and Glucocorticoids.⁵

RA, if not treated properly may leads to permanent damage to the joints and is the number one cause of early retirement, disability payments, and loss of employment. It is a serious condition characterized by destructive polyarthritis and damages major organs including the skin, eye, heart, lungs, renal, nervous and gastrointestinal systems. The cardiac complications are directly proportional to the severity of the disease which include atherosclerosis, arterial stiffness, risk for myocardial infarction, myocarditis with presence of rheumatoid nodules and myocardial fibrosis.⁶

The pleiotropic effects of statins like anti-inflammatory, immune modulating and anabolic effects, strongly support a potential role of these drugs in the prevention and/or treatment of cardiovascular risk factors and joint damage associated with RA.⁷

Pitavastatin, the seventh statin reduces elevated levels of total cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, and triglycerides and increases high-density lipoprotein cholesterol levels.⁸ It appears to exert a number of beneficial effects on patients at risk of cardiovascular events by reducing the size and composition of atherosclerotic plaques, improvements in cardiovascular function, and improvements in markers of inflammation, oxidative stress, and renal function^{9,10}.

Pitavastatin has anabolic effect on bone and prevents osteoporosis induced by RA. Substantial cardiovascular protection offered by it can reduce cardiovascular morbidity and mortality associated with RA.^{9,10}

Many pivotal studies like TARA trial, JUPITER trial and PATROL trial have demonstrated that Statins have a beneficial role in the management of RA⁷. Only limited number of studies available on the effect of Pitavastatin in RA. Hence this study is structured to evaluate the efficacy and safety of Pitavastatin in patients with active Rheumatoid arthritis.

AIM AND OBJECTIVES

The present study was structured for evaluating the effect of pitavastatin in patients with active rheumatoid arthritis treated at a tertiary care hospital

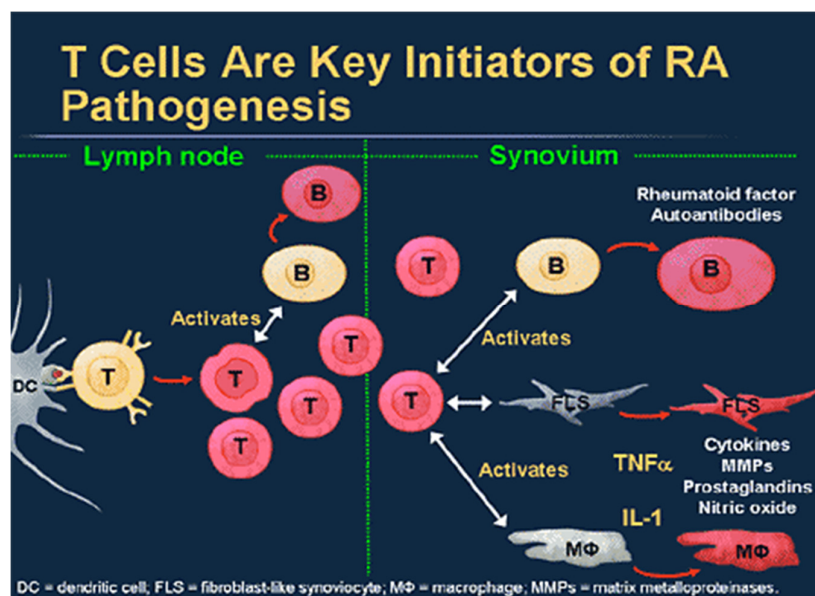
The secondary objectives of the study was to evaluate the reduction in

- (i) Disease activity score
- (ii) Inflammatory markers like Rheumatoid Factor and Antibodies to cyclic citrullinated peptide
- (iii) Acute phase reactants &
- (iv) Improvement in lipid profile.

REVIEW OF LITERATURE

Rheumatoid Arthritis - An overview

Rheumatoid arthritis (RA) is an autoimmune disorder with strong genetic and environmental etiology leading to severe disability and premature mortality.⁴ The pathogenesis of RA comprises of both cellular and molecular mechanisms. Predominant cell types involved in synovial inflammation include activated T cells, B cells monocyte/macrophages and neutrophils. The mediators involved include 1. Receptor activator of NF- κ B ligand (RANKL) and its receptor RANK. 2. Proinflammatory cytokines (e.g., tumour necrosis factor- α (TNF- α)).3. Interleukins 1 (IL-1), IL-6, IL-17, and IL-18). 4. Matrix degrading enzymes (e.g., matrix metalloproteinases (MMPs) 4. CathepsinK (Cat K). Inflammation can induce bone damage and these two processes are linked via common mediators.¹¹



Antigens are typically presented to T cells by B cells via HLA-DR4. The presence of autoantibodies, such as rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA) (tested as anti-cyclic citrullinated peptide [anti CCP]), can precede the clinical manifestation of RA by many years. HLA DR3 and DRH genes are associated with a greater frequency of extra-articular diseases. Hematological abnormalities like anemia (normocytic, normochromic), thrombocytopenia, eosinophilia and raised Erythrocyte Sedimentation Rate (ESR) and raised C- Reactive Protein (CRP) are also present in RA patients. ¹¹

A joint working group of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) in 2010 , developed a new approach for classification of RA. In the new criteria, classification as “definite RA” is based on the confirmed presence of synovitis in at least 1 joint.^{4,5,12} The achievement of a total score of at least 6 (of a possible 10) from the individual scores in four domains .The highest score achieved in a given domain is used for this calculation.

The domains and their values are:

1. Number and site of involved joints :-

- a) 2 to 10 large joints (from among shoulders, elbows, hips, knees, and ankles) = 1 point.

b). 1 to 3 small joints (from among the metacarpophalangeal joints, proximal interphalangeal joints, second through fifth metatarsophalangeal joints, thumb interphalangeal joints, and wrists) = 2 points.

c). 4 to 10 small joints = 3 points.

d). Greater than 10 joints (including at least 1 small joint) = 5 points.

Early bone loss is well evident from decrease in bone mineral density (BMD) in the metacarpal bones and forearm measured by dual X-ray absorptiometry (DXA) and digital X-ray radiometry (DXR) and radiological alterations in patients with early and established RA.¹³

2. Serological abnormality (rheumatoid factor or anti-citrullinated peptide/protein antibody) :-

a). Low positive (above the upper limit of normal [ULN]) = 2 points.

b). High positive (greater than three times the ULN) = 3 points.

3. Elevated acute phase response :-

Erythrocyte sedimentation rate [ESR] or C-reactive protein [CRP]) above the ULN = 1 point.

4. Symptom duration:-

Atleast six weeks=1point.^{5,14}

The synovitis of multiple joints in RA causes widespread pain, and the succeeding destruction of the joints will lead to severe disability affecting of motor functions particularly the fine movements of the hand.¹²It can also affects other organs like lungs, pleura, pericardium, sclera and subcutaneous tissue.³

SIGNS AND SYMPTOMS

The signs and symptoms include pain, swelling, tenderness and warmth around the joint, stiffness following a period of rest mostly in the morning, poor grip strength, tiredness leading to psychological disturbances like irritability and depression, flu-like symptoms, loss of weight and the presence of rheumatoid nodules – fleshy lumps typically seen on hands, feet and elbows. Flare-ups can occur often particularly in the winter , following any systemic illnesses for a few days to a couple of months.⁴

EFFECT OF RA ON BONE AND JOINT

The rheumatoid pannus (neovascularisation) dynamically invades and destroys the underlying cartilage and also the subchondral bone. Angiogenesis is a key event for the expansion of the synovial lining of joints in RA; vascular endothelial growth factor (VEGF) appears to have a essential role. The serum VEGF level is an index of the activity of the disease and a prognostic factor regarding joint destruction. The serum angiopoietin-1 (Ang-

1) level is used as a marker of sustained arthritis. The serum angiopoietin-2 (Ang-2) level may reflect a state of marked angiogenesis.¹

Macrophage-like synoviocytes leads to overproduction of proinflammatory cytokines, Fibroblast-like synoviocytes and causes osteoclast activation a vital process leading to bone erosion. Specific inhibition of osteoclast activation can reduce joint destruction without affecting joint inflammation. Osteoporosis ensues due to reduced mobility, inflammation, and also due to the drugs (steroids).

RA can directly or indirectly affect most organ systems in the body and leads to premature death. RA needs an apt management not only to reduce the impact on joints, but also to focus on the whole body, to reduce morbidity.^{1,4} Extra-articular manifestations of RA ensue in about 40% of patients, occur at any age or at any stage after the onset of the disease, involving the oral, cutaneous, ocular, cardiac, pulmonary, renal, nervous, haematopoietic and gastrointestinal systems.¹⁵

MANAGEMENT

The primary goal of managing rheumatoid arthritis is to prolong the long-term health-related quality of life which can be achieved by reduction of the inflammatory process.¹⁶ The non-pharmacotherapy in RA include aerobic activities, dynamic muscular reinforcement, and therapeutic patient education.¹⁷

Symptomatic management

Pharmacotherapy include Symptom-modifying anti-rheumatic drugs (SMARDs): analgesics (opioid and nonopioid analgesics) to reduce pain, and nonsteroidal anti-inflammatory drugs (NSAIDs) (including “traditional” or nonselective NSAIDs, cyclooxygenase-2 [COX-2] inhibitors to lessen pain and stiffness. Both groups of drugs are widely used to control symptoms of RA. Though there are justifications for using NSAIDs for control of RA symptoms are strong¹⁸ they have lost their historical role as a first-line management because of concerns about their limited effectiveness, inability to modify the long-term course of the disease, and toxic gastrointestinal and cardiac effects.¹⁹

Disease modifying anti rheumatic drugs (DMARDs)

DMARDs are a heterogeneous collection of agents grouped together by use and convention. They arrest or slow down the disease progress by modifying the disease process. Effect may take two weeks to six months to become clinically evident. Generally they have been the mainstay of treatment for rheumatoid arthritis.^{6,20}

These agents are widely classified in to non-biological agents and biological agents. Non biologicals include Methotrexate (MTX), Azathioprine, Sulphasalazine (SSZ), Chloroquine,Hydroxychloroquine (HCQ),Cyclophosphamide, Cyclosporine, Leflunomide and Mycophenolate

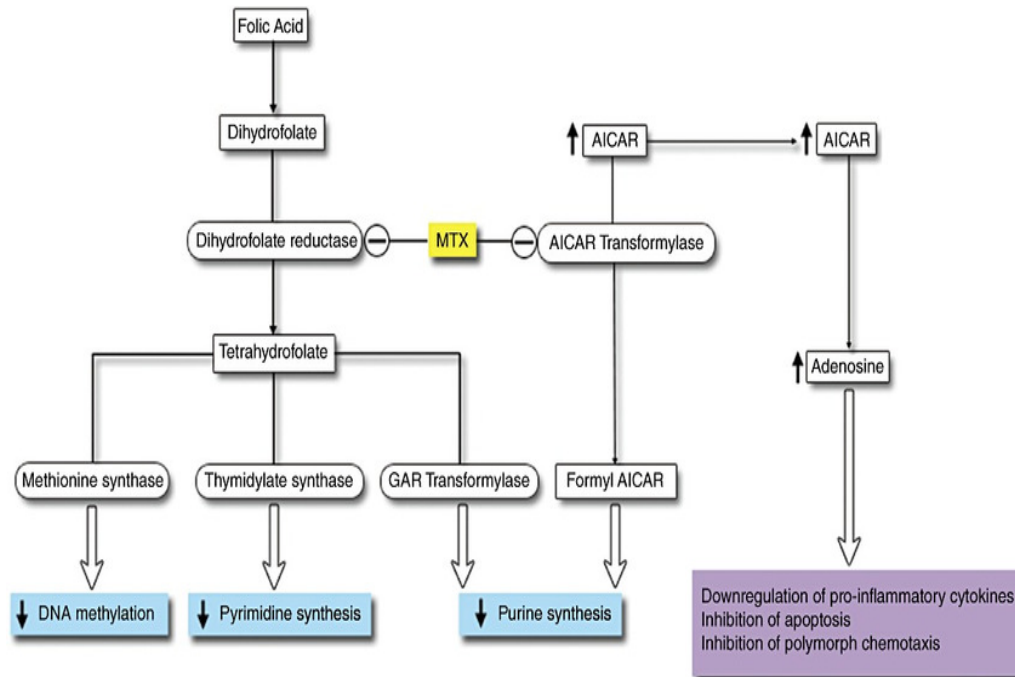
mofetil. These are small molecule drugs. Biologics are large molecule drugs mostly proteins, that are produced by recombinant DNA technology. Abatacept, a T cell modulating biologic, Rituximab – a B cell cytotoxic agent, Tocilizumab an anti-IL-6 antibody, IL-1 antagonists (Anakinra, Rilocept, Canakinumab) and TNF α inhibitors like Adalimumab, Certolizumab, Etanercept, Golimumab and Infliximab are the currently available biologics.^{6,20}

METHOTREXATE

It is an antimetabolite, effective in doses lower than those used in cancer chemotherapy. The first line of treatment in RA involves MTX monotherapy, aimed at reduction of the C-reactive protein (CRP) level and radiographic progression in RA significantly. The protective effect of MTX is more in subjects seropositive for anticyclic citrullinated peptide (anti-CCP) antibodies. In patients with active RA the dose of MTX has to be raised or switched over to combination therapy.²¹

Mechanism of action:

MTX inhibits amino-imidazole carbamoylase (AICAR) transformylase and thymidylate synthetase. AICAR inhibits AMP deaminase, leading to the accumulation of adenosine, which is an inhibitor of inflammation.



It inhibits proliferation, promotes apoptosis of immune inflammatory cells and inhibits the release of proinflammatory cytokines. Almost 70% of the drug is absorbed orally and metabolized in liver by hydroxylation, gets excreted in urine. 30% of the drug is excreted unchanged in urine. The dose used in RA is less compared to that used in cancer chemotherapy. To start with the dosage in RA is 7.5 mg once weekly. Upto 30 – 35 mg can be given per week depends on the response and tolerability of the patient.

Frequent adverse effects involve nausea, mouth ulcers, stomatitis and GI ulceration. It has the potency to exert toxicity on bonemarrow leading to Leukopenia, and anemia. Progressive dose related hepatotoxicity in the form of elevated liver enzymes can occur. The incidence of GI and liver function test abnormalities can be prevented by giving folic acid 5mg orally, one day

after the MTX dose. HCQ can reduce the clearance or increase the tubular reabsorption of MTX. Aspirin and Sulphonamides decrease its renal tubular secretion and potentiate its toxicity. Salicylates, Dicumerol and Sulphonamides displace MTX from its protein binding sites. It is contraindicated in pregnancy.²⁰

Combination therapy in active RA

Glucocorticoids may be used as adjuvants to MTX in combination therapy. Although the pain-relieving effect of the steroidal agents is prompt and obvious, they may cause many side effects like osteoporosis, unhealed wounds, upper gastrointestinal bleeding and may aggravate existing conditions, such as hypertension, diabetes, etc. Thus, steroidal agents are currently used only in certain limited conditions.

Pharmacotherapy for active RA at present includes one or a combination of the following four classes of drugs: Nonsteroidal anti-inflammatory drugs, analgesics, corticosteroids (prednisolone and methylprednisolone), and disease modifying antirheumatic drugs (DMARDs). Modern RA management stresses the importance of early diagnosis and aggressive treatment with DMARDs, particularly methotrexate, hydroxychloroquine, and sulfasalazine. In spite of the availability of so many conventional DMARDs, favorable outcomes are frequently not achieved with combination DMARDs resulting in

persistent active disease. Of late, however, newer biologic therapies are the order of the day for successful management of active RA. Leflunomide, etanercept, and adalimumab are the popular biologics which are frequently used either alone or in combination with methotrexate. A number of trials have shown that these newer drugs to be more effective than traditional agents because of their ability to alter joint remodeling as well as attenuate disease symptoms.^{20,21}

Biological agents in active RA

Despite promising and successful outcome with newer biologic agents, their adverse effect profile limited their usage particularly in young patients. They may activate latent TB, cause bone marrow suppression, fungal infections, lymphomas, drug induced lupus etc. Their benefit largely remains confined to the small subset of patients and in a resource poor country like India, only few can afford the high cost of the therapy. Thus, it is apparent that further therapeutic advances are required for better treatment of RA for those patients who do not respond to conventional DMARDs combination therapy and particularly for those who cannot afford the costly new biologic treatments. Therefore, there is still a need in the market for a medicament or method that can efficiently improve the anti-inflammation activity. Recently statin group of drugs is emerging as adjuvants with DMARDs. A study demonstrates a significant negative association between persistence with statin therapy and RA

onset, particularly in adult patients who began treatment at a relatively young age and with high efficacy statins.^{22,23,24}

Statins have a reasonable bioactivity profile that makes them possible adjunct therapeutic agents in addition to standard antirheumatic treatment to target both vascular risk reduction and synovial inflammation.²² This has the potential to reduce the need for the relatively toxic long-term treatments currently used for RA, such as several disease-modifying anti rheumatic drugs (DMARDs).²⁵

PLEIOTROPIC EFFECTS OF STATINS

Statins display immune modulatory effects by mainly triggering the major histocompatibility complex (MHC), the co-stimulatory molecules in inflammation, the leukocyte migration, and the cytokine network. Statins interfere with the interaction between MHC (class I/class II) and CD8/CD4 required to achieve efficient T-cell activation.²⁶

Statins selectively block the lymphocyte function-associated antigen-1 (LFA-1),^{26,27} a α/β heterodimeric receptor belonging to the $\beta 2$ integrin subfamily that plays a central role in lymphocyte homing and leukocyte trafficking. The interaction between activated LFA-1 and the intracellular adhesion molecule-1 (ICAM-1) providing signals for both leukocyte migration and co-stimulation is also blocked by statin. Other adhesion molecules inhibited by statins include ICAM-1, CD11b, CD18,

and CD49. Statins suppress the cytokine-induced maturation of dendritic cells resulting in the failure to express the costimulatory molecules and to induce T-cell response.^{9,28} Numerous studies suggest inhibitory effects of statins on proinflammatory cytokine production, such as IFN- γ , tumour necrosis factor- α , interleukin (IL)-1 β , and IL-6 in several cells. Another mechanism of immunomodulation is the regulation of isoprenylated proteins such as Rho and Rac and their function.²⁹

Trial of Atorvastatin in Rheumatoid Arthritis (TARA), showed reduction in DAS28, C-reactive protein and erythrocyte sedimentation rate.⁷ Some studies highlighted the effect of rosuvastatin on RA patient showing an improvement in CRP not in rheumatoid disease activity.^{30,31}

A placebo control study with rosuvastatin along with methotrexate declared a reduced clinical disease activity index (CDAI) significantly. This may suggest that rosuvastatin can be beneficial and may be used as adjuvant therapy to other medications for treatment of RA.³²

Another clinical study with 16 highly active RA patients who were on methotrexate, with either atorvastatin 40 mg or rosuvastatin 10 mg as adjuvant therapy show an improvement in clinical parameters like morning stiffness, swollen joint count, visual analogue scale and DAS28 score. ESR also show improvement. Both the drugs improve the clinical activity and 10 mg rosuvastatin is equivalent to 40 mg atorvastatin in the management of RA when used as an adjuvant therapy.³³

ROSUVASTATIN

Rosuvastatin is a hydrophilic statin with extensive first-pass metabolism. The absorption of rosuvastatin is not affected by food and maximum plasma concentration is reached in 3 to 5 h. It is 88% protein bound, mainly to albumin. Rosuvastatin is metabolized mainly by CYP2C9 isoenzyme, excreted in feces and the elimination half-life is approximately 19 hours. The usual dose is 5- 10 mg once daily.³⁴ CYP2C9 inhibitors like warfarin interfere with the metabolism of rosuvastatin. Cyclosporine, Gemfibrozil and antiretroviral agents have pharmacokinetic interactions. No interaction with grape juice, fibrates and ezetimibe.³⁴

Important side effects include myopathy and rhabdomyolysis. Contraindicated in hepatic failure since it may cause a rise in hepatic transaminases. Also contraindicated in pregnancy and lactation. It should be used cautiously in patients with Diabetes, since it increases the HbA_{1C} levels.³⁴

The effects of rosuvastatin on LDL cholesterol are dose-related. Higher doses are more efficacious in improving the lipid profile of patients with hypercholesterolemia. As an adjunct to DMARDs, rosuvastatin can effectively bring out remission in active RA patients.³⁴

PITAVASTATIN

Pitavastatin has a unique structure that contributes to a number of pharmacological benefits, including increased systemic bioavailability, a high level of oral absorption and potent effects on LDL-C and HDL-C. Being a lipophilic statin it can easily penetrate hepatic and extra hepatic tissues like bone and exert anti-inflammatory effects.^{31,32,33} Pitavastatin forms a structural analogue of HMG-CoA intermediate and reversibly competes with the inhibitors of HMG Co-A. The bioavailability of pitavastatin is 80%. Food intake does not alter its bioavailability. Half-life of the drug is eleven hours.

Pitavastatin is rapidly glucuronized by UGT1A3 and UGT2B7 and then converted to its major inactive metabolite, Pitavastatin lactone. It is metabolized to some extent by CYP2C9 and CYP3A4 in hepatic microsomes.³⁵

USES

Pitavastatin reduces oxidation of LDL-C and protects the endothelium from oxidative stress. In patients with stable CAD, postprandial endothelium-dependent vasodilation is ameliorated by inhibiting oxidative stress. It is also effective in the treatment of patients with metabolic syndrome or Type 2 Diabetes, because of its beneficial effects on the atherogenic lipid triad, neutral effects on glycemic control

and reduced potential for drug Interactions.Pitavastatin is found to have anti epileptogenic effect in Pentylenetetrazol induced seizure in mice.³⁶

DOSE, ADMINISTRATION and DURATION:

Available in tablet form in 1,2 and 4 mg dosage forms.Once daily dosage is enough. Generally other statins are usually administered during night time due to peak enzyme activity but pitavastatin can be taken at any time during the day. Almost 80% of the administered dose is absorbed.

SIDE EFFECTS, EFFICACY AND SAFETY:

Common statin-related side effects (headaches, stomach upset, abnormal liver function tests and muscle cramps are similar to other statins.Increased levels of serum uric acid have been reported with pitavastatin. No data available regarding occurrence of myopathy and rhabdomyolysis with Pitavastatin. Gemfibrozil reduces clearance of Pitavastatin and raises blood concentrations of the drug.

Pitavastatin is generally well tolerated in hyperlipidemic patients with or without type 2 diabetes, with the most common treatment-related adverse events being musculoskeletal or gastrointestinal in nature. Increases in plasma creatine kinase levels were seen in <5% of pitavastatin recipients and the incidence of myopathy or rhabdomyolysis are extremely low.^{37,38,39}

Pitavastatin should be carefully administered in patients with liver diseases since plasma concentration of the drug increases in hepatic failure. Pitavastatin is contraindicated in pregnancy and lactation.³³

Drug interactions

Pitavastatin like Rosuvastatin appears to be a substrate of CYP2C9, and not CYP3A4 (which is a common source of interactions in other statins). As a result, pitavastatin is less likely to interact with drugs that are metabolized via CYP3A4, which might be important for patients with active RA with co-morbid conditions. Pitavastatin is contraindicated only in patients treated with cyclosporine or lopinavir/ritonavir combination therapy. Administration should be temporarily suspended in patients receiving erythromycin or fusidic acid, however, and the dosage should be limited to 2 mg in people treated with rifampicin. As for other statins, pitavastatin should be used with caution in people treated with fibrates or niacin.³⁵

CLINICAL OUTCOME OF PITAVASTATIN IN RHEUMATOID ARTHRITIS

Loss of bone mass is frequently seen in patients with RA and the main causes of osteoporosis are steroid therapy, postmenopausal changes in hormone balance (postmenopausal osteoporosis), and disuse bone atrophy associated with periarticular impairment. Bone and cartilage

damage in RA results from an imbalance between synthesis and degradation due to cellular and cytokine-mediated inflammation. Increased bone resorption in RA is linked to the facilitation of osteoclast differentiation and activation by inflammatory cytokines of TNF- α and IL-1. Osteoprotegerin (OPG), a soluble decoy receptor with homology to the members of the TNF receptor family, binds to the receptor activator of NF- κ B ligand (RANKL) and blocks interactions with the receptor activator of NF- κ B. An imbalance in this system may play a part in the skeletal complications of RA. Statins have recently been reported to stimulate bone formation in vivo by stimulating osteoblastogenesis, and by inhibiting osteoclastogenesis in human bone marrow cell culture and also by inhibiting bone loss induced by steroids in animal studies. They also increase new bone formation from osteoblasts and accelerate the promoter activity of bone morphogenic protein-2 (BMP-2), a member of the BMP family.^{40,41}

A study comparing cost effectiveness of Pitavastatin versus Atorvastatin showed Pitavastatin is cost effective in managing hypercholesterolemia. Compared to other statins Pitavastatin is less likely to cause myopathy and maintains a good glycemic control in diabetic patients. It effectively increases HDL-C levels also.³⁰

This review of literature clearly depicted that depicted that pleiotropic effect of Pitavastatin and its beneficial role in cardiovascular disorders, malignancies, autoimmune disorders,Alzheimers disease etc. Pitavatatin as an adjuvant with DMARDs in active RA, may mitigates inflammation,prevents osteoporosis and risk for CVD and thereby reduces morbidity along with early mortality.

MATERIALS AND METHODS

Ethics Approval

The study was conducted after obtaining institutional ethical clearance certificate from Institutional Ethical Committee (IEC), Research Cell of Chennai Medical College Hospital and Research Centre (Affiliated to The Tamilnadu Dr. M.G.R. Medical University), Irungalur, Tiruchirapalli. The approval letter was enclosed as Appendix A.

Study Design

A prospective, open labelled, parallel arm, randomized, single centre study performed in a tertiary care teaching hospital(Chennai Medical College Hospital & Research Centre (SRM Groups), Irungalur, Tiruchirapalli) conducted at outpatient clinics. Total duration of the study period was 24 weeks. All patients were having active RA and on oral first line DMARD,Methotrexate at the time of recruitment.

Chemicals: Methotrexate, Pitavastatin, Rosuvastatin

Informed Consent

Written informed consent was obtained from each subject who were willing to participate in the study, after being explained personally about the purpose, potential risks regarding the study.

Inclusion criteria:-

Active Rheumatoid arthritis patients of both sex, in the age group of 20 – 60 years according to American College of Rheumatology (ACR) criteria and on a dose of Methotrexate 7.5mg weekly for the last three months will be selected for this study.

Active RA at the time of screening:-Patients with More than or equal to 6 swollen joints / 6 tender joints(from 68 joint count), CRP more than or equal to 1.5mg/dl, ESR more than or equal to 28mm in the 1sthour, Morning stiffness more than or equal to 45 minutes)

Exclusion criteria

Patients on hypolipidemic drugs, steroids therapy, Vitamin D3 therapy, Patient with severe Rheumatoid arthritis as per ACR Criteria-Stage IV, Diabetic patients, Pregnancy and lactation, Liver failure, Renal failure, Patients with myopathies and pancytopenia.

Sample Size

Total 90 active Rheumatoid arthritis patients who fulfilled the inclusion and exclusion criteria attending the medicine outpatient department at Chennai Medical College Hospital and Research Centre, Irungalur, Tiruchirapalli were selected after obtaining written informed consent. Selected study subjects were

randomized by simple randomization technique and divided in to 3 groups of 30 each. The detailed study description was depicted in table 1.

Subjects in each group were treated as follows and continued without any changes in the treatment for the entire course of the study.

Table 1: Description of study groups (n=90)

Group	No. of subjects	Subject descriptions
I	30	Patients with Rheumatoid arthritis with active disease on Tab. Methotrexate 12.5 mg weekly.
II	30	Patients with Rheumatoid arthritis with active disease on Methotrexate 7.5 mg weekly + Tab. Rosuvastatin 10 mg once Daily.
III	30	Patients with Rheumatoid arthritis with active disease on Methotrexate 7.5mg weekly + Tab. Pitavastatin 1mg once daily

All the subjects were provided with a general questionnaire which includes thorough past and present medical history and detailed medication information. None of the subjects included in this study are allowed to change their medication regimens during the entire study period in order to avoid the experimentation bias. Blood samples were collected from the subjects on 0th day at the end of 4th, 8th and 12th weeks of the study period.

Demographic and Clinical Data

Baseline demographic data including age, sex were determined, medications prescribed for diabetes treatment were documented using a structured questionnaire during the subject's visit and validated from medical records. Clinical characteristics including body weight, height, body mass index, systolic and diastolic blood pressure of all subjects were measured.

Anthropometric measurements

- ❖ All the measurements were recorded by a single observer
- ❖ A digital scale was used for measuring the weight, which was adjusted to the nearest 0.1 kg.
- ❖ A wall - mounted stadiometer was used for measuring the height and was adjusted to the Nearest 0.1cm. BMI was calculated as $BMI = \text{Weight (kg)} / \text{Height (m)}^2$

Blood pressure determination

Blood pressure is measured by means of a sphygmomanometer

Blood pressure levels

Criteria(s)	Blood pressure levels	
	Systolic (mmHg)	Diastolic (mmHg)
Normal	Less than 120	Less than 80
At risk (pre hypertension)	120-139	80-89
High	140 and above	90 and above

Disease Activity Score (DAS)

DAS is calculated according to the standard formula based on tender joint count (TJC),swollen joint count (SJC),ESR and assessment of general health (GH) based on the scores between 0- 100 from the patient. The joints involved include shoulders,metacarpophalangeal joints,proximal interphalangeal joints,elbows,wrists and knees of both sides contributing to a score of 28.Estimation done at every visit.

$$DAS- 28= 0.56\sqrt{TJC28} + 0.28\sqrt{SJC28} + 0.70 \log ESR + (0.014 \times GH)$$

Blood sample collection:

About 4 ml of blood was collected during each visit by vene puncture under aseptic precautions in a sterile dry clean container.EDTA was the anticoagulant added.Serum was used for analysis.

Immunological Parameters.

The immunological parameters were estimated by Enzyme Linked Immuno Sorbent Assay (ELISA)

Rheumatoid Factor (RF) test

Detects IgM antibodies to IgG antigen. The purified antigen is bound to a solid phase microassay well. Patient serum samples are diluted and added to each well. If antibody is present in the patient's serum, antigen-antibody

complexes are formed. The absorbance of the solution, measured at 450 nm, is directly related to the concentration of IgM antibody. Values more than 7.7 IU are considered to be positive, with the presence of detectable antibodies.

Anti-CCP

Intended for the quantitative determination of IgG class antibodies directed against cyclic citrullinated peptides, present in human serum or plasma. Procedure same as estimation of RF. The lowest concentration of Anti-CCP detected is 1.12 U/ml with 98% confidence value.

- ❖ Complete hemogram was done by Auto Analyzer method. ESR was measured by Westergren method as the method of choice. The Westergren method uses EDTA as an anticoagulant. The reference range is for men < 15 mm/hr - 20 mm/hr and for women < 20 mm/hr - 30 mm/hr. CRP measured by Latex Agglutination test. The reference range is normal upto 10 mg/L and High-sensitivity if < 3 mg/L.

Biochemical evaluation

Blood samples were collected from the subjects to measure the biochemical parameters in all the three test groups on 0th day at the end of 4th, 8th and 12th weeks of the study period.

The following biochemical parameters were determined

1. Blood Glucose
2. Blood Urea
3. Serum Creatinine
4. SGOT,SGPT
5. ALP
6. Lipid Profile
 - i. Total cholesterol
 - ii. Triglycerides
 - iii. High density lipoprotein (HDL)
 - iv. Low density lipoprotein (LDL)

Blood glucose estimation

Blood glucose estimation was done by glucose oxidase-peroxidase method . Random blood glucose was measured.Reference value is 140 to 160 mgs /dl .Blood urea was estimated by urease GLDH method . Reference value is 10 to 50 mg / dl.

❖ Estimation of serum creatinine was done by Modified JAFFE'S method.

When sodium hydroxide is added to creatine containing sample,reddish orange colour has been formed.Results are analysed by calorimetry.The reference value is 0.5 to 1.5 mg / dl.

- ❖ Estimation of liver enzymes ,Serum Glutamic Oxaloacetic Transaminase, (SGOT), Serum Glutamic Pyruvic Transaminase(SGPT), and serum Alkaline Phosphatase (ALP) were done by International Federation of Clinical Chemistry and Laboratory medicine (IFCC) method.

Lipid Profile

Blood should be collected after a 12-hour fast (no food or drink, except water).

Total Cholesterol (TC)

The TC was estimated by CHOD method. The normal range of the total cholesterol is 75-169 mg/dL for those age 20 and younger and 100-199 mg/dL for those over age 21.

High Density Lipoprotein (HDL)

HDL levels were calculated by spectrophotometric method .The value of HDL is better if it is greater than 40 mg/dL. A high HDL level is related to lower risk of heart and blood vessel disease.

Low Density Lipoprotein (LDL)

LDL fractions were precipitated using PEG 6000 and determined spectrometrically.The ranges of LDL in blood are

- Less than 70 mg/dL for those with heart or blood vessel disease and for other patients at very high risk of heart disease (those with metabolic syndrome)
- Less than 100 mg/dL for high risk patients (multiple risk factors for coronary vascular diseases)

- Less than 130 mg/dL for individuals who are at low risk for coronary artery disease

Triglycerides (TG)

Triglycerides are quantitatively determined spectrometrically by enzymatic measurement of glycerol and total triglycerides in serum at 540 nm. A normal fasting level is 150 milligrams per deciliter (mg/dL). Borderline high level is 150 to 199 mg/dL. A high level is 200 to 499 mg/dL.

The estimation of VLDL cholesterol was done by Friedwald calculation method.

$$\text{VLDL} = \frac{\text{Triglycerides}}{5}$$

STATISTICAL ANALYSIS

All the data was initially entered to Microsoft Excel 2010 and later these spreadsheets were used for analysis. Statistical analysis was done using SPSS version 20.0.

- ❖ Descriptive statistics were calculated as frequency, percentage, mean and standard deviation. Descriptive data were represented using various tables, graphs, diagrams etc.
- ❖ For all the statistical tests of significance, p value of <0.05 was considered to reject the null hypothesis.
- ❖ After the normality tests showed normal distribution of continuous variables, ANOVA test for repeated measures using a General linear model was done to test the difference in means at various time intervals between the three groups of study subjects followed by Bonferroni post-Hoc test for inter-group comparisons. Profile plots and estimated marginal means were studied for each variable.
- ❖ For categorical nominal variables, Chi-square test was done to test the association between the variables.

RESULTS

Ninety active Rheumatoid arthritis patients who were included at the start of the study were followed till the end of the study. No lost to follow up or adverse drug reactions were reported.

Table 1 Age distribution of the study population (n=90)

About 41% of the study subjects were in the age group of 41 to 50 years while 35% were aged 51-60 years.

Age group	Frequency	Percentage
31-40 years	19	21.1
41-50 years	37	41.1
51-60 years	32	35.6
61-70 years	2	2.2
Total	90	100.0

Mean age (\pm S.D): 48.32 (7.49) years, minimum: 34 years, maximum: 70 years.

Fig.1: Bar chart showing age distribution of the study population

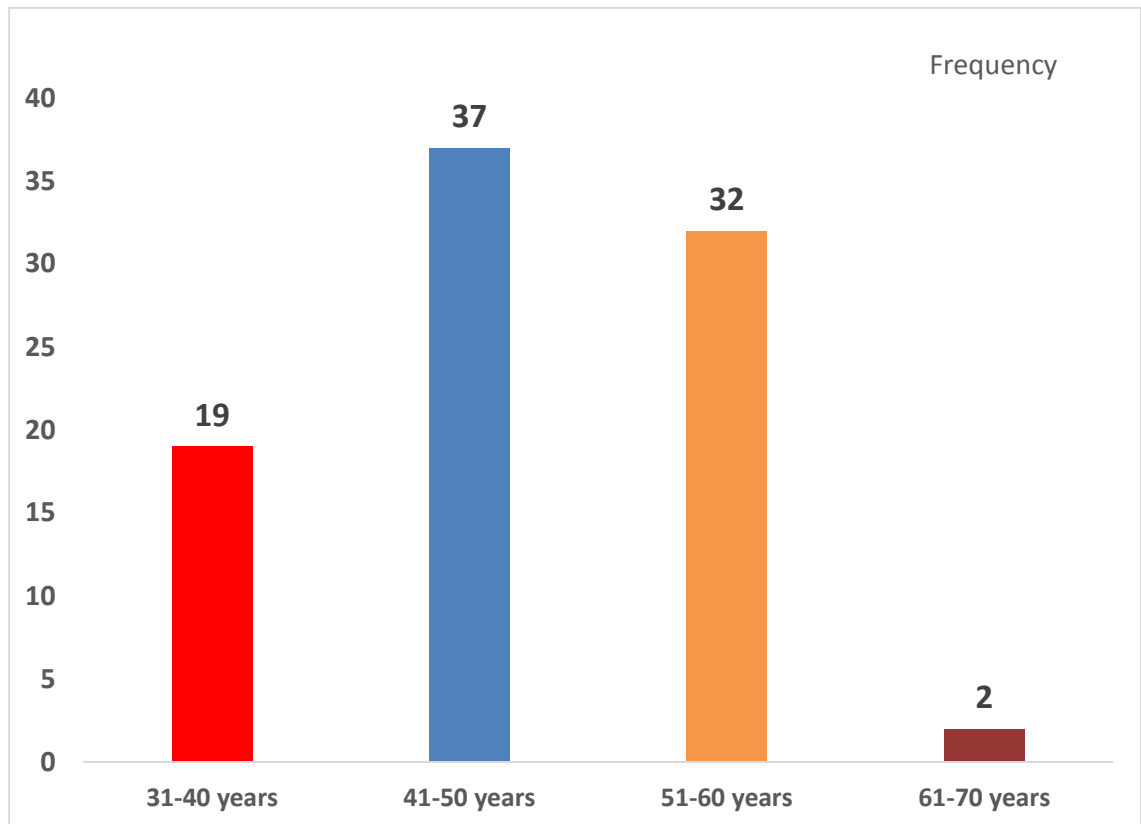


Table 2 Gender distribution of the study population (n=150)

Though the number of females were more in each group, Males and females were equally distributed across all 3 groups as the difference was not statistically significant.

Gender	Group 1 N (%)	Group 2 N (%)	Group 3 N (%)	Total N (%)
Female	19 (32.2)	20 (33.9)	20 (33.9)	59 (100)
Male	11 (35.5)	10 (32.3)	10 (32.3)	31 (100)
Total	30 (33.3)	30 (33.3)	30 (33.3)	90 (100)

Chi square p value: 0.952

Fig.2: Clustered Bar chart showing gender distribution of the study population

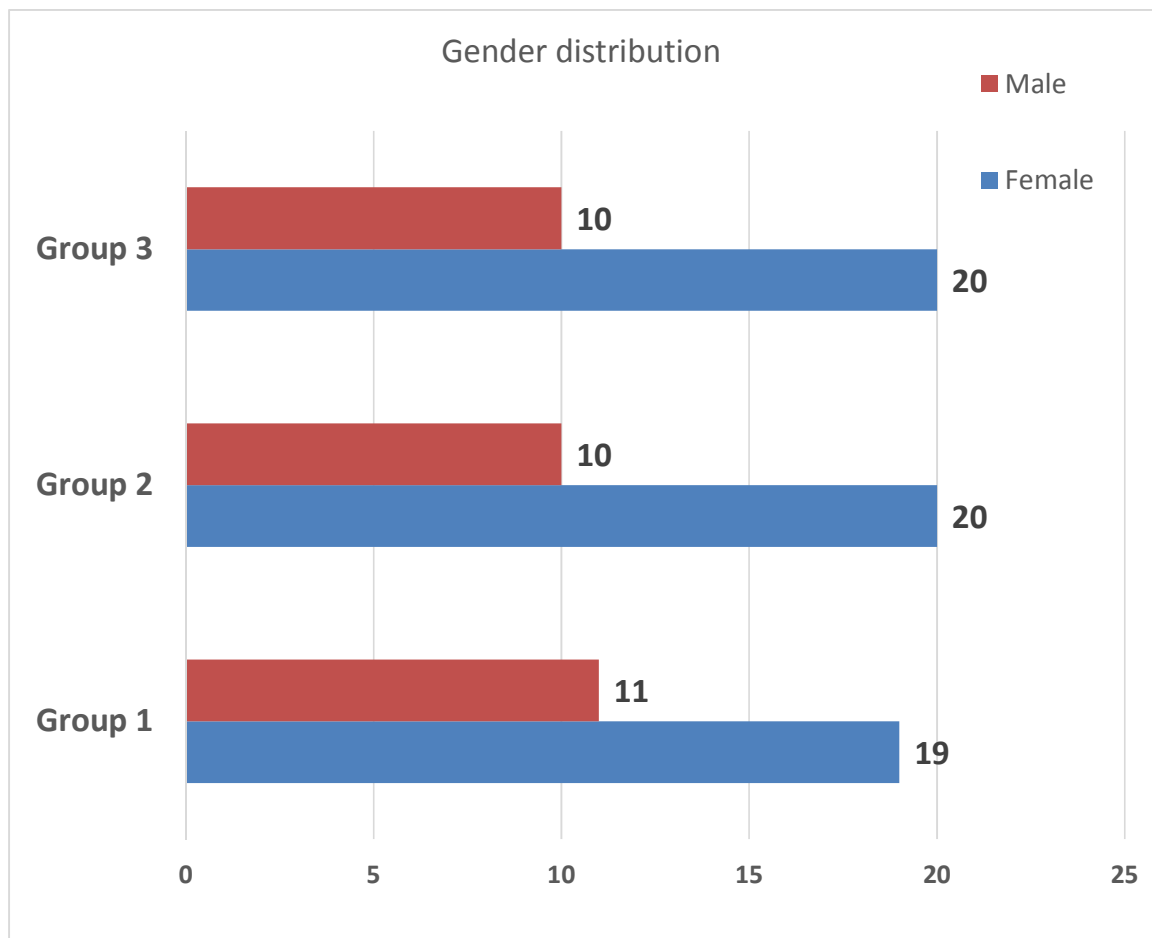


Table 3 Descriptive statistics of various parameters in the study population (n=90)

Statistic	Mean (\pm Std. Deviation)	Minimum	Maximum
Weight (Kg)	69.11 \pm 13.43	47	97
Height (in cm)	163.0 \pm 11.14	142	184
BMI (Kg/m ²)	25.73 \pm 3.80	15.60	36.16

Table 4 Distribution of BMI across the 3 groups (n=90)

The differences in the distribution of overweight and obese individuals across the groups were not statistically significant.

BMI group	Group			Total
	1	2	3	
Underweight (<18.5)	0	2	0	2
	0.0%	100.0%	0.0%	100.0%
Normal (18.5-22.9)	5	7	6	18
	27.8%	38.9%	33.3%	100.0%
Overweight (23 - 24.9)	8	7	5	20
	40.0%	35.0%	25.0%	100.0%
Obesity (\geq 25)	17	14	19	50
	34.0%	28.0%	38.0%	100.0%
Total	30	30	30	90
	33.3%	33.3%	33.3%	100.0%

Chi square p value: 0.447

Fig.3: Stacked Bar chart showing Distribution of BMI across the 3 groups

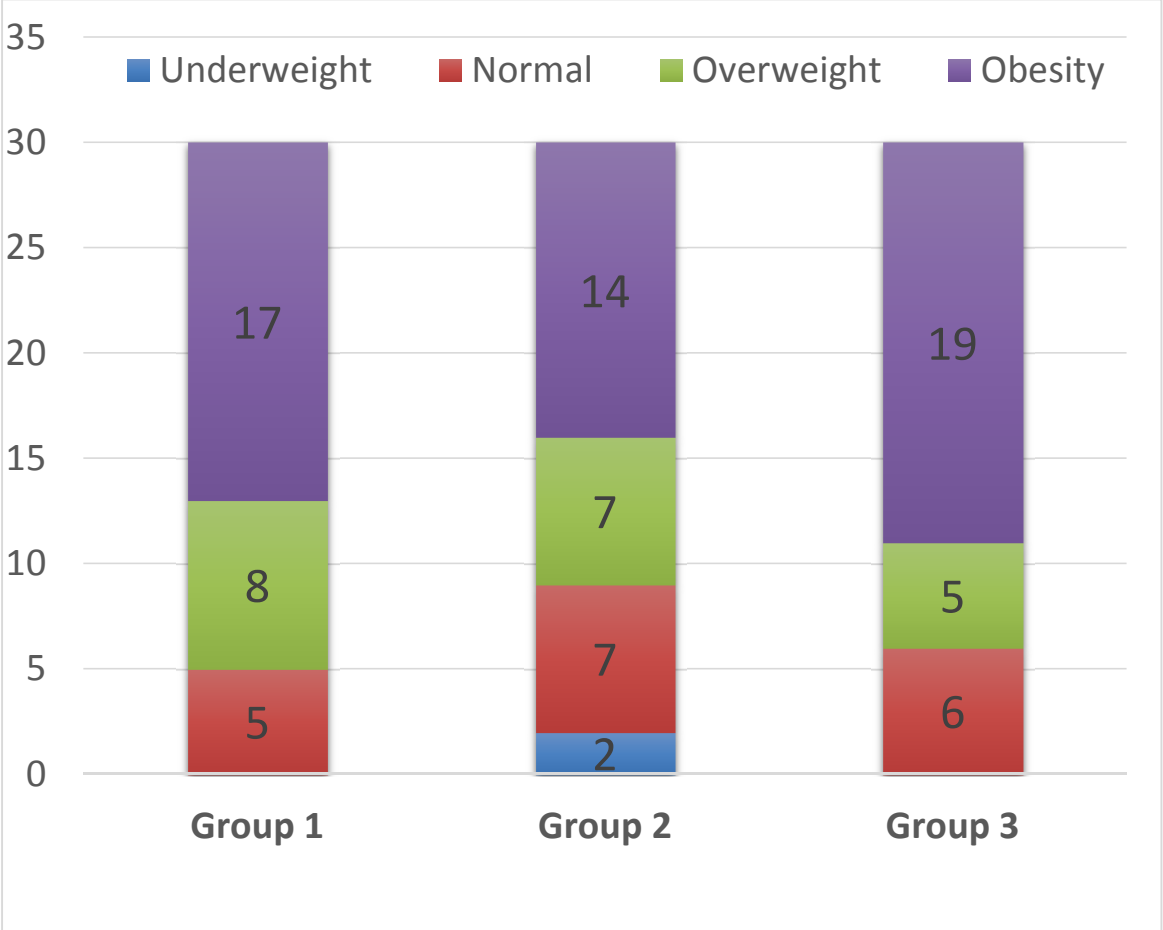


Table 5 Distribution of Disease activity score across the 3 groups at various time periods (n=90)

A mean reduction in DAS was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant reduction is seen in group 3, having baseline value of 6.54 to 3.03 at the end of the study.

Disease activity score	Group		
	1	2	3
	Mean ± Std. Deviation	Mean ± Std. Deviation	Mean ± Std. Deviation
Baseline	6.86 ± 0.76	6.49 ± 0.85	6.54 ± 0.67
4 weeks	6.34 ± 0.73	5.96 ± 0.73	5.39 ± 0.54
8 weeks	5.96 ± 0.75	5.56 ± 0.72	4.14 ± 0.54
12 weeks	5.60 ± 0.91	5.11 ± 0.74	3.03 ± 0.50

ANOVA for repeated measures using a General linear model was done to test the difference in mean Disease activity scores at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

p value	<0.001
F statistic	36.63
Degree of freedom	2
Partial Eta square	0.457

Estimated marginal means of DAS

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	6.188 \pm 0.120	5.949	6.426
2	5.783 \pm 0.120	5.544	6.022
3	4.776 \pm 0.120	4.537	5.015

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean DAS scores between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.001). This implies group 3 can effectively decrease DAS.

Dependent Variable (DAS score)	Mean Difference (1 st - 2 nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	0.404	0.058	-0.009	0.819
Group 1 Vs Group 3	1.411	<0.001	0.996	1.82
Group 2 Vs Group 3	1.006	<0.001	0.5922	1.421

Fig.4: Profile plot showing distribution of Disease activity score across the 3 groups at various time periods

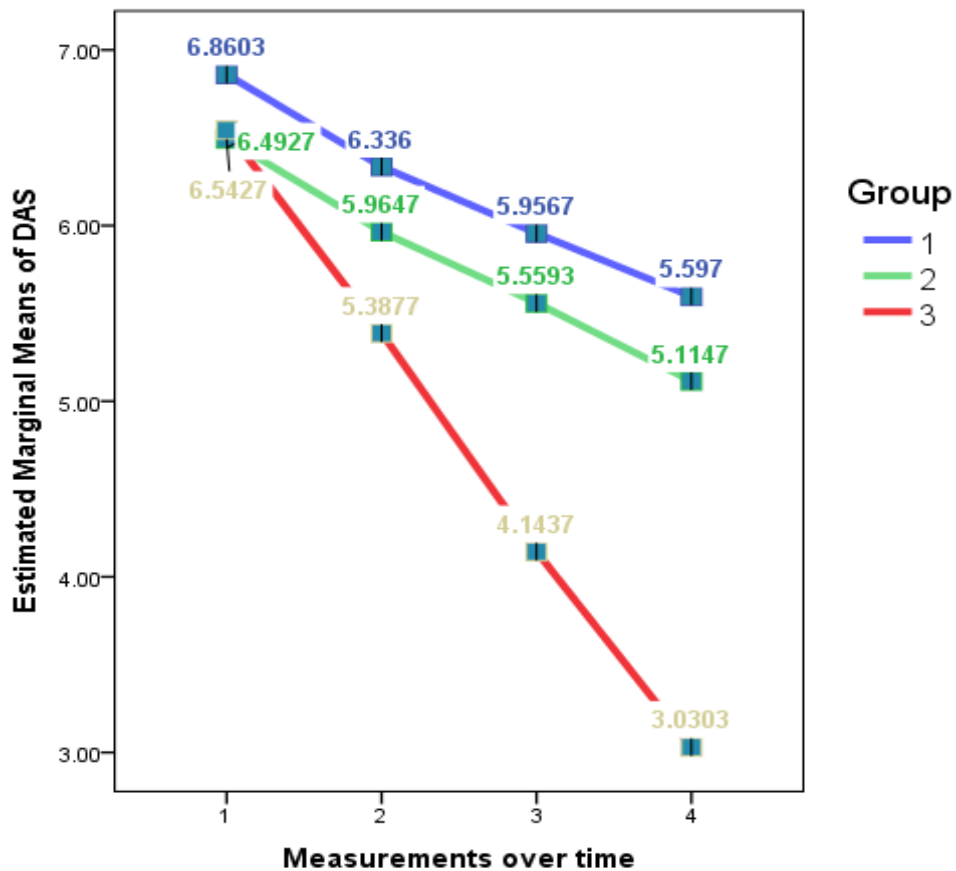


Table 6 Distribution of serum Rheumatoid Factor levels across the 3 groups at various time periods (n=90)

A mean reduction in Rheumatoid factor was seen from the baseline to 12th week of the study in all the groups and a significant reduction is seen in group 3, having baseline value of 88.5 to 42.3 at the end of the study.

Serum RF levels	Group		
	1	2	3
	Mean \pm Std Deviation	Mean \pm Std Deviation	Mean \pm Std Deviation
Baseline	94.3 \pm 97.3	93.5 \pm 98.3	88.5 \pm 73.8
12 weeks	52.8 \pm 43.6	52.5 \pm 71.7	42.3 \pm 35.5
Mean RF reduction	30.29 \pm 25.15	40.45 \pm 41.21	77.50 \pm 82.70

ANOVA test was done to test the difference in mean Rheumatoid factor reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean Rheumatoid factor levels between the three groups.

p value	0.003
F statistic	6.062
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean RF levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). This data shows group 3 effectively decrease RF compared to other groups.

Dependent Variable (RF reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-10.1610	1.000	-45.008	24.686
Group 1 Vs Group 3	-47.2166	0.004	-82.064	-12.368
Group 2 Vs Group 3	-37.0556	0.033	-71.903	-2.207

Fig.5: Profile plot showing distribution of RF levels across the 3 groups at various time periods

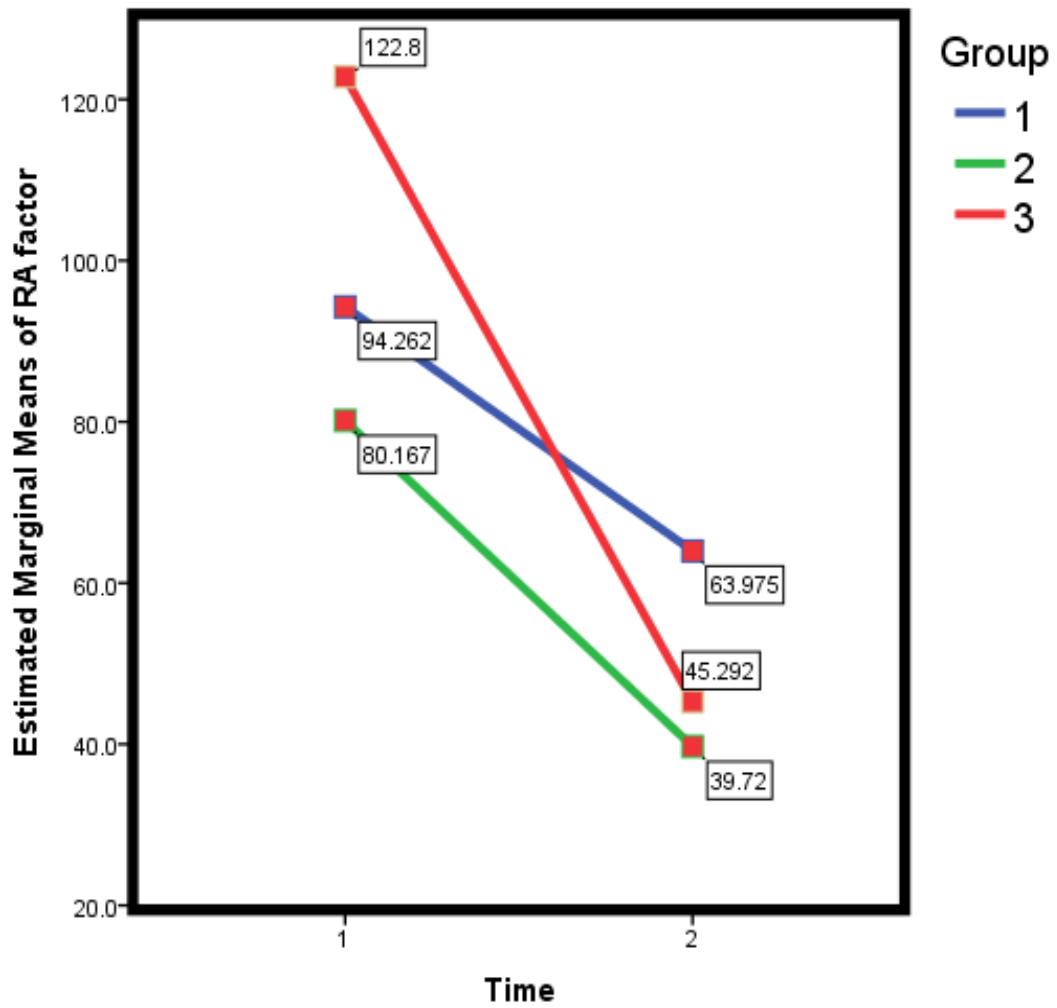


Table 7 Distribution of serum anti-CCP levels across the 3 groups at various time periods (n=90)

A mean reduction in anti-CCP level was seen from the baseline to 12th week of the study in all the groups and a significant reduction is seen in group 3, having baseline value of 38.06 to 18.33 at the end of the study.

Serum anti-CCP levels	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	41.61 ± 44.35	48.84 ± 43.57	38.06 ± 34.41
12 weeks	21.79 ± 17.29	29.82 ± 34.16	18.33 ± 14.89
Mean anti-CCP reduction	11.15 ± 12.80	18.36 ± 13.47	32.40 ± 25.88

ANOVA test was done to test the difference in mean anti-CCP reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean anti-CCP levels between the three groups.

p value	<0.001
F statistic	10.356
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean anti-CCP levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). Group 3 is superior in reducing the anti-CCP values.

Dependent Variable (Anti-CCP reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-7.211	0.398	-18.804	4.382
Group 1 Vs Group 3	-21.250	<0.001	-32.843	-9.657
Group 2 Vs Group 3	- 14.039	0.012	-25.632	-2.446

Fig.6: Profile plot showing distribution of serum anti-CCP levels across the 3 groups at various time periods

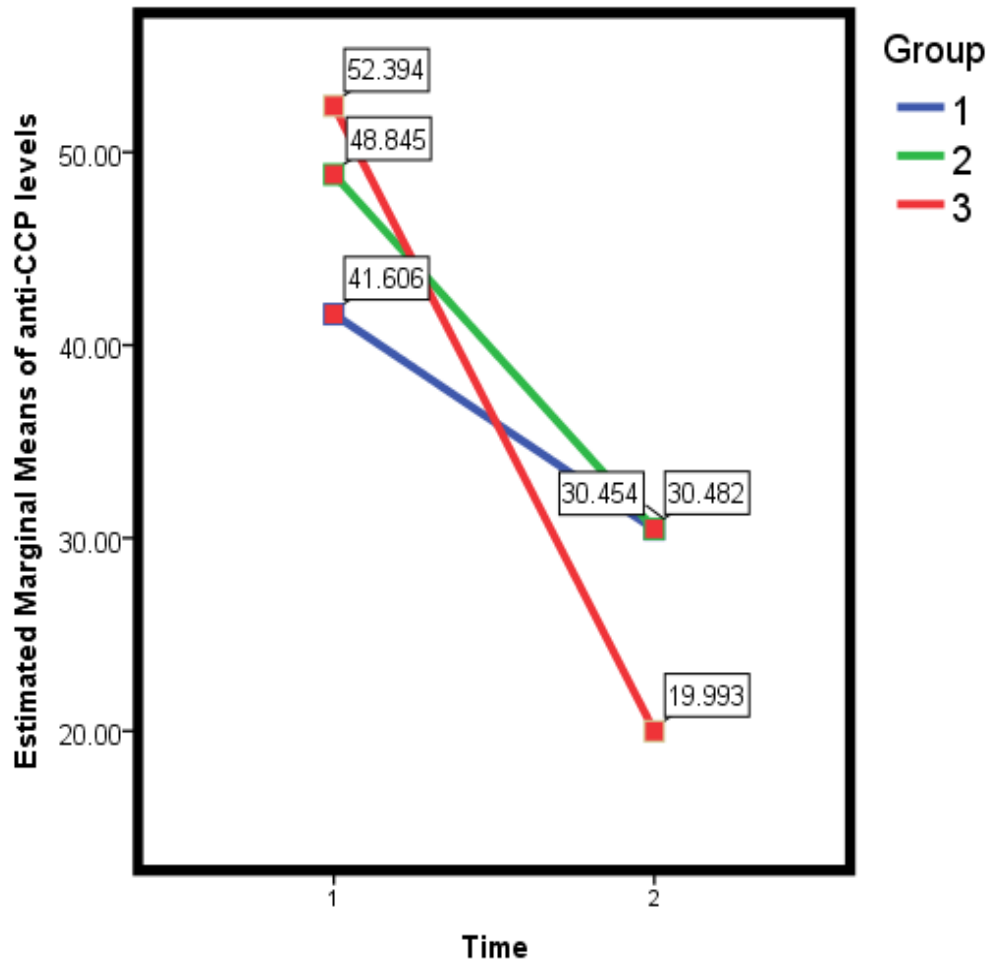


Table 8 Distribution of mean hemoglobin levels across the 3 groups at various time periods (n=90)

A reduction in mean hemoglobin levels was found in all the groups but not statistically significant.

Hemoglobin levels	Group		
	1	2	3
	Mean \pm Std Deviation	Mean \pm Std Deviation	Mean \pm Std Deviation
Baseline	12.8 \pm 15.4	12.8 \pm 14.6	10.4 \pm 1.2
4 weeks	12.7 \pm 16.1	10.0 \pm 1.0	10.1 \pm 1.1
8 weeks	12.6 \pm 16.5	9.7 \pm 0.9	9.9 \pm 1.1
12 weeks	12.4 \pm 15.8	9.6 \pm 0.9	9.7 \pm 1.0

ANOVA for repeated measures using a General linear model was done to test the difference in mean hemoglobin levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

Since the ANOVA test for repeated measures was not statistically significant, post-hoc test was not done. Hence, the difference in mean hemoglobin levels at various time intervals between the three groups was not statistically significant. (p value: > 0.1).

p value	0.535
F statistic	0.631
Degree of freedom	2
Partial Eta square	0.014

Estimated marginal means of Hemoglobin levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	12.620 \pm 1.730	9.182	16.058
2	10.528 \pm 1.730	7.090	13.967
3	10.032 \pm 1.730	6.593	13.470

Table 9 Distribution of total WBC count across the 3 groups at various time periods (n=90)

A reduction in mean WBC count was found among groups 1 & 3 but not statistically significant.

Total WBC count	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	9778 ± 1152	10103 ± 1082	10063 ± 1477
4 weeks	9280 ± 1155	10800 ± 5700	9667 ± 1535
8 weeks	8918 ± 1851	9627 ± 1195	9560 ± 1314
12 weeks	8970 ± 1165	12137 ± 14920	9070 ± 1875

ANOVA for repeated measures using a General linear model was done to test the difference in mean total WBC count at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

As the ANOVA for repeated measures was not statistically significant, post-hoc test was not done. Hence, the difference in mean total WBC count at various time intervals between the three groups was not statistically significant. (p value: > 0.01).

p value	0.093
F statistic	2.43
Degree of freedom	2
Partial Eta square	0.053

Estimated marginal means of Total WBC count

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	9236.58 \pm 477.085	8288.325	10184.842
2	10666.66 \pm 477.085	9718.408	11614.925
3	9590.00 \pm 477.085	8641.741	10538.259

Table 10 Distribution of platelet count across the 3 groups at various time periods (n=90)

The mean platelet levels were not found to be significant among the groups.

Platelet count (in lakhs)	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	1.8 ± 0.2	2.5 ± 3.7	1.9 ± 0.2
4 weeks	1.8 ± 0.2	1.8 ± 0.2	8.5 ± 36.5
8 weeks	1.7 ± 0.2	5.2 ± 18.9	8.4 ± 36.4
12 weeks	1.7 ± 0.2	5.1 ± 19.0	1.7 ± 0.2

ANOVA for repeated measures using a General linear model was done to test the difference in mean platelet count at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

As the ANOVA for repeated measures was not statistically significant, post-hoc test was not done. Hence, the difference in mean platelet count at various time intervals between the three groups was not statistically significant.(p value: > 0.1).

p value	0.549
F statistic	0.603
Degree of freedom	2
Partial Eta square	0.014

Estimated marginal means of platelet count

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	1.761 \pm 2.169	-2.550	6.071
2	3.650 \pm 2.169	-0.661	7.961
3	5.120 \pm 2.169	0.809	9.431

Table 11 Distribution of erythrocyte sedimentation rate (ESR) across the 3 groups at various time periods (n=90)

A mean reduction in ESR was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant reduction is seen in group 3, having baseline value of 49.7 to 17.1 at the end of the study.

ESR (in mm)	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	49.0 ± 19.7	52.1 ± 21.3	49.7 ± 11.7
4 weeks	39.0 ± 18.0	44.8 ± 19.0	37.7 ± 10.7
8 weeks	34.2 ± 16.2	39.7 ± 17.8	27.6 ± 8.4
12 weeks	29.7 ± 14.4	34.1 ± 18.4	17.1 ± 3.5
Mean ESR reduction	19.3 ± 16.0	18.0 ± 13.9	32.6 ± 10.3

ANOVA test was done to test the difference in mean ESR reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean ESR levels between the three groups.

p value	<0.001
F statistic	10.482
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean ESR levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). Compared to other groups Pitavastatin, methotrexate group reduces ESR values significantly.

Dependent Variable (ESR reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	1.367	1.000	-7.23	9.97
Group 1 Vs Group 3	-13.233	0.001	-21.83	-4.63
Group 2 Vs Group 3	-14.600	<0.001	-23.20	-6.00

Table 12 Distribution of C-reactive protein levels (CRP) across the 3 groups at various time periods (n=90)

A mean reduction in CRP was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant reduction is seen in group 3, having baseline value of 29.9 to 8.7 at the end of the study.

CRP levels	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	26.4 ± 8.6	32.8 ± 18.1	29.9 ± 7.6
4 weeks	20.9 ± 8.3	27.3 ± 19.4	22.1 ± 7.0
8 weeks	17.4 ± 7.3	21.4 ± 20.3	14.9 ± 5.8
12 weeks	14.4 ± 6.6	16.7 ± 22.5	8.7 ± 5.0
Mean CRP reduction	12.1 ± 5.7	16.1 ± 9.0	21.2 ± 6.8

ANOVA test was done to test the difference in mean CRP reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean CRP levels between the three groups.

p value	<0.001
F statistic	11.756
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean CRP levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). Pitavastatin ,Methotrexate combination effectively reduces CRP levels.

Dependent Variable (CRP reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-4.067	0.100	-8.66	0.52
Group 1 Vs Group 3	-9.100	0.001	-13.69	-4.51
Group 2 Vs Group 3	-5.033	0.027	-9.62	-0.44

Table 13 Distribution of blood glucose levels across the 3 groups at various time periods (n=90)

Blood glucose levels (mgs %)	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	115 ± 25	106 ± 25	112 ± 20
4 weeks	112 ± 23	108 ± 27	111 ± 13
8 weeks	116 ± 23	110 ± 28	109 ± 12
12 weeks	113 ± 23	112 ± 28	108 ± 10

ANOVA for repeated measures using a General linear model was done to test the difference in mean blood glucose levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

As the ANOVA for repeated measures was not statistically significant, post-hoc test was not done. Hence, the difference in mean blood glucose levels at various time intervals between the three groups was not statistically significant. (p value: > 0.1).

p value	0.659
F statistic	0.419
Degree of freedom	2
Partial Eta square	0.010

Estimated marginal means of blood glucose levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	113.917 \pm 3.907	106.151	121.683
2	109.142 \pm 3.907	101.376	116.908
3	110.083 \pm 3.907	102.317	117.849

Table 14 Distribution of blood urea levels across the 3 groups at various time periods (n=90)

Blood urea levels (mgs %)	Group		
	1	2	3
	Mean \pm Std Deviation	Mean \pm Std Deviation	Mean \pm Std Deviation
Baseline	29.2 \pm 3.2	28.2 \pm 5.8	28.8 \pm 2.5
4 weeks	28.8 \pm 2.7	28.6 \pm 5.8	29.4 \pm 2.5
8 weeks	29.3 \pm 3.5	28.4 \pm 5.6	29.3 \pm 2.3
12 weeks	29.6 \pm 2.7	28.6 \pm 5.8	29.1 \pm 2.0

ANOVA for repeated measures using a General linear model was done to test the difference in mean blood urea levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA for repeated measures was not statistically significant. So, post-hoc test was not done. Hence, the difference in mean blood urea levels at various time intervals between the three groups was not statistically significant. (p value: > 0.1).

p value	0.666
F statistic	0.409
Degree of freedom	2
Partial Eta square	0.009

Estimated marginal means of blood urea levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	29.233 \pm 0.681	27.880	30.586
2	28.445 \pm 0.681	27.092	29.798
3	29.158 \pm 0.681	27.805	30.511

Table 15 Distribution of serum creatinine levels across the 3 groups at various time periods (n=90)

Serum creatinine levels (mgs%)	Group		
	1	2	3
	Mean \pm Std Deviation	Mean \pm Std Deviation	Mean \pm Std Deviation
Baseline	0.940 \pm 0.128	1.817 \pm 4.946	0.873 \pm 0.083
4 weeks	0.897 \pm 0.093	1.880 \pm 5.123	0.907 \pm 0.087
8 weeks	0.937 \pm 0.107	2.117 \pm 5.163	0.890 \pm 0.088
12 weeks	0.913 \pm 0.107	2.137 \pm 5.158	0.903 \pm 0.081

ANOVA for repeated measures using a General linear model was done to test the difference in mean serum creatinine levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

Since the ANOVA for repeated measures was not statistically significant, post-hoc test was not done. Hence, the difference in mean serum creatinine levels at various time intervals between the three groups was not statistically significant. (p value: > 0.1).

p value	0.257
F statistic	1.382
Degree of freedom	2
Partial Eta square	0.031

Estimated marginal means of serum creatinine levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	0.922 \pm 0.531	-0.133	1.976
2	1.987 \pm 0.531	0.933	3.042
3	0.893 \pm 0.531	-0.161	1.948

Table 16 Distribution of serum SGOT levels across the 3 groups at various time periods (n=90)

A mean increment in serum SGOT was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant increase is seen in group 3, having baseline value of 29.300 to 29.600 at the end of the study.

Serum SGOT levels	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	28.000 ± 1.576	28.700 ± 2.087	29.300 ± 2.003
4 weeks	28.533 ± 1.383	28.967 ± 1.586	29.467 ± 1.776
8 weeks	28.733 ± 1.574	29.067 ± 1.680	29.433 ± 1.675
12 weeks	28.167 ± 1.392	29.467 ± 1.525	29.600 ± 1.567

ANOVA for repeated measures using a General linear model was done to test the difference in mean serum SGOT levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in mean serum SGOT levels between the three groups.

p value	0.012
F statistic	4.685
Degree of freedom	2
Partial Eta square	0.097

Estimated marginal means of serum SGOT levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	28.358 \pm 0.255	27.851	28.866
2	29.050 \pm 0.255	28.543	29.557
3	29.450 \pm 0.255	28.943	29.957

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in serum SGOT levels between Group 1 Vs Group 3 was statistically significant (p value: < 0.05) and group 3 increases SGOT levels.

Dependent Variable (serum SGOT levels)	Mean Difference (1 st - 2 nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-0.69	0.176	-1.57	0.19
Group 1 Vs Group 3	-1.09	0.010	-1.97	-0.21
Group 2 Vs Group 3	-0.40	0.812	-1.28	0.48

Fig.7: Profile plot showing distribution of SGOT levels across the 3 groups at various time periods

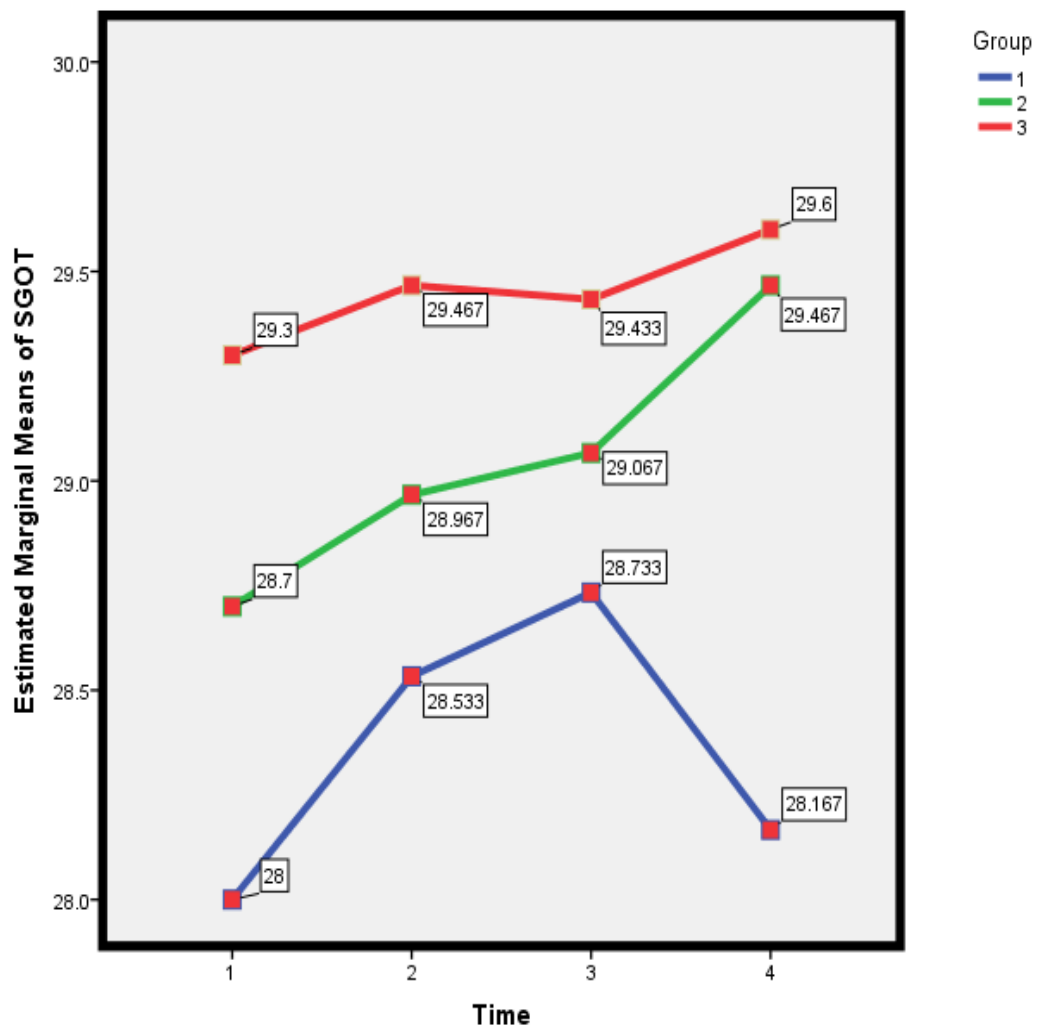


Table 17 Distribution of serum SGPT levels across the 3 groups at various time periods (n=90)

A slight increment in mean serum SGPT was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant increase is seen in group 3, having baseline value of 32.30 to 32.83 at the end of the study.

Serum SGPT levels	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	31.10 ± 1.99	31.63 ± 2.24	32.30 ± 2.00
4 weeks	30.90 ± 2.16	31.67 ± 2.35	32.50 ± 1.55
8 weeks	30.70 ± 1.99	32.03 ± 2.44	32.60 ± 1.52
12 weeks	31.20 ± 1.73	32.17 ± 2.49	32.83 ± 1.29

ANOVA for repeated measures using a General linear model was done to test the difference in mean serum SGPT levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in mean serum SGPT levels between the three groups.

p value	0.002
F statistic	6.598
Degree of freedom	2
Partial Eta square	0.132

Estimated marginal means of serum SGPT levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	30.975 \pm 0.309	30.360	31.590
2	31.875 \pm 0.309	31.260	32.490
3	32.558 \pm 0.309	31.944	33.173

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in serum SGPT levels between Group 1 Vs Group 3 was statistically significant (p value: <0.05). Hence SGPT value elevation was found in group 3 treated individuals.

Dependent Variable (serum SGPT levels)	Mean Difference (1 st - 2 nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-0.90	0.128	-1.97	0.17
Group 1 Vs Group 3	-1.58	0.001	-2.65	-0.52
Group 2 Vs Group 3	-0.68	0.365	-1.75	0.38

Fig.8: Profile plot showing distribution of SGPT levels across the 3 groups at various time periods

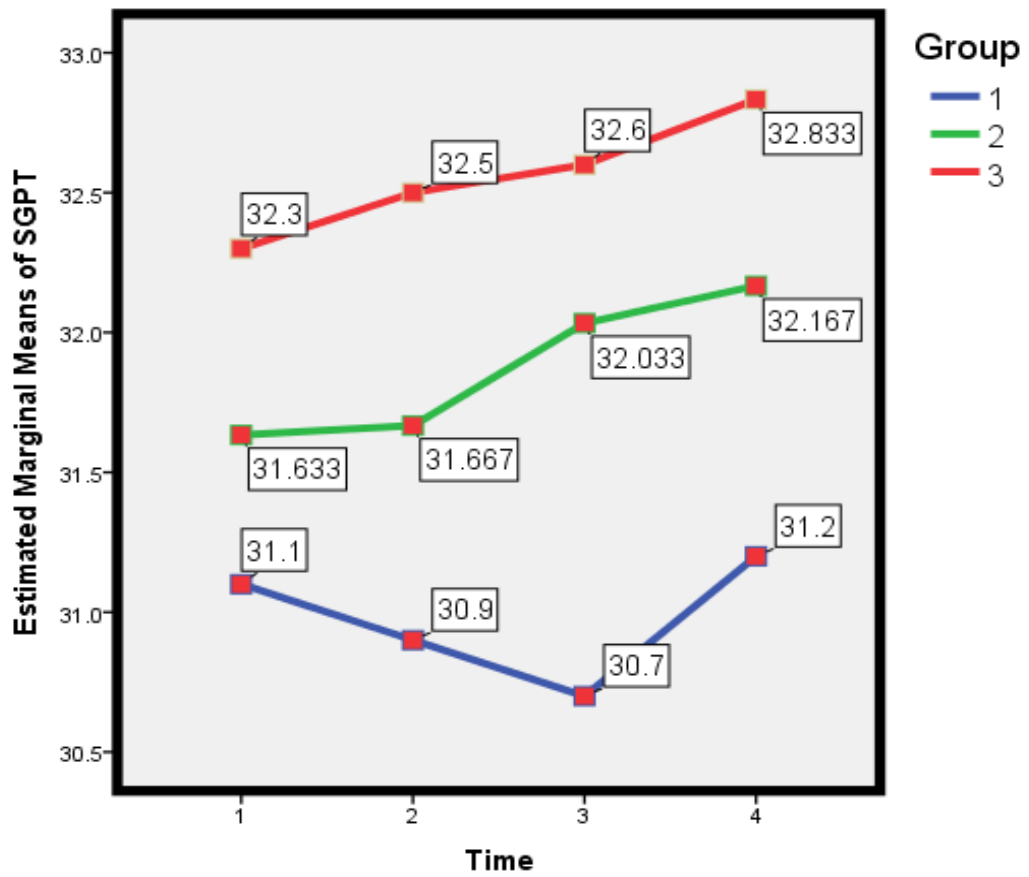


Table 18 Distribution of serum Alkaline phosphatase (ALP) levels across the 3 groups at various time periods (n=90)

An insignificant rise in serum ALP was seen from the baseline and at 12th weeks of the study group 3 and an insignificant reduction was seen in groups 2 & 3 as per table:18.

Serum ALP levels	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	10.40 ± 0.93	20.73 ± 36.79	10.93 ± 1.14
4 weeks	10.10 ± 0.96	20.40 ± 36.88	10.70 ± 1.06
8 weeks	10.20 ± 1.00	20.35 ± 36.55	10.33 ± 1.06
12 weeks	10.47 ± 0.78	20.33 ± 36.49	10.53 ± 1.04

ANOVA for repeated measures using a General linear model was done to test the difference in mean serum ALP levels at various time intervals between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

As the ANOVA for repeated measures was not statistically significant, post-hoc test was not done. Hence, the difference in mean serum ALP levels at various time intervals between the three groups was not statistically significant (p value: > 0.1).

p value	0.114
F statistic	2.229
Degree of freedom	2
Partial Eta square	0.049

Estimated marginal means of serum ALP levels

Group	Mean \pm Std. Error	95% Confidence Interval	
		Lower Bound	Upper Bound
1	10.292 \pm 3.867	2.606	17.977
2	20.454 \pm 3.867	12.769	28.140
3	10.625 \pm 3.867	2.940	18.310

Table 19 Distribution of serum triglyceride (TGL) levels across the 3 groups at various time periods (n=90)

A mean reduction in serum TGL was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant increase is seen in group 3, having baseline value of 182.9 to 175.5 at the end of the study.

Serum TGL levels (mgs %)	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	170.3 ± 23.0	189.0 ± 33.2	182.9 ± 24.0
4 weeks	169.3 ± 22.3	188.5 ± 33.7	180.4 ± 23.9
8 weeks	168.9 ± 22.9	187.7 ± 34.5	178.0 ± 23.2
12 weeks	168.3 ± 22.0	186.6 ± 35.5	175.5 ± 23.4
Mean TG reduction	2.0 ± 7.7	2.4 ± 5.7	7.3 ± 3.1

ANOVA test was done to test the difference in mean triglyceride reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean TG levels between the three groups.

p value	0.001
F statistic	7.954
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean TG levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). This data implies the superiority of group 3 in reducing triglyceride levels.

Dependent Variable (TG reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-0.380	1.000	-4.03	3.27
Group 1 Vs Group 3	-5.347	0.002	-9.00	-1.69
Group 2 Vs Group 3	-5.033	0.004	-8.62	-1.31

Fig.9: Profile plot showing distribution of TGL levels across the 3 groups at various time periods

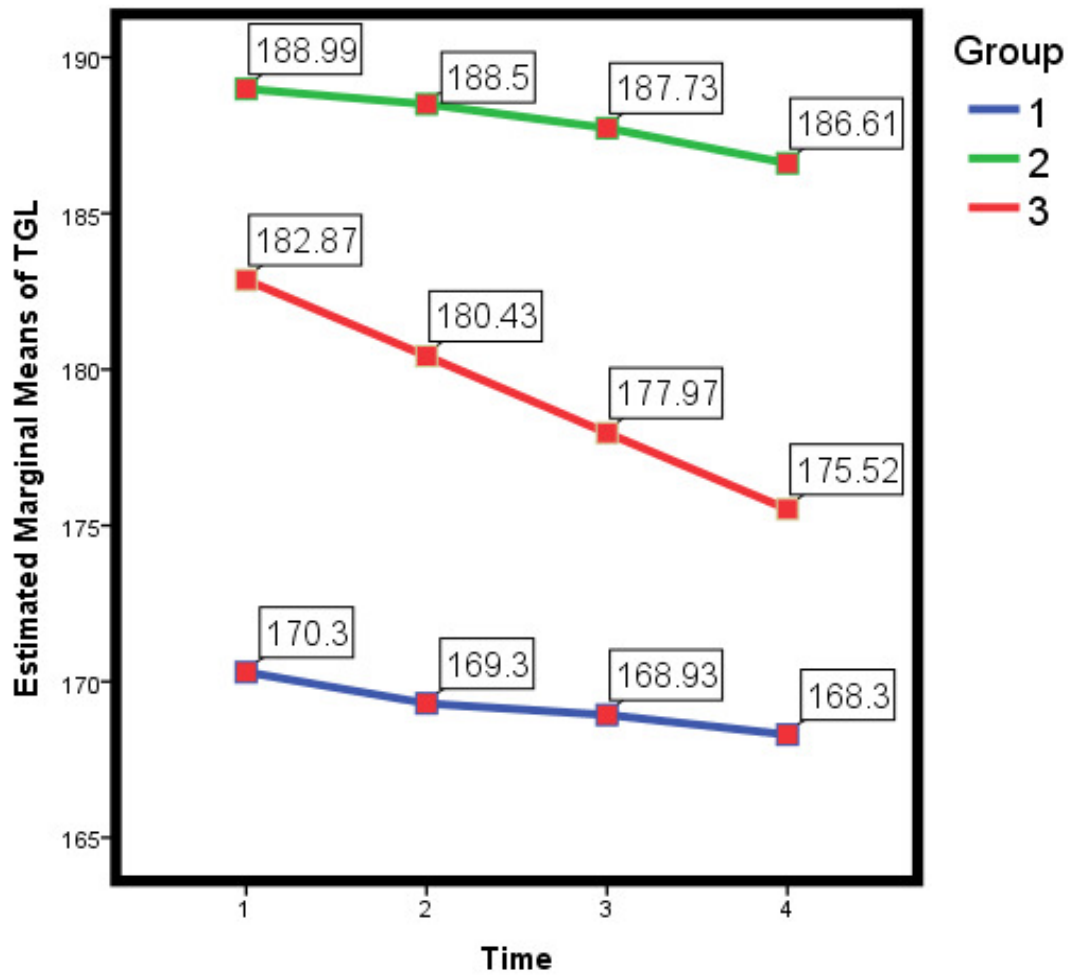


Table 20 Distribution of serum LDL levels across the 3 groups at various time periods (n=90)

A mean reduction in serum HDL was seen from the baseline at 4th, 8th and 12th weeks of the study in all the groups and a significant increase is seen in group 3, having baseline value of 132.3 to 123.2 at the end of the study.

Serum LDL levels (mgs %)	Group		
	1	2	3
	Mean ± Std Deviation	Mean ± Std Deviation	Mean ± Std Deviation
Baseline	124.5 ± 21.8	119.7 ± 36.3	132.3 ± 19.2
4 weeks	123.8 ± 22.0	118.1 ± 36.0	129.6 ± 18.4
8 weeks	123.8 ± 21.7	115.7 ± 35.0	126.6 ± 18.0
12 weeks	124.5 ± 21.9	113.0 ± 34.5	123.2 ± 17.1
Mean LDL reduction	0.00 ± 1.76	6.76 ± 3.56	9.13 ± 3.76

ANOVA test was done to test the difference in mean LDL reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean LDL levels between the three groups.

p value	<0.001
F statistic	67.582
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean LDL levels between Group 1 Vs Group 3, Group 1 Vs Group 2 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). Group 3 can significantly reduce serum LDL levels compared to other groups.

Dependent Variable (LDL reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-6.756	<0.001	-8.75	-4.77
Group 1 Vs Group 3	-9.130	<0.001	-11.12	-7.14
Group 2 Vs Group 3	-2.374	0.014	-4.36	-0.38

Fig.10: Profile plot showing distribution of LDL levels across the 3 groups at various time periods

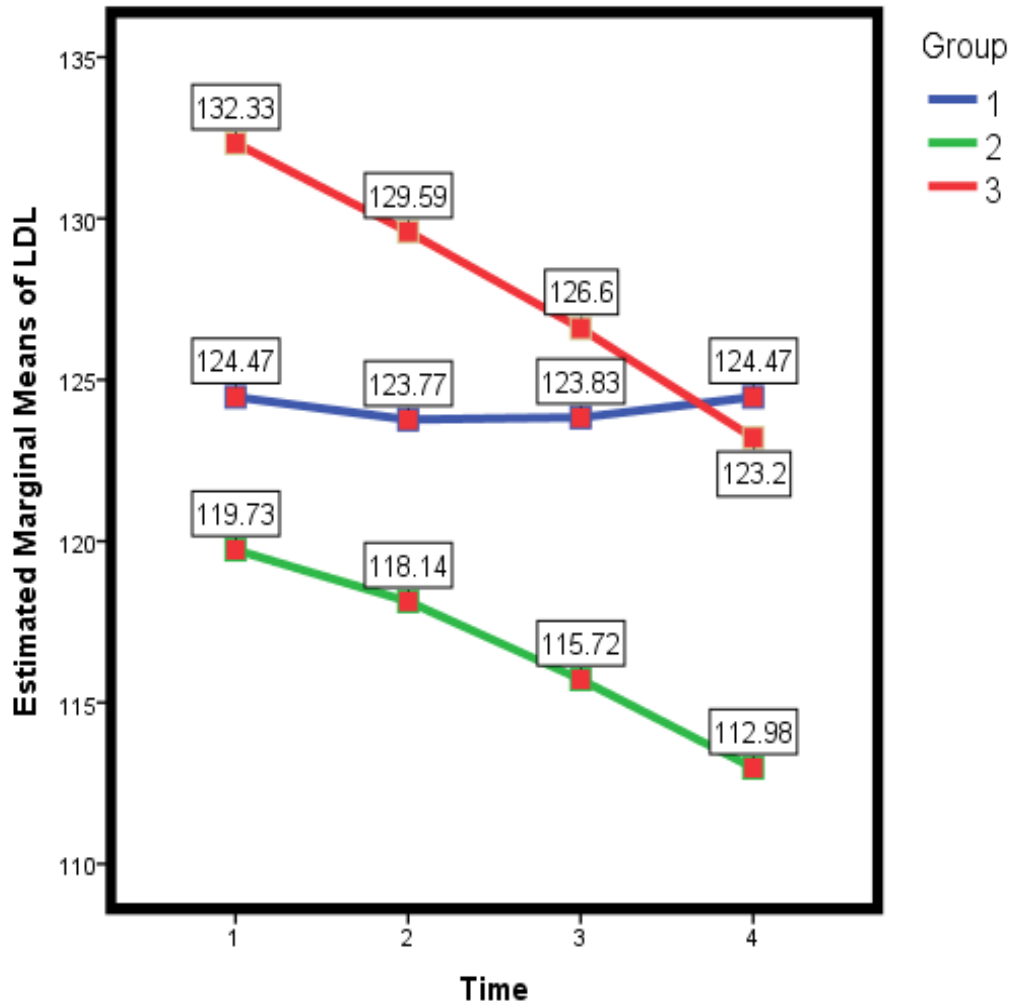


Table 21 Distribution of serum HDL levels across the 3 groups at various time periods (n=90)

A mean increment in serum HDL was seen from the baseline at 4th, 8th and 12th weeks of the study in groups 2 & 3 and a significant increase is seen in group 3, having baseline value of 35.79 to 37.87 at the end of the study.

Serum HDL levels (mgs %)	Group		
	1	2	3
	Mean Std Deviation	Mean Std Deviation	Mean Std Deviation
Baseline	33.33 ± 1.77	37.73 ± 23.04	35.79 ± 3.41
4 weeks	32.87 ± 1.78	37.76 ± 23.08	36.45 ± 3.03
8 weeks	32.90 ± 1.94	37.78 ± 23.08	37.00 ± 3.15
12 weeks	32.83 ± 1.74	37.89 ± 22.99	37.87 ± 2.91
Mean HDL increase	-0.50 ± 0.90	0.15 ± 0.51	2.09 ± 0.73

ANOVA test was done to test the difference in mean HDL increase after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in mean HDL increase between the three groups.

p value	<0.001
F statistic	101.793
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in rise in mean HDL levels between Group 1 Vs Group 3, Group 1 Vs Group 2 and Group 2 Vs Group 3 was statistically significant (p value: <0.05). This data implies that group 3 was effective in increasing HDL levels.

Dependent Variable (HDL rise after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-0.653	0.002	-1.11	-.19
Group 1 Vs Group 3	-2.587	<0.001	-3.05	-2.13
Group 2 Vs Group 3	-1.933	<0.001	-2.39	-1.47

Fig.11: Profile plot showing distribution of HDL levels across the 3 groups at various time periods

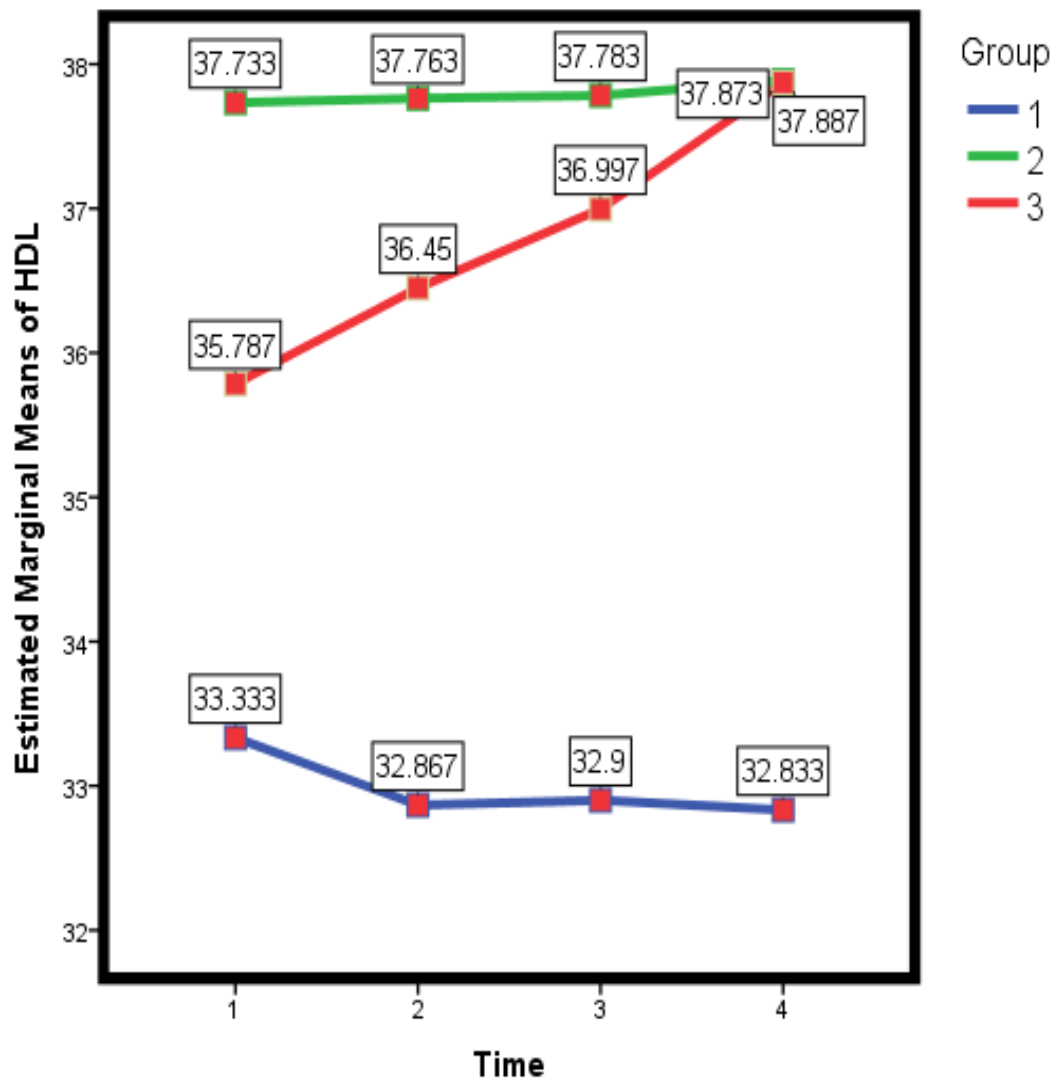


Table 22 Distribution of serum total cholesterol (TC) levels across the 3 groups at various time periods (n=90)

A reduction in the mean serum TC level was seen from the baseline at 4th, 8th and 12th weeks of the study in groups 2 & 3 a significant reduction is seen in group 3, having baseline value of 156.13 to 152.63 at the end of the study.

Serum TC levels (mgs%)	Group		
	1	2	3
	Mean Std Deviation	Mean Std Deviation	Mean Std Deviation
Baseline	160.13 ± 24.24	169.47 ± 17.87	156.13 ± 18.89
4 weeks	159.67 ± 23.77	168.95 ± 17.91	154.93 ± 18.65
8 weeks	159.33 ± 23.68	168.18 ± 18.17	153.65 ± 18.68
12 weeks	159.73 ± 23.81	167.35 ± 18.57	152.63 ± 18.30
Mean TC reduction	0.40 ± 1.33	2.13 ± 1.84	3.50 ± 2.73

ANOVA test was done to test the difference in mean total cholesterol reduction after 12 weeks of therapy between the three groups followed by Bonferroni post-Hoc test for inter-group comparisons.

ANOVA test

ANOVA test showed that there was a statistically significant difference in reduction of the mean total cholesterol levels between the three groups.

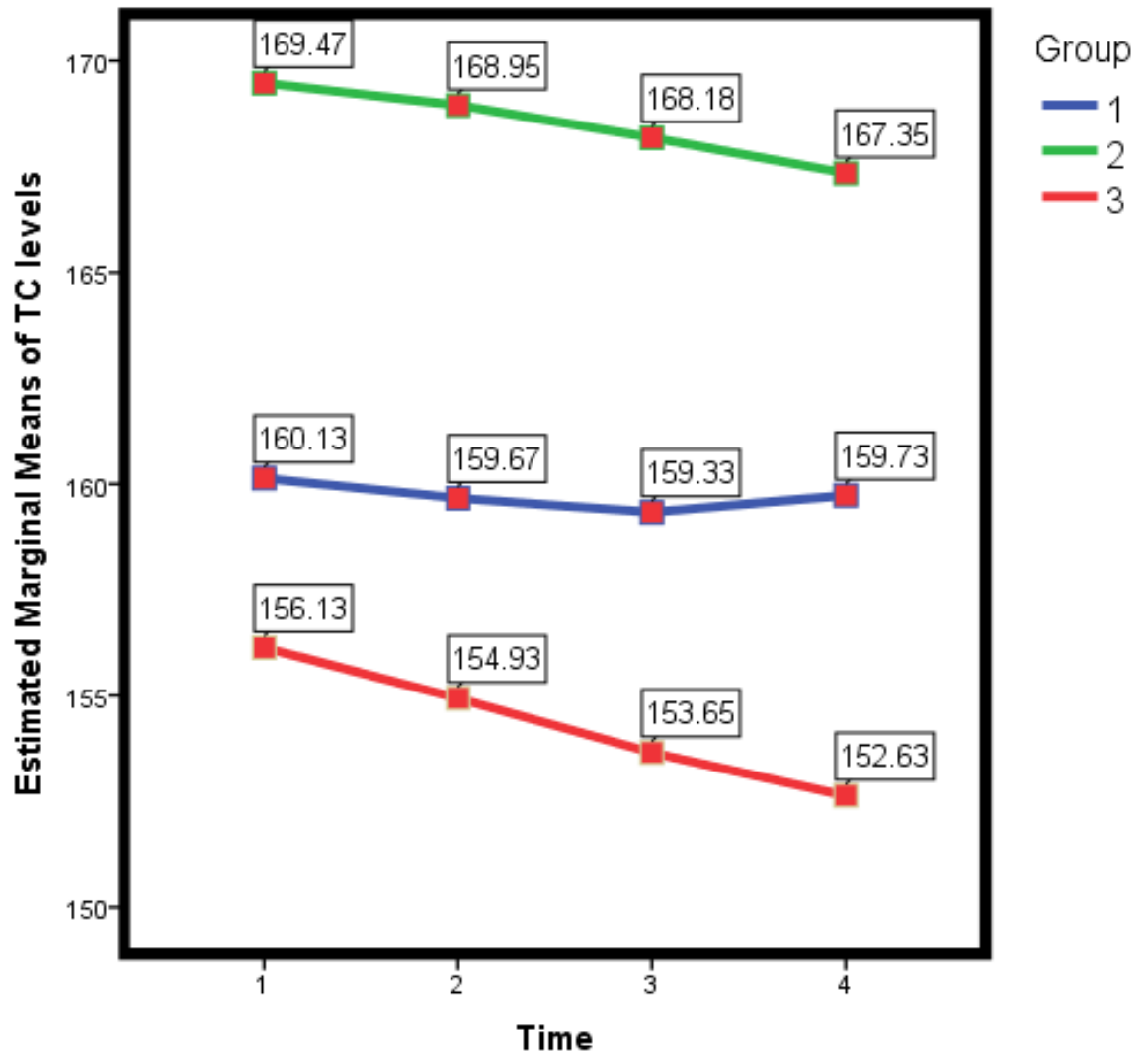
p value	<0.001
F statistic	17.270
Degree of freedom	2

Bonferroni Post-Hoc test

Bonferroni test showed that the difference in reduction in mean total cholesterol levels between Group 1 Vs Group 3, Group 1 Vs Group 2 and Group 2 Vs Group 3 was statistically significant (p value: <0.05), denoting the superiority of group 3 in reducing total cholesterol.

Dependent Variable (TC reduction after 12 weeks)	Mean Difference (1st - 2nd)	p value	95% Confidence Interval	
			Lower	Upper
Group 1 Vs Group 2	-1.727	0.005	-3.02	-0.44
Group 1 Vs Group 3	-3.100	<0.001	-4.39	-1.81
Group 2 Vs Group 3	-1.373	0.033	-2.66	-0.08

Fig.12: Profile plot showing distribution of TC levels across the 3 groups at various time periods



DISCUSSION

Rheumatoid arthritis is a chronic inflammatory, autoimmune disease which leads to rapid onset of clinically significant functional impairment, particularly if not controlled properly by DMARDs. Statins, because of their pleiotropic effects have been used in various trials to prove their efficacy in RA.

The present study was conducted to find out the effect of Pitavastatin in active RA patients along with Methotrexate, compared to Methotrexate monotherapy and Methotrexate ,Rosuvastatin combination therapy. This study was undertaken in 90 active RA patients who attended the medicine outpatient department of Chennai Medical College Hospital and Research Centre ,Trichy. The study population were divided into 3 groups of 30 each. A daily oral dose of 1 mg of Pitavastatin was administered to the 30 subjects with active RA belonging to group 3, along with Methotrexate 7.5 mg once weekly for a period of 12 weeks. The immunological parameters were tested at the end of the study i.e) after 3rd month and compared with the baseline. The biochemical parameters of all the three groups were evaluated at the end of each months, (4th week, 8th week. 12th week) and the results were statistical analysed by ANOVA method. Additionally, post-hoc test (Bonferroni test) was used to compare the intergroup means.

Effect of Pitavastatin on DAS score:

The reduction in mean DAS scores was maximum among the subjects under pitavastatin + methotrexate group. Bonferroni test showed that the difference in reduction in mean DAS scores between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: 0.004). Hence pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the DAS scores. Though there is a difference in reduction in mean DAS scores between Group 1 Vs Group 2, it was not statistically significant (p value: >0.05). This result is comparable with the result of Kumar et al,³² but against the studies conducted by Ekabmukther et al, Mc carrey et al & Das et al.^{7,22,31}

Effect of Pitavastatin on Immunological Parameters:

The reduction in mean RA factor levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under rosuvastatin and methotrexate. Bonferroni test showed that the difference in reduction in mean RA factor levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.002). Hence pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the mean RA factor levels. The difference in reduction of mean RA factor levels between Group 1 Vs Group 2 was not statistically significant (p value: >0.05).

This correlates with the studies conducted by Abeles AM et al, Chan AU et al, Niwa S et al.^{43,44,45}

The reduction in mean anti-CCP levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under rosuvastatin and methotrexate. Bonferroni test showed that the difference in reduction in mean anti-CCP levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.001). Hence pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the mean anti-CCP levels. This correlates with the studies conducted by Abeles AM et al, Chan AU et al and Niwa S et al.^{43,44,45}

Effect of Pitavastatin on Acute Phase Reactants:

The reduction in mean ESR levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under methotrexate monotherapy. Bonferroni test showed that the difference in reduction in mean ESR levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.001). Pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the mean ESR levels. However, difference in reduction of mean ESR levels between Group 1 Vs Group 2 was not statistically significant (p value: >0.05). This

result favours the previous studies by Kumar et al, Ekabmukther et al, Mccarrey et al and Das et al.^{7,22,31,32}

The reduction in mean ESR levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under rosuvastatin and methotrexate. Bonferroni test showed that the difference in reduction in mean CRP levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.001). This shows that pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the mean CRP levels. Difference in reduction of mean CRP levels between Group 1 Vs Group 2 was not statistically significant (p value: >0.05), comparable to the studies by Kumar et al, Ekabmukther et al, Mc carrey et al and Das et al.^{7,22,31,32}

All the three groups did not show a statistically significant change in blood glucose levels. This is in contrast with studies by Sattar Net et al, Ray K et al and Preiss et al.^{46,47,48,49}

The renal parameters like blood urea, serum creatinine were also not showed any variations among the groups which is in contrast with studies by Mc carrey et al and Ogata et al.^{7,51}

The serum SGOT, serum SGPT levels was maximum among the subjects under pitavastatin + methotrexate group. Bonferroni test showed that the difference in serum SGOT, serum SGPT levels between Group 1 Vs Group 3 was statistically significant (p value: <0.010) and (p value: <0.001) respectively. Hence pitavastatin and methotrexate combined therapy raised the serum SGOT levels in comparison to methotrexate monotherapy. However, difference in mean serum SGOT, serum SGPT levels between Group 1 Vs Group 2 and Group 2 Vs Group 3 was not statistically significant (p value: >0.05). No change in the mean ALP levels among the groups were noticed. Though the elevation in serum transaminases were statistically significant, there was no clinical significance. This result is in consistent with the study by Mukthar et al.⁵⁰

Effect of Pitavastatin on lipid profile:

The reduction in mean TG levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under rosuvastatin and methotrexate. Bonferroni test showed that the difference in reduction in mean TG levels between Group 1 Vs Group 3 and Group 2 Vs Group 3 was statistically significant (p value: <0.002). The difference in reduction of mean TG levels between Group 1 Vs Group 2 was not statistically significant (p value: >0.05). Hence pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the mean TG levels.

This correlates with the studies conducted by Jick et al, LIVES study, JAPAN-ACS study, CHIBA study and PATROL trial.^{14,37,38,39}

The reduction in mean LDL levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under rosuvastatin and methotrexate. Bonferroni test showed that the difference in reduction in mean LDL levels between Group 1 Vs Group 3, Group 1 Vs Group 2 and Group 2 Vs Group 3 was statistically significant (p value: <0.001). Hence pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in reducing the mean LDL levels, comparable to studies by Jick et al, LIVES study, JAPAN-ACS study, CHIBA study, PATROL trial, Fujino et al and Sailo et al.^{14,35,36,37,38,39}

The mean increment in HDL levels of 3 groups in descending order is Group 3 > Group 2 > Group 1. The rise in mean HDL levels was maximum among the subjects under pitavastatin + methotrexate group followed by subjects under rosuvastatin and methotrexate. Bonferroni test showed that the difference in rise in mean HDL levels between Group 1 Vs Group 3, Group 1 Vs Group 2 and Group 2 Vs Group 3 was statistically significant (p value: <0.001). Hence pitavastatin and methotrexate combined therapy is superior to methotrexate monotherapy and combined therapy with rosuvastatin and methotrexate in rising the mean HDL levels which is in relevant to the LIVES

study, JAPAN-ACS study, CHIBA study, PATROL trial and study by Jick et al.^{14,37,38,39}

The reduction in mean total cholesterol levels was maximum among the subjects under pitavastatin + methotrexate group (p value: <0.001), compared to other groups showing the superiority in reducing the mean total cholesterol levels as seen in the LIVES study, JAPAN-ACS study, CHIBA study, PATROL trial and study by Jick et al.^{14,37,38,39}

The highlight of the present study is the identification of superiority of pitavastatin as an adjuvant therapy along with methotrexate in the management of patients with active RA with marked inflammation.

CONCLUSION

Pitavastatin decreases the disease activity score, and improves the well-being of patients with active RA by lowering the rheumatoid factors and anti CCP levels. It significantly reduces inflammation in active RA which is evident from the decrease in the ESR and CRP levels. Further the side effects such as myopathy, precipitation of diabetes seen with others statins are not that much pronounced while using Pitavastatin except a slight elevation in the hepatic transaminases ,which is not clinically significant but statistically significant, which may be attributed to the concurrent use of methotrexate. Further studies with large sample size can clearly justify the occurrence of this side effect. Further it raises the HDL level, lowers TG, TC and LDL levels and have a favouring effect in reducing the cardiovascular risk factors .Considering the increasing morbidity and mortality in crippling disease-RA, particularly involving the cardiovascular system, addition of a potent statin like Pitavastatin as an adjuvant to DMARDs can improve the quality of life of patients.

S.no	Group	Name	Age	Agegroup	Sex	Wt	Ht	BMI	BMIgroup	DAS.0	DAS.1	DAS.2	DAS.3	ESR.0	ESR.1	ESR.2	ESR.3
1	1	Chitra	41	41 to 50 years	Female	54	1.43	26.40716	>25	7.68	7.43	7.02	6.92	27	25	25	24
2	1	Haridoss	52	51 to 60 years	Male	62	1.64	23.05176	23 to 24.9	7.74	6.82	4.72	2.66	46	34	38	40
3	1	Kalaiselvi	40	31 to 40 years	Female	50	1.42	24.79667	23 to 24.9	7.15	6.98	6.78	6.62	62	60	62	66
4	1	Mehraj Banu	38	31 to 40 years	Female	69	1.58	27.6398	>25	5.97	5.47	5.38	5.12	33	25	25	24
5	1	Sangeetha	48	41 to 50 years	Female	78	1.64	29.0006	>25	6.46	6.04	5.73	5.28	38	32	32	32
6	1	kermals	39	31 to 40 years	Female	58	1.63	21.82995	18.5 to 22.9	6.88	6.25	5.9	5.67	48	39	31	24
7	1	Mani Kandan	52	51 to 60 years	Male	82	1.68	29.05329	>25	6.51	5.85	5.66	5.61	36	29	22	24
8	1	Mohamed Ismail	55	51 to 60 years	Male	66	1.72	22.30936	18.5 to 22.9	6.6	6.11	5.83	5.67	32	28	22	20
9	1	Kasthuri	60	51 to 60 years	Female	56	1.49	25.22409	>25	5.95	5.31	5.13	4.92	24	20	20	18
10	1	Mallika	36	31 to 40 years	Female	52	1.49	23.42237	23 to 24.9	6.69	6.27	5.79	5.66	36	38	38	40
11	1	Kanagasabai, 43	43	41 to 50 years	Male	75	1.78	23.778	23 to 24.9	6.34	5.85	5.47	4.99	32	29	24	20
12	1	Ayeesha Begum 6	60	51 to 60 years	Female	88	1.56	36.16042	>25	8.07	7.68	7.32	7.16	85	88	80	60
13	1	Mageshwaran	43	41 to 50 years	Male	97	1.8	29.93827	>25	7.01	6.14	5.56	5.26	52	48	48	46
14	1	Nagavalli 59/F	59	51 to 60 years	Female	65	1.62	24.76757	23 to 24.9	6.82	6.27	5.72	5.42	38	32	24	19
15	1	Thambidhurai 38	38	31 to 40 years	Male	69	1.68	24.44728	23 to 24.9	7.16	6.6	6.11	5.83	36	28	24	24
16	1	Rajakumari 3/F	34	31 to 40 years	Female	62	1.54	26.14269	>25	7.82	7.13	6.98	6.71	64	56	54	54
17	1	Angayarkanni 56	56	51 to 60 years	Female	54	1.57	21.90758	18.5 to 22.9	6.47	6.14	5.94	5.74	36	20	16	12
18	1	Dharmambal 60/F	60	51 to 60 years	Female	54	1.62	20.57613	18.5 to 22.9	6.42	6.22	6	5.31	36	24	20	18
19	1	Mariyapushpam 4	43	41 to 50 years	Female	72	1.59	28.47989	>25	5.97	5.46	5.34	5.06	28	19	17	14
20	1	Anbuselvi 58/F	58	51 to 60 years	Female	82	1.6	32.03125	>25	7.77	7.24	6.82	6.28	86	67	44	26
21	1	Manoharan 49/M	49	41 to 50 years	Male	80	1.76	25.82645	>25	6.74	5.89	5.64	5.23	48	21	18	12
22	1	Mohanambal 52/F	52	51 to 60 years	Female	77	1.6	30.07813	>25	6.72	6.04	5.92	5.63	38	21	15	14
23	1	Suriyanarayanan	50	41 to 50 years	Male	75	1.8	23.14815	23 to 24.9	7.11	6.82	6.74	5.73	60	50	48	34

S.no	Group	Name	Age	Agegroup	Sex	Wt	Ht	BMI	BMIgroup	DAS.0	DAS.1	DAS.2	DAS.3	ESR.0	ESR.1	ESR.2	ESR.3
24	1	Abdul rehman 58	58	51 to 60 years	Male	86	1.78	27.14304	>25	7.97	7.41	6.62	6.52	78	62	49	48
25	1	Lakhsmi 34/F	34	31 to 40 years	Female	62	1.59	24.52435	23 to 24.9	6.67	6.21	5.82	5.36	39	24	22	22
26	1	Vishalatchi 40/	40	31 to 40 years	Female	72	1.49	32.43097	>25	7.61	6.82	6.52	6.34	84	68	52	36
27	1	Mohanraj 52/M	52	51 to 60 years	Male	64	1.6	25	>25	8.15	7.37	7.06	6.55	95	62	54	39
28	1	Vijayalakshmi 4	49	41 to 50 years	Female	54	1.56	22.18935	18.5 to 22.9	6.54	6.32	6.02	5.96	62	50	42	29
29	1	Radhabai 60/F	60	51 to 60 years	Female	62	1.56	25.47666	>25	4.92	4.52	3.94	3.62	48	32	20	14
30	1	Soundarajan 50/	50	41 to 50 years	Male	82	1.79	25.59221	>25	5.9	5.42	5.22	5.08	44	38	39	38
31	2	Selvi	40	31 to 40 years	Female	85	1.62	32.38836	>25	8.21	7.34	7.06	6.09	37	33	26	19
32	2	Ramasamy 53/M	53	51 to 60 years	Male	75	1.78	23.67125	23 to 24.9	7.49	7	6.76	6.29	35	29	21	14
33	2	Vedivazhagi 70/	70	61 to 70 years	Female	59	1.62	22.48133	18.5 to 22.9	8.07	6.52	5.49	4.27	85	52	45	23
34	2	Suriya Begum 55	55	51 to 60 years	Female	71	1.56	29.17489	>25	7.66	7.06	6.36	6.04	85	69	56	42
35	2	Mangayarkarashi	39	31 to 40 years	Female	49	1.63	18.44255	<18.5	5.47	5.12	4.76	4.39	42	38	41	43
36	2	Samsunisha 50/F	50	41 to 50 years	Female	89	1.62	33.91251	>25	6.08	5.68	5.22	4.98	33	25	28	20
37	2	Chitradevi 49/F	49	41 to 50 years	Female	68	1.6	26.5625	>25	6.57	6.14	5.93	5.6	44	37	28	20
38	2	Therasa 60/F	60	51 to 60 years	Female	59	1.55	24.55775	23 to 24.9	6.99	6.32	5.94	5.69	63	56	44	32
39	2	Ponnammal 62/F	62	61 to 70 years	Female	47	1.54	19.81784	18.5 to 22.9	5.4	4.94	4.78	4.3	52	41	30	21
40	2	Malathi 50/F	50	41 to 50 years	Female	85	1.58	34.04903	>25	7.02	6.48	6.48	5.98	84	71	54	42
41	2	Jeenath koloru	48	41 to 50 years	Female	86	1.59	34.01764	>25	6.16	5.95	5.75	5.38	45	33	25	17
42	2	Jeenath 44/F	44	41 to 50 years	Female	78	1.78	24.6181	23 to 24.9	7.27	6.77	6.36	5.93	95	82	73	73
43	2	Murugesan 43/M	43	41 to 50 years	Male	91	1.75	29.71429	>25	6.18	5.97	5.46	5.19	46	38	32	27
44	2	Dhanalakshmi48/	48	41 to 50 years	Female	59	1.68	20.9042	18.5 to 22.9	5.9	5.51	5.07	4.82	46	38	32	27
45	2	Rajagopalan 56	56	51 to 60 years	Male	86	1.81	26.25073	>25	6.53	6.09	5.71	5.22	62	58	57	55
46	2	Abdul Rahman 50	50	41 to 50 years	Male	90	1.8	27.77778	>25	5.77	5.39	4.89	4.54	33	28	22	18

S.no	Group	Name	Age	Agegroup	Sex	Wt	Ht	BMI	BMIgroup	DAS.0	DAS.1	DAS.2	DAS.3	ESR.0	ESR.1	ESR.2	ESR.3
47	2	Navmadha 48/F	48	41 to 50 years	Female	52	1.5	23.11111	23 to 24.9	6.18	5.85	5.47	4.96	32	27	24	18
48	2	Fousal Hithaua	39	31 to 40 years	Female	62	1.49	27.92667	>25	5.95	5.33	4.98	4.78	30	28	28	28
49	2	Marimuthu 52/M	52	51 to 60 years	Male	60	1.75	19.59184	18.5 to 22.9	7.11	6.7	6.18	5.69	62	57	56	54
50	2	Swarnalatha46/F	46	41 to 50 years	Female	48	1.56	19.72387	18.5 to 22.9	5.5	5.06	4.61	4.18	29	24	20	16
51	2	Usharani 48/F	48	41 to 50 years	Female	70	1.58	28.04038	>25	6.58	6.08	5.49	5.08	48	40	33	25
52	2	Shanmugasundram	50	41 to 50 years	Male	50	1.79	15.60501	<18.5	5.23	4.82	4.71	3.48	22	19	18	16
53	2	Mohan kumar 54	54	51 to 60 years	Male	90	1.81	27.47169	>25	7.18	6.5	6.12	5.96	68	60	52	43
54	2	Vasanthi, 51/F	51	51 to 60 years	Female	54	1.47	24.98959	23 to 24.9	6.29	5.87	5.52	5.02	54	49	46	40
55	2	Jeyashankar, 48	48	41 to 50 years	Male	60	1.65	22.03857	18.5 to 22.9	7.26	6.73	6.39	5.97	76	78	70	64
56	2	Narendran, 39/M	39	31 to 40 years	Male	74	1.81	22.58783	18.5 to 22.9	5.68	5.2	4.68	4.3	28	22	20	20
57	2	Saravanaperumal	52	51 to 60 years	Male	72	1.75	23.5102	23 to 24.9	6.18	5.73	5.16	4.82	33	30	30	30
58	2	Vetriselvi 56/F	56	51 to 60 years	Female	62	1.64	23.05176	23 to 24.9	7.27	6.51	6.11	5.55	88	81	80	78
59	2	Thamarai, 49/F	49	41 to 50 years	Female	69	1.51	30.26183	>25	6.69	5.96	5.23	5.16	73	70	69	67
60	2	Abirami, 36/F	36	31 to 40 years	Female	75	1.63	28.22839	>25	4.91	4.32	4.11	3.78	32	32	31	31
61	3	Chandra, 55/F	55	51 to 60 years	Female	75	1.51	32.89329	>25	6.53	5.86	4.92	2.96	45	36	25	14
62	3	Mahendran, 34/F	34	31 to 40 years	Female	90	1.82	27.17063	>25	5.9	4.98	3.55	2.99	42	34	23	14
63	3	Jeyakodi, 46/F	46	41 to 50 years	Female	55	1.54	23.1911	23 to 24.9	7.08	5.08	3.63	2.83	48	33	22	18
64	3	Manivannan, 52/	52	51 to 60 years	Male	80	1.75	26.12245	>25	5.91	4.86	4.14	2.97	34	24	19	15
65	3	Chitra, 43/F	43	41 to 50 years	Female	49	1.52	21.20845	18.5 to 22.9	6.11	4.89	4.06	2.97	42	25	18	15
66	3	Thenmozhi, 60/F	60	51 to 60 years	Female	66	1.52	28.56648	>25	5.18	4.33	3.78	2.92	31	24	18	15
67	3	Prabakaram, 46/	46	41 to 50 years	Male	94	1.82	28.37822	>25	6.92	5.87	4.99	4.27	60	30	23	18
68	3	Anushuya, 46/f	46	41 to 50 years	Female	51	1.53	21.78649	18.5 to 22.9	5.77	5.15	4.21	2.92	30	22	18	14
69	3	Sivakami, 54/F	54	51 to 60 years	Female	49	1.58	19.62827	18.5 to 22.9	6.63	5.5	4.28	3.03	40	36	22	12

S.no	Group	Name	Age	Agegroup	Sex	Wt	Ht	BMI	BMIgroup	DAS.0	DAS.1	DAS.2	DAS.3	ESR.0	ESR.1	ESR.2	ESR.3
70	3	Savithri, 52/F	52	51 to 60 years	Female	72	1.6	28.125	>25	5.93	4.73	3.69	2.84	61	42	28	14
71	3	Padma, 42/F	42	41 to 50 years	Female	61	1.54	25.72103	>25	6.39	5.42	4.02	2.96	49	35	25	18
72	3	Radha krishnan,	49	41 to 50 years	Male	94	1.84	27.76465	>25	6.93	5.83	4.17	2.99	45	41	30	21
73	3	Ambika, 49/F	49	41 to 50 years	Female	65	1.56	26.7094	>25	6.33	5.52	4.02	3.09	54	46	35	22
74	3	Majibhur ghari,	58	51 to 60 years	Male	94	1.8	29.01235	>25	6.04	5.17	3.41	2.73	42	33	21	13
75	3	RehmathNisha, 3	35	31 to 40 years	Female	72	1.61	27.77671	>25	5.72	4.6	3.28	2.04	38	30	22	15
76	3	Grace mary, 51/	51	51 to 60 years	Female	50	1.49	22.52151	18.5 to 22.9	6.27	5.08	4.1	2.8	41	32	22	13
77	3	Rajarajan, 50/M	50	41 to 50 years	Male	68	1.79	21.22281	18.5 to 22.9	7.16	5.52	4.16	3.18	42	38	43	21
78	3	Mariyakokila, 5	54	51 to 60 years	Female	60	1.6	23.4375	23 to 24.9	7.6	6.12	4.64	3.03	68	66	32	19
79	3	Muthulakshmi, 4	40	31 to 40 years	Female	69	1.64	25.65437	>25	6.34	5.01	3.63	2.06	54	29	22	14
80	3	Narayanan, 52/M	52	51 to 60 years	Male	80	1.75	26.12245	>25	7	6.04	4.68	3.25	60	49	41	20
81	3	G.Chandra, 46/F	46	41 to 50 years	Female	54	1.5	24	23 to 24.9	8.35	5.75	4.39	2.76	62	40	29	18
82	3	Malathi, 52/f	52	51 to 60 years	Female	70	1.62	26.67276	>25	7.18	5.69	4.43	3.43	78	59	44	23
83	3	Riswan Beevi, 4	40	31 to 40 years	Female	64	1.52	27.70083	>25	6.56	5.2	3.42	2.67	41	32	21	15
84	3	Zaheer hussari,	44	41 to 50 years	Male	82	1.79	25.59221	>25	7.28	6.43	5.5	4.54	70	60	42	20
85	3	Neournisha, 38/	38	31 to 40 years	Female	56	1.58	22.4323	18.5 to 22.9	6.35	5.43	4.2	3.38	56	48	39	25
86	3	Ranjani, 44/F	44	41 to 50 years	Female	74	1.63	27.85201	>25	6.58	5.41	4.2	2.86	55	45	41	22
87	3	Sivaraman, 39/M	39	31 to 40 years	Male	85	1.81	25.94548	>25	7.66	6.49	5.12	3.73	48	32	27	21
88	3	Rajendran, 50/M	50	41 to 50 years	Male	85	1.76	27.4406	>25	6.2	5.97	4.38	2.78	48	36	22	14
89	3	Dheergasumangal	49	41 to 50 years	Female	52	1.49	23.42237	23 to 24.9	6.4	5.11	3.83	3.06	62	41	32	14
90	3	Devarajan, 45/M	45	41 to 50 years	Male	70	1.68	24.80159	23 to 24.9	5.98	4.59	3.48	2.87	44	32	21	16

S.no	Group	Name	ESR.reduction	BL.H6.0	BL.H6.1	BL.H6.2	BL.H6.3	TC.0	TC.1	TC.2	TC.3	Platelet.0	Platelet.1	Platelet.2	Platelet.3	CRP.0	CRP.1	CRP.2	CRP.3	CRP.reduction
1	1	Chitra	3	9.1	8.8	7.8	9	9400	8000	7000	6200	1.6	1.5	1.5	2	40	35	32	24	16
2	1	Haridoss	6	12.2	12.4	12	12.1	9200	8700	9000	9300	1.5	2	2	1.8	32	30	24	22	10
3	1	Kalaiselvi	-4	12.8	11.8	12	11.5	13600	10100	950	9900	2.2	2	2	1.8	30	28	24	26	4
4	1	Mehraj Banu	9	8.1	8	7.8	8	10700	9800	9400	8800	2	2	1.8	1.8	20	18	20	20	0
5	1	Sangeetha	6	9.4	9.8	10	9.6	10900	10200	9900	10100	1.8	1.6	1.6	1.7	22	20	19	15	7
6	1	kermals	24	9	9	8.8	8.8	10920	10800	10300	10400	2	2	1.8	2	33	30	27	24	9
7	1	Mani Kandan	12	9.2	9	9.2	8.8	9900	9800	9900	9400	1.8	1.8	1.6	1.8	29	27	20	18	11
8	1	Mohamed Ismail	12	9.4	9.6	9.2	9.2	9900	9600	9700	9400	2.2	2.2	2	2	28	24	20	16	12
9	1	Kasthuri	6	9.2	9	9.2	9	10200	10400	10300	10100	1.8	2	1.8	1.8	11	10	9	7	4
10	1	Mallika	-4	9.6	9	9.2	9	9200	9400	9500	9300	2	1.8	1.8	1.8	13	11	11	8	5
11	1	Kanagasabai, 43	12	9.8	9.6	9.4	9.4	9200	9100	8900	8900	2.2	2	2	2.1	11	10	8	8	3
12	1	Ayeesha Begum 6	25	10.6	10.7	9	10.1	8000	6400	6800	6300	1.6	1.5	1.6	1.6	26	22	16	14	12
13	1	Mageshwaran	6	11.6	11	10.8	10.6	9400	8800	9200	9300	1.7	1.8	1.8	1.7	34	28	22	16	18
14	1	Nagavalli 59/F	19	9	8.8	9	8.6	8900	9100	9100	9000	1.8	2	1.8	1.6	30	26	20	11	19
15	1	Thambidhurai 38	12	9	8.4	8.6	8.8	7900	8000	8400	8100	1.8	2	1.6	1.8	19	12	9	7	12
16	1	Rajakumari 3/F	10	9.6	9.6	9.4	9	8600	8000	7800	7300	1.8	1.6	1.6	1.5	19	12	9	8	11
17	1	Angayarkanni 56	24	10.2	10	9.4	9.4	9500	9600	9300	8900	2	2	1.8	1.6	28	12	9	9	19
18	1	Dharmambal 60/F	18	9.8	9.8	9.6	9.6	9720	9600	9800	9300	2	2	1.8	1.6	29	21	19	11	18
19	1	Mariyapushpam 4	14	8.8	8.4	8.6	8.4	10200	9800	9200	9400	1.6	1.8	1.6	1.6	13	9	7	7	6
20	1	Anbuselvi 58/F	60	11.2	10.8	10.8	10.4	8600	6100	6600	6400	1.8	1.6	1.6	1.6	30	22	16	11	19
21	1	Manoharan 49/M	36	8.4	8.4	8.6	8.4	10400	10200	10100	9800	1.8	1.6	1.5	1.5	24	13	11	9	15
22	1	Mohanambal 52/F	24	10.2	10.4	10	10	9800	9600	9600	9200	1.8	1.8	2	1.8	20	11	9	7	13
23	1	Suriyanarayanan	26	11.6	10.6	9.8	9.8	9600	9400	9200	9000	2	1.8	1.8	1.6	31	22	18	16	15

S.no	Group	Name	ESR.reduction	BL.H6.0	BL.H6.1	BL.H6.2	BL.H6.3	TC.0	TC.1	TC.2	TC.3	Platelet.0	Platelet.1	Platelet.2	Platelet.3	CRP.0	CRP.1	CRP.2	CRP.3	CRP.reduction
24	1	Abdul rehman 58	30	9.6	9.2	8.8	8.8	10800	10600	10600	9800	1.5	1.5	1.5	1.5	42	30	26	19	23
25	1	Lakshmi 34/F	17	10.6	10.2	10.2	10.2	9800	9400	9600	9200	2	1.8	1.8	1.6	20	13	11	9	11
26	1	Vishalatchi 40/	48	9	8.8	8.6	8.4	9400	9200	9800	9500	1.5	1.5	1.5	1.4	32	28	20	13	19
27	1	Mohanraj 52/M	56	10.2	9.8	9.8	8.8	11000	10600	10200	10200	1.5	1.5	1.6	1.5	38	32	26	20	18
28	1	Vijayalakshmi 4	33	9.8	9.6	9.8	9.4	8600	8500	8600	8200	1.6	1.6	1.5	1.6	40	31	29	29	11
29	1	Radhabai 60/F	34	12	11.6	11.6	10.4	11400	11000	10900	10600	1.5	1.8	1.8	1.6	30	28	24	20	10
30	1	Soundarajan 50/	6	11.2	11	10.6	10.8	8600	8600	7900	7800	2	1.8	1.8	1.8	19	12	8	7	12
31	2	Selvi	18	10.9	12.8	12	11.6	8100	7300	7200	6900	1.5	1.6	1.6	1.5	36	30	22	14	22
32	2	Ramasamy 53/M	21	10.3	10.2	9.8	9.6	10300	10000	9800	9600	2	2	1.8	1.8	38	30	22	16	22
33	2	Vedivazhagi 70/	62	10.6	10.7	9.9	10.1	8000	6400	6200	7000	2	2	1.5	1.8	40	32	28	20	20
34	2	Suriya Begum 55	43	9	9	8.6	8.4	8800	8600	8600	8200	1.6	1.6	1.5	1.5	42	32	24	13	29
35	2	Mangayarkarashi	-1	10.6	10.4	9.8	9.6	9400	9500	9400	8900	2	1.8	1.8	1.8	30	22	16	8	22
36	2	Samsunisha 50/F	13	11.2	11.2	10.8	11	10600	9200	9700	8600	1.8	1.8	1.8	1.6	26	20	15	6	20
37	2	Chitradevi 49/F	24	9.6	9.2	9	8.8	11200	11000	11000	10800	1.6	1.6	1.5	1.5	24	18	11	8	16
38	2	Therasa 60/F	31	10.8	10.6	10.4	10.4	9800	9900	9700	9600	1.6	1.5	1.5	1.4	35	29	20	11	24
39	2	Ponnammal 62/F	31	9.6	9.4	9.2	9.2	9800	9400	9100	8900	2	1.8	1.8	1.6	36	28	20	12	24
40	2	Malathi 50/F	42	10.6	10.6	10.4	10	11200	11000	9500	9300	1.9	1.8	1.8	1.8	42	34	26	45	-3
41	2	Jeenath koloru	28	10.2	10	9.8	10	9600	9800	9400	9700	1.8	1.8	1.8	1.6	28	20	11	17	11
42	2	Jeenath 44/F	22	10.9	10.6	10.4	10.2	9000	8800	9000	8500	2	2	2	1.8	50	40	29	17	33
43	2	Murugesan 43/M	19	10.4	10.6	10.4	10.2	11200	11000	10600	10400	2	2	1.8	1.8	28	22	16	9	19
44	2	Dhanalakshmi48/	19	8.9	8.6	8.6	8.4	9900	9700	9800	9500	1.8	1.8	1.6	1.6	28	22	16	9	19
45	2	Rajagopalan 56	7	11.6	11.4	11	10.8	11600	10900	10500	10200	2	2	2	2	34	28	23	14	20
46	2	Abdul Rahman 50	15	8.9	9	8.8	8.6	10500	10400	10400	10500	1.6	1.6	1.6	1.6	25	20	14	7	18

S.no	Group	Name	ESR.reduction	BL.H6.0	BL.H6.1	BL.H6.2	BL.H6.3	TC.0	TC.1	TC.2	TC.3	Platelet.0	Platelet.1	Platelet.2	Platelet.3	CRP.0	CRP.1	CRP.2	CRP.3	CRP.reduction
47	2	Navmadha 48/F	14	90	8.8	8.8	8.8	11200	11000	11100	10800	1.6	1.6	1.5	1.5	15	13	9	6	9
48	2	Fousal Hithaua	2	9.4	9.2	9.2	9	10600	10400	10500	10500	2	1.8	1.6	1.5	116	122	124	129	-13
49	2	Marimuthu 52/M	8	11.2	11	10.8	10.6	11500	11400	11300	11100	22	2.2	2.1	2	28	24	19	12	16
50	2	Swarnalatha46/F	13	8.8	8.6	8.6	8.5	10600	10400	10500	10400	1.8	1.6	1.6	1.5	14	11	8	5	9
51	2	Usharani 48/F	23	10.6	10.4	10	9.8	10600	10500	10600	10200	2	2.1	2	1.9	24	19	14	10	14
52	2	Shanmugasundram	6	9.6	9.2	9	9	9500	9300	8900	8700	1.8	1.6	1.6	1.6	16	13	9	7	9
53	2	Mohan kumar 54	25	9.8	9.8	9.4	9	11600	11200	10700	10400	2	1.8	1.6	1.6	30	22	16	11	19
54	2	Vasanthi, 51/F	14	8.8	8.6	8.4	8.4	9400	8900	8800	8500	1.6	1.5	1.6	1.5	24	19	16	12	12
55	2	Jeyashankar, 48	12	11.2	11	11.2	11	10400	40300	10200	10300	2.2	2.1	2.1	2	38	32	24	16	22
56	2	Narendran, 39/M	8	11	9.9	9.8	9.6	7900	8000	7600	7500	1.8	1.6	1.6	1.6	14	11	9	7	7
57	2	Saravanaperumal	3	10.8	10.6	10.4	9.8	10900	10500	10100	90900	2	2	2	1.8	29	25	20	15	14
58	2	Vetriselvi 56/F	10	8.8	8.6	8.4	8.2	9800	9700	9300	9100	1.6	1.6	1.6	1.5	43	37	29	21	22
59	2	Thamarai, 49/F	6	10.4	10.4	10	9.6	11200	11000	10900	10700	1.8	1.8	105	106	31	25	20	16	15
60	2	Abirami, 36/F	1	9.6	9.6	9.2	9	8900	8500	8400	8400	1.8	1.6	1.6	1.6	21	18	11	8	13
61	3	Chandra, 55/F	31	10.7	10.1	10	9.6	11400	9800	9300	9400	1.6	1.5	1.5	1.5	42	34	22	11	31
62	3	Mahendran, 34/F	28	13.6	12.4	11.8	11.4	7400	7500	7400	6900	1.8	1.8	1.6	1.6	36	26	18	9	27
63	3	Jeyakodi, 46/F	30	11	10.3	10.1	9.8	8600	6200	6500	5800	1.6	1.8	1.6	1.5	32	24	28	30	2
64	3	Manivannan, 52/	19	9.6	9.4	9.2	9.4	10900	10700	10500	10000	2	1.6	1.5	1.6	20	15	9	6	14
65	3	Chitra, 43/F	27	12.1	10.8	11.4	11	10900	10900	10500	10400	2	2	1.8	1.9	20	12	9	5	15
66	3	Thenmozhi, 60/F	16	9.4	9.2	9	9	11700	11500	11600	11500	1.8	1.8	1.6	1.6	21	14	9	5	16
67	3	Prabakaram, 46/	42	12.4	12	11.6	11.4	12500	11000	10500	10200	2.1	2	2	1.8	29	22	16	9	20
68	3	Anushuya, 46/f	16	9.2	9	8.9	8.8	9600	9500	9500	9500	2	1.8	1.8	1.5	21	15	10	6	15
69	3	Sivakami, 54/F	28	10.8	10.6	10.4	10.4	11000	9900	9800	9500	1.9	1.8	1.6	1.5	29	20	11	7	22

S.no	Group	Name	ESR.reduction	BL.H6.0	BL.H6.1	BL.H6.2	BL.H6.3	TC.0	TC.1	TC.2	TC.3	Platelet.0	Platelet.1	Platelet.2	Platelet.3	CRP.0	CRP.1	CRP.2	CRP.3	CRP.reduction
70	3	Savithri, 52/F	47	9.8	9.5	9.4	9.2	8900	9000	9100	8800	1.6	1.6	1.5	1.5	29	20	13	7	22
71	3	Padma, 42/F	31	9.2	9.1	9	8.8	10900	10700	10600	10200	2	202	201	2	26	20	15	9	17
72	3	Radha krishnan,	24	9.6	9.4	9.2	9	8900	8700	8600	8500	1.8	1.6	1.6	1.5	31	25	18	11	20
73	3	Ambika, 49/F	32	10.2	10.4	10.2	10.2	9900	9800	9700	9500	1.8	1.6	1.5	1.5	29	22	15	9	20
74	3	Majibhur ghari,	29	9.6	9.4	9.2	8.8	8900	9000	8800	8600	1.8	1.7	1.8	1.6	24	16	9	5	19
75	3	RehmathNisha, 3	23	8.8	8.6	8.4	8.2	11400	11200	11000	10800	1.8	1.6	1.6	1.5	20	13	8	4	16
76	3	Grace mary, 51/	28	9.8	9.8	9.6	9.2	11200	10900	10500	10600	2	2	1.8	1.9	22	15	9	5	17
77	3	Rajarajan, 50/M	21	11.2	11.4	10.8	10.2	10700	10600	10100	9800	2.2	2.2	2.2	2.2	29	20	12	8	21
78	3	Mariyakokila, 5	49	8.8	8.8	8.6	8.6	11500	10600	10200	10000	2	1.8	1.8	1.8	42	32	21	10	32
79	3	Muthulakshmi, 4	40	10	9.8	9.4	9.4	10300	9700	9500	9200	1.9	1.8	1.8	1.6	24	17	10	7	17
80	3	Narayanan, 52/M	40	11.4	11.2	11.2	11	9500	8900	8800	8600	1.8	1.8	1.6	1.6	39	24	15	8	31
81	3	G.Chandra, 46/F	44	9.8	8.7	8.3	8.8	4900	4200	5500	6800	1.5	1.6	1.6	1.8	43	42	30	20	23
82	3	Malathi, 52/f	55	9.8	9.6	9.4	9.2	11000	10800	10800	1500	2	1.8	1.6	1.5	40	30	19	9	31
83	3	Riswan Beevi, 4	26	8.9	8.8	8.6	8.5	9700	9500	9600	9300	1.9	1.8	1.6	1.6	26	18	10	5	21
84	3	Zaheer hussari,	50	12	11.8	11.2	11	10900	10900	10800	10500	2.1	2	2	2	40	31	22	11	29
85	3	Neournisha, 38/	31	10.8	10.6	10.6	10.2	9400	9200	8900	8800	1.8	1.7	1.7	1.5	30	22	15	8	22
86	3	Ranjani, 44/F	33	10.2	10.4	10.2	9.8	10200	10100	10000	9800	2	2	1.7	1.8	37	29	20	7	30
87	3	Sivaraman, 39/M	27	10.8	10.8	10.6	10.5	9900	9700	9500	9100	2.2	2.2	2.2	2.1	41	28	18	10	31
88	3	Rajendran, 50/M	34	11.4	11.4	11.6	11.2	9200	9200	9000	8900	2.4	2.2	2.2	2	23	18	12	7	16
89	3	Dheergasumangal	48	8.8	8.6	8.5	8.7	9700	9500	9400	9100	1.8	1.8	1.6	1.5	28	20	12	7	21
90	3	Devarajan, 45/M	28	11.4	11.2	11	10.9	10900	10800	10800	10500	2.1	1.9	2	1.9	24	18	11	7	17

S.no	Group	Name	Bl.Glucose.0	Bl.Glucose.1	Bl.Glucose.2	Bl.Glucose.3	urea.0	urea.1	urea.2	urea.3	Creatinine.0	Creatinine.1	Creatinine.2	Creatinine.3	SGOT.0	SGOT.1	SGOT.2	SGOT.3	SGPT.0	SGPT.1	SGPT.2	SGPT.3	ALP.0	ALP.1	ALP.2	ALP.3	TGL.0
1	1	Chitra	102	98	98	104	27	30	32	30	0.9	0.9	0.9	0.8	26	26	28	28	30	34	29	32	9	10	11	10	140
2	1	Haridoss	96	108	112	104	32	36	38	36	1	0.9	0.9	0.9	29	28	28	28	31	34	32	30	12	11	11	11	160
3	1	Kalaiselvi	98	94	98	106	22	28	24	27	0.8	0.8	0.9	0.8	25	28	25	25	29	26	29	30	11	12	9	10	154
4	1	Mehraj Banu	90	92	98	94	23	24	22	30	0.8	0.8	0.8	0.9	24	25	26	26	31	29	31	30	12	12	10	12	164
5	1	Sangeetha	94	98	100	96	28	26	28	28	0.9	0.9	0.9	0.8	26	27	27	26	29	29	28	30	11	9	11	10	168
6	1	kermals	99	106	102	116	30	26	28	28	0.9	0.8	0.9	0.9	30	28	30	30	32	30	30	30	11	11	12	11	156
7	1	Mani Kandan	142	128	138	134	34	32	32	30	1.1	0.9	0.9	0.9	28	28	28	28	30	30	28	30	11	11	10	11	164
8	1	Mohamed Ismail	96	98	98	98	28	26	24	28	0.8	0.9	0.9	0.9	26	28	28	26	28	28	28	29	9	10	10	10	146
9	1	Kasthuri	112	114	108	116	28	26	28	28	0.9	0.9	0.9	0.8	28	29	30	28	30	30	30	29	11	9	10	10	136
10	1	Mallika	116	108	104	112	30	28	30	28	1	0.9	0.9	0.9	28	29	28	26	30	29	29	28	11	11	12	11	146
11	1	Kanagasabai, 43	112	106	114	108	28	32	30	28	0.9	0.9	1	0.9	28	28	29	28	30	29	31	31	9	9	9	9	196
12	1	Ayeesha Begum 6	134	102	148	112	36	34	34	36	1.2	1.2	1.2	1	29	31	34	31	36	36	35	36	10	11	10	11	178
13	1	Mageshwaran	122	116	108	118	34	28	32	34	1.1	1	1.1	1	28	30	31	28	35	32	35	34	11	10	11	11	168
14	1	Nagavalli 59/F	112	118	106	110	32	28	28	30	0.8	0.8	0.9	0.8	28	28	29	29	30	29	29	30	9	9	10	9	176
15	1	Thambidhurai 38	106	98	104	96	32	30	32	32	1.1	0.9	1	1	28	28	29	29	30	28	30	30	11	11	11	12	165
16	1	Rajakumari 3/F	128	132	134	130	28	28	32	30	1	0.9	0.9	1	28	29	28	28	29	29	28	30	11	10	10	11	175
17	1	Angayarkanni 56	118	116	120	114	26	28	26	30	0.8	0.8	0.9	0.9	29	29	29	29	31	32	31	31	10	9	9	9	156
18	1	Dharmambal 60/F	106	112	116	104	26	26	28	26	0.8	0.8	0.9	0.8	30	28	30	30	32	32	32	32	11	10	11	10	155
19	1	Mariyapushpam 4	142	138	140	136	28	28	26	28	1.2	0.9	1	1	28	30	28	28	29	32	32	32	11	10	10	10	188
20	1	Anbuselvi 58/F	102	96	112	102	32	32	30	28	0.9	0.8	0.8	0.8	26	27	28	27	32	32	30	32	11	9	11	10	233
21	1	Manoharan 49/M	122	131	128	124	27	28	26	27	0.8	0.8	0.8	0.9	26	28	28	28	30	32	32	32	9	10	9	10	173
22	1	Mohanambal 52/F	133	128	150	138	28	27	29	30	0.9	0.9	1	1	28	28	29	28	32	30	30	32	9	9	11	10	172
23	1	Suriyanarayanan	96	98	112	94	26	26	26	28	0.8	0.9	0.8	0.8	29	29	29	28	31	31	30	31	10	9	9	10	162

S.no	Group	Name	Bl.Glucose.0	Bl.Glucose.1	Bl.Glucose.2	Bl.Glucose.3	urea.0	urea.1	urea.2	urea.3	Creatinine.0	Creatinine.1	Creatinine.2	Creatinine.3	SGOT.0	SGOT.1	SGOT.2	SGOT.3	SGPT.0	SGPT.1	SGPT.2	SGPT.3	ALP.0	ALP.1	ALP.2	ALP.3	TGL.0
24	1	Abdul rehman 58	163	159	160	150	32	30	30	28	1	0.9	0.9	0.9	29	30	30	30	36	34	34	34	11	11	11	11	241
25	1	Lakshmi 34/F	116	98	109	112	28	28	29	28	0.8	0.9	0.9	0.9	29	28	29	28	31	30	32	32	10	9	11	10	172
26	1	Vishalatchi 40/	158	144	138	152	30	28	30	28	1.1	1	1	1	30	31	28	29	32	32	30	31	11	9	8	11	179
27	1	Mohanraj 52/M	34	32	36	36	34	32	36	36	1	1	1.2	1.2	30	29	30	30	34	32	34	34	10	11	9	11	189
28	1	Vijayalakshmi 4	156	146	138	150	30	32	30	32	1.1	1.1	1.1	1.2	30	31	29	29	32	32	30	32	10	11	9	11	179
29	1	Radhabai 60/F	108	106	108	104	30	30	28	28	0.9	0.8	0.8	0.8	29	30	28	29	31	32	30	32	11	10	11	11	162
30	1	Soundarajan 50/	136	128	132	134	28	28	30	28	0.9	0.9	1	0.9	28	28	29	28	30	32	32	30	9	10	10	11	156
31	2	Selvi	96	100	100	106	36	36	32	34	0.9	0.9	0.9	0.9	26	26	28	26	29	30	29	29	13	11	11	12	166
32	2	Ramasamy 53/M	102	100	104	104	28	30	28	28	0.9	1	0.9	0.9	24	26	28	28	29	29	29	29	11	10	11	10	200
33	2	Vedivazhagi 70/	134	102	148	112	36	34	34	36	1.2	0.9	1	1	30	29	31	31	36	37	36	35	11	13	11	11	182
34	2	Suriya Begum 55	128	128	130	130	27	26	26	26	1	1	0.9	0.9	34	32	32	32	39	38	39	39	12	13	12	13	180
35	2	Mangayarkarashi	94	94	96	96	26	26	26	28	0.8	0.8	0.8	0.9	32	32	30	30	33	35	33	33	10	11	12	12	196
36	2	Samsunisha 50/F	140	142	140	142	24	26	26	26	0.9	0.9	0.9	0.9	24	28	26	28	29	29	28	29	9	11	11	10	242
37	2	Chitradevi 49/F	98	98	102	102	32	30	30	30	0.9	0.9	0.9	0.8	26	26	27	27	29	26	27	27	10	10	9	10	234
38	2	Therasa 60/F	116	118	118	118	30	32	30	32	0.9	1	0.9	0.8	29	30	32	31	30	31	36	35	11	10	11	10	232
39	2	Ponnammal 62/F	98	102	100	110	28	28	30	28	0.9	1	0.8	0.9	30	28	26	28	32	30	30	32	11	10	11	10	204
40	2	Malathi 50/F	116	116	108	110	30	30	32	30	1	1	1	0.9	30	30	28	28	32	32	30	30	13	12	11	12	232
41	2	Jeenath koloru	110	110	108	112	26	26	28	30	0.9	1	1	1	26	26	28	30	30	30	32	29	11	11	12	10	229
42	2	Jeenath 44/F	108	108	110	110	26	28	28	32	0.9	1	0.9	1	29	28	26	28	34	32	30	32	12	10	9	12	236
43	2	Murugesan 43/M	142	140	136	144	32	32	32	30	1.1	1.1	10	10	30	30	28	30	32	30	32	30	12	12	11	12	110
44	2	Dhanalakshmi48/	30	28	30	28	0.8	0.8	0.9	0.9	28	29	28	28	30	31	31	32	32	32	32	34	11	11	11	10	200
45	2	Rajagopalan 56	108	99	112	116	30	28	29	28	0.9	0.8	1	0.9	28	29	29	29	30	31	32	30	156	156	155	155	111
46	2	Abdul Rahman 50	102	110	110	116	28	28	30	30	0.9	0.9	1	1	28	29	29	30	32	31	33	33	156	156	155	154	139

S.no	Group	Name	Bl.Glucose.0	Bl.Glucose.1	Bl.Glucose.2	Bl.Glucose.3	urea.0	urea.1	urea.2	urea.3	Creatinine.0	Creatinine.1	Creatinine.2	Creatinine.3	SGOT.0	SGOT.1	SGOT.2	SGOT.3	SGPT.0	SGPT.1	SGPT.2	SGPT.3	ALP.0	ALP.1	ALP.2	ALP.3	TGL.0
47	2	Navmadha 48/F	103	164	172	168	32	33	30	30	1	1.1	1	1	29	29	29	30	31	31	34	33	10	9	10	10	200
48	2	Fousal Hithaua	30	31	29	26	30	31	29	26	1	1	1	0.9	28	30	30	30	32	33	32	34	11	12	11	11	176
49	2	Marimuthu 52/M	124	128	126	126	30	28	28	28	0.9	1	0.9	1	28	30	31	31	29	31	33	32	9	10	9	10	204
50	2	Swarnalatha46/F	116	114	109	115	28	29	30	32	0.9	1	0.9	1.1	28	30	32	30	29	32	34	32	10	9	9	9	166
51	2	Usharani 48/F	121	118	122	124	28	26	28	29	0.9	0.9	0.8	0.9	30	30	29	30	34	34	33	33	13	12	12	12	193
52	2	Shanmugasundram	98	96	106	110	28	32	32	29	0.8	0.9	0.9	0.8	28	29	30	30	32	31	33	33	11	10	10	12	173
53	2	Mohan kumar 54	104	105	108	106	32	30	28	30	0.8	0.9	0.8	1	28	29	30	31	31	33	32	36	11	10	12	11	201
54	2	Vasanthi, 51/F	124	126	126	128	28	30	32	30	0.9	0.9	1	1	30	30	28	28	32	33	31	32	13	12	11	10	169
55	2	Jeyashankar, 48	102	104	108	112	26	29	26	26	0.8	0.8	0.9	0.9	30	30	29	29	32	33	31	32	11	11	11	10	185
56	2	Narendran, 39/M	100	104	98	106	28	29	28	26	0.9	1	0.8	0.9	29	28	29	28	31	32	33	32	10	9	11	9	168
57	2	Saravanaperumal	110	112	112	114	28	28	30	30	0.8	0.9	0.8	0.9	30	28	29	28	32	30	30	30	11	10	10	10	178
58	2	Vetriselvi 56/F	139	142	136	144	29	30	30	32	1	1.1	1	1.1	29	28	29	30	33	30	32	34	10	10	11	12	214
59	2	Thamarai, 49/F	94	98	98	96	28	29	32	34	0.8	0.8	0.9	0.9	28	29	30	32	30	33	33	34	11	12	11	10	168
60	2	Abirami, 36/F	104	110	112	114	30	32	28	28	0.9	0.9	0.9	0.9	30	29	28	29	33	31	32	32	12	9	10	11	182
61	3	Chandra, 55/F	121	118	116	118	25	36	27	29	0.9	1	1	1	25	26	28	29	30	32	32	33	13	11	9	10	186
62	3	Mahendran, 34/F	94	94	92	94	20	24	24	24	0.8	0.9	0.9	0.9	32	30	30	30	35	33	32	32	13	13	13	13	168
63	3	Jeyakodi, 46/F	98	102	94	92	32	24	28	30	0.9	0.8	0.9	0.9	26	27	26	24	35	32	38	29	11	11	10	11	162
64	3	Manivannan, 52/	104	106	108	102	26	28	26	29	0.9	0.9	0.8	1	28	30	31	30	29	32	33	34	10	11	12	9	234
65	3	Chitra, 43/F	201	142	140	126	32	28	30	30	0.9	0.9	0.8	0.8	26	24	25	28	28	29	29	32	11	10	11	10	240
66	3	Thenmozhi, 60/F	102	108	109	99	26	28	28	28	0.9	0.9	1	1	30	29	28	30	32	31	32	33	11	10	9	10	215
67	3	Prabakaram, 46/	110	112	108	116	28	30	28	26	0.9	0.9	0.9	1	25	28	29	29	28	29	33	31	10	9	10	9	176
68	3	Anushuya, 46/f	108	120	122	118	28	30	27	28	0.9	0.9	0.8	0.8	30	29	28	29	33	32	31	34	12	11	10	12	167
69	3	Sivakami, 54/F	146	150	132	129	32	30	30	30	1.1	1	1	1	33	31	30	30	35	34	32	32	13	12	11	12	204

S.no	Group	Name	Bl.Glucose.0	Bl.Glucose.1	Bl.Glucose.2	Bl.Glucose.3	urea.0	urea.1	urea.2	urea.3	Creatinine.0	Creatinine.1	Creatinine.2	Creatinine.3	SGOT.0	SGOT.1	SGOT.2	SGOT.3	SGPT.0	SGPT.1	SGPT.2	SGPT.3	ALP.0	ALP.1	ALP.2	ALP.3	TGL.0
70	3	Savithri, 52/F	126	128	116	120	28	28	27	28	0.9	0.9	0.8	0.8	30	31	30	30	32	33	33	32	9	10	11	9	178
71	3	Padma, 42/F	120	108	110	116	29	28	27	26	0.9	0.8	0.8	0.8	28	30	32	31	32	32	34	33	11	10	12	10	172
72	3	Radha krishnan,	110	108	112	96	30	31	32	29	0.9	0.9	1	0.8	28	29	28	29	31	32	33	32	10	11	11	10	168
73	3	Ambika, 49/F	104	108	102	112	32	30	28	30	1.1	1	1	1	29	28	29	30	33	32	33	33	10	11	11	10	174
74	3	Majibhur ghari,	108	110	112	110	28	32	30	30	0.8	1.1	0.9	1	28	29	30	29	30	32	33	34	11	12	9	11	216
75	3	RehmathNisha, 3	94	97	98	102	28	29	30	28	0.8	0.8	0.9	0.9	28	30	31	30	30	32	32	31	10	11	10	11	190
76	3	Grace mary, 51/	122	124	118	114	28	28	30	29	0.9	0.9	0.9	1	30	29	30	29	32	33	32	32	10	11	10	11	167
77	3	Rajarajan, 50/M	96	98	96	96	29	30	32	30	0.8	0.8	0.9	0.8	32	32	32	32	35	35	33	34	11	11	10	10	193
78	3	Mariyakokila, 5	99	98	100	98	29	30	28	29	0.8	0.9	0.8	0.9	30	30	32	33	32	32	34	35	10	11	10	11	173
79	3	Muthulakshmi, 4	120	118	122	109	29	30	27	29	0.8	0.9	0.8	0.9	30	28	28	29	34	31	32	32	12	9	9	10	161
80	3	Narayanan, 52/M	102	106	104	98	29	30	32	28	0.8	0.9	0.9	0.9	30	30	28	29	32	33	30	32	11	10	9	10	159
81	3	G.Chandra, 46/F	108	108	106	108	30	32	30	34	1	0.9	0.9	0.9	28	29	28	28	33	33	33	34	12	11	11	12	180
82	3	Malathi, 52/f	108	104	98	104	29	29	32	30	0.8	0.8	0.8	0.9	30	29	30	30	34	32	32	34	11	10	10	11	177
83	3	Riswan Beevi, 4	111	112	114	110	28	30	32	30	0.8	1.1	1.1	0.9	29	30	28	29	32	33	31	33	11	9	10	11	156
84	3	Zaheer hussari,	118	120	121	121	28	28	30	29	0.8	0.9	0.9	0.8	30	30	30	29	34	35	34	34	13	13	12	12	194
85	3	Neournisha, 38/	99	97	98	97	32	30	29	31	0.9	0.9	0.8	1	30	29	30	29	32	32	33	32	9	10	9	9	152
86	3	Ranjani, 44/F	112	108	119	105	29	28	30	31	0.8	0.9	0.8	0.9	32	31	30	29	35	33	32	33	11	11	10	11	163
87	3	Sivaraman, 39/M	94	96	98	96	29	31	30	27	0.8	0.9	0.8	0.8	30	30	31	30	32	31	33	34	10	9	10	11	196
88	3	Rajendran, 50/M	121	118	122	120	32	35	33	32	0.9	1.1	1	1	30	32	31	32	32	35	34	35	10	11	11	10	231
89	3	Dheergasumangal	110	98	99	112	29	27	28	28	0.9	0.8	0.8	0.8	31	32	30	31	33	35	32	33	10	10	9	9	163
90	3	Devarajan, 45/M	105	102	98	99	29	29	34	32	0.8	0.8	1	0.9	31	32	30	31	34	35	33	33	12	12	11	11	171

S.no	Group	Name	TGL.1	TGL.2	TGL.3	TG.reduction	LDL.0	LDL.1	LDL.2	LDL.3	LDLdecrease	HDL.0	HDL.1	HDL.2	HDL.3	HDLincrease	TCH.0	TCH.1	TCH.2	TCH.3	TC.reduction	RF	RF.12wks	RFreduction	ANTICCP	ANTICCP3	ACCP.reduction
1	1	Chitra	150	144	148	-8	153	156	150	152	1	36	36	36	36	0	168	168	166	168	0	82	70	12	13	6	7.3
2	1	Haridoss	160	162	160	0	160	158	158	160	0	32	30	32	31	-1	188	188	188	186	2	43	28	15	16	12	4.2
3	1	Kalaiselvi	154	154	156	-2	146	146	146	148	-2	33	32	32	33	0	172	174	174	174	-2	539	402	137	200	157	43
4	1	Mehraj Banu	164	162	162	2	160	162	162	160	0	32	33	33	33	1	186	186	184	184	2	21	10	11	9	5	4
5	1	Sangeetha	168	168	170	-2	156	150	152	152	4	33	33	30	32	-1	212	212	208	210	2	41	32	8.6	13	8	5
6	1	kermals	156	160	158	-2	124	122	121	124	0	35	35	35	34	-1	178	178	178	178	0	47	31	17	0	13	-13
7	1	Mani Kandan	160	162	162	2	126	124	126	126	0	32	30	32	32	0	196	194	192	194	2	61	42	18	18	14	3.7
8	1	Mohamed Ismail	146	142	142	4	98	96	98	98	0	34	33	33	32	-2	135	134	134	135	0	43	34	8.9	18	11	7.2
9	1	Kasthuri	138	132	138	-2	102	98	100	100	2	34	33	33	33	-1	120	121	121	121	-1	31	20	10	17	12	4.6
10	1	Mallika	138	138	140	6	102	95	100	100	2	33	32	32	33	0	163	164	163	164	-1	52	39	13	26	18	8.1
11	1	Kanagasabai, 43	188	190	192	4	116	116	110	114	2	34	32	33	32	-2	174	172	174	174	0	36	34	2	19	17	2.1
12	1	Ayeesha Begum 6	178	175	176	2	135	133	133	135	0	34	34	33	33	-1	152	152	151	152	0	208	160	48	133	108	25
13	1	Mageshwaran	166	168	170	-2	128	132	130	132	-4	34	35	35	33	-1	148	147	148	147	1	56	32	24	13	9.8	3.2
14	1	Nagavalli 59/F	176	178	178	-2	109	108	109	110	-1	33	32	33	33	0	158	158	159	158	0	58	32	26	21	13	8.3
15	1	Thambidurai 38	160	164	162	3	104	106	105	105	-1	34	32	31	33	-1	136	138	138	138	-2	75	30	45	13	8	5.3
16	1	Rajakumari 3/F	173	175	175	0	130	132	131	132	-2	32	32	31	32	0	156	154	154	154	2	173	140	33	109	91	18
17	1	Angayarkanni 56	156	155	156	0	110	112	110	110	0	38	38	38	38	0	130	130	129	130	0	64	30	35	21	11	10
18	1	Dharmambal 60/F	155	155	155	0	98	96	98	98	0	35	35	33	33	-2	129	130	129	129	0	49	30	18	17	11	5.8
19	1	Mariyapushpam 4	185	183	188	0	109	107	107	107	2	32	32	33	32	0	160	161	160	160	0	62	30	32	19	9	10
20	1	Anbuselvi 58/F	227	228	224	9	169	167	169	169	0	30	32	30	30	0	195	192	193	193	2	119	69	50	72	88	-16
21	1	Manoharan 49/M	173	173	172	1	122	123	122	122	0	33	33	32	32	-1	148	146	145	146	2	92	40	52	61	26	34
22	1	Mohanambal 52/F	163	170	170	2	116	112	112	116	0	35	34	35	33	-2	153	152	152	154	-1	36	19	17	18	10	8.1
23	1	Suriyanarayanan	162	162	162	0	95	96	95	95	0	33	32	34	35	2	148	147	148	147	1	83	33	50	36	21	15

S.no	Group	Name	TGL.1	TGL.2	TGL.3	TG.reduction	LDL.0	LDL.1	LDL.2	LDL.3	LDLdecrease	HDL.0	HDL.1	HDL.2	HDL.3	HDLincrease	TCH.0	TCH.1	TCH.2	TCH.3	TC.reduction	RF	RF.12wks	RFreduction	ANTICCP	ANTICCP3	ACCP.reduction
24	1	Abdul rehman 58	243	241	240	1	116	115	116	116	0	35	34	35	35	0	210	208	210	210	0	146	130	16	68	38	30
25	1	Lakshmi 34/F	174	172	172	0	95	98	98	98	-3	34	33	34	33	-1	160	158	156	160	0	84	48	36	37	20	17
26	1	Vishalatchi 40/	178	178	179	0	142	142	144	143	-1	32	31	31	31	-1	138	139	139	139	-1	121	78	43	78	42	36
27	1	Mohanraj 52/M	190	190	150	39	150	148	148	150	0	30	32	30	30	0	168	164	166	168	0	212	159	54	98	86	12
28	1	Vijayalakshmi 4	180	178	180	-1	135	135	135	136	-1	30	30	30	30	0	153	153	152	150	3	73	39	34	30	20	10
29	1	Radhabai 60/F	162	160	162	0	120	122	122	122	-2	33	32	33	33	0	140	140	141	141	-1	56	32	24	17	12	5.1
30	1	Soundarajan 50/	156	149	150	6	108	106	108	104	4	35	34	35	35	0	130	130	128	128	2	64	45	19	36	16	20
31	2	Selvi	160	164	164	2	130	126	122	122	8	30	30	30	30	0	142	142	140	140	2	26	18	7.9	17	10	6.8
32	2	Ramasamy 53/M	207	205	202	-2	170	172	166	164	6	34	34	33	33	-1	178	178	176	176	2	29	12	16	7.9	5.1	2.8
33	2	Vedivazhagi 70/	180	169	154	28	160	158	152	150	10	32	33	33	33	1	168	164	164	164	4	208	102	106	133	91	42
34	2	Suriya Begum 55	182	182	180	0	163	160	157	154	9	32	32	32	32	0	152	153	152	152	0	110	95	15	200	148	52
35	2	Mangayarkarashi	196	197	195	1	150	148	146	142	8	32	32	32	32	0	164	164	164	163	1	62	30	31	23	12	11
36	2	Samsunisha 50/F	242	242	242	0	146	144	142	138	8	35	35	35	35	0	197	196	196	196	1	127	79	48	65	36	28
37	2	Chitradevi 49/F	234	234	233	1	109	107	104	101	8	36	36	36	36	0	188	188	187	188	0	82	32	50	54	23	31
38	2	Therasa 60/F	232	232	230	2	136	135	132	128	8	33	32	33	34	1	198	198	197	197	1	84	42	42	53	21	32
39	2	Ponnammal 62/F	204	202	202	2	116	114	110	104	12	37	36	37	37	0	164	163	163	163	1.5	49	18	31	15	7	8.3
40	2	Malathi 50/F	232	231	230	2	127	125	122	117	10	33	33	32	33	0	187	187	187	185	2	69	42	27	43	26	17
41	2	Jeenath koloru	227	228	228	1	105	104	100	94	11	36	36	36	37	1	185	184	184	183	2	108	67	40	84	50	34
42	2	Jeenath 44/F	234	234	236	0.5	108	107	102	99	8.8	36	36	37	36	0	193	193	192	190	3	75	38	37	42	21	21
43	2	Murugesan 43/M	108	105	102	8	39	38	39	39	0	154	154	154	154	0	194	194	194	194	0.5	39	20	19	20	14	6.5
44	2	Dhanalakshmi48/	200	199	199	1	108	106	104	99	9	38	38	37	38	0	146	146	145	145	1	106	69	37	76	51	25
45	2	Rajagopalan 56	109	105	102	9	35	35	36	35	0	10	9	10	11	1	192	192	192	192	0	57	24	34	16	8.2	8.1
46	2	Abdul Rahman 50	137	132	127	12	36	36	35	35	1	10	10	9	10	0	194	193	193	193	0.8	43	22	21	27	12	15

S.no	Group	Name	TGL.1	TGL.2	TGL.3	TG.reduction	LDL.0	LDL.1	LDL.2	LDL.3	LDLdecrease	HDL.0	HDL.1	HDL.2	HDL.3	HDLincrease	TCH.0	TCH.1	TCH.2	TCH.3	TC.reduction	RF	RF.12wks	RFreduction	ANTICCP	ANTICCP3	ACCP.reduction
47	2	Navmadha 48/F	198	199	199	1	152	149	148	145	7.5	36	35	36	35	-1	176	175	174	174	2	65	35	30	49	22	27
48	2	Fousal Hithaua	176	177	177	-1	110	107	105	102	7.9	37	38	37	37	0	157	157	157	157	0	38	17	21	18	9.8	8.2
49	2	Marimuthu 52/M	203	203	203	1	142	140	138	136	6	34	35	35	35	0.5	176	177	176	176	0	295	68	227	98	52	46
50	2	Swarnalatha46/F	166	165	165	1	95	95	93	92	3.4	39	40	40	40	0.5	143	143	143	143	0	49	24	25	12	8.8	3.6
51	2	Usharani 48/F	193	192	193	0	130	127	125	121	8.7	36	36	36	36	0	164	164	162	162	2.5	47	23	25	21	15	6
52	2	Shanmugasundram	173	173	173	0.5	132	129	126	121	11	34	35	34	34	0	159	158	157	154	5	29	17	11	14	11	3.6
53	2	Mohan kumar 54	200	200	200	1	114	112	108	105	8.7	40	40	41	41	0.5	163	162	162	160	3	99	43	56	79	62	18
54	2	Vasanthi, 51/F	168	168	169	0	103	102	100	98	4.8	41	41	41	41	0	149	149	148	144	5	38	22	16	16	10	5.6
55	2	Jeyashankar, 48	184	184	184	0.4	122	120	121	117	5	37	38	37	38	0.5	165	164	163	161	4.5	63	31	33	32	19	13
56	2	Narendran, 39/M	168	169	169	-1	95	95	94	94	1	40	40	40	40	0	146	145	142	139	7	97	30	67	40	20	20
57	2	Saravanaperumal	178	178	179	-1	129	127	125	121	8	38	37	38	38	-0.4	154	153	153	151	3	29	16	13	15	10	5
58	2	Vetriselvi 56/F	214	214	214	0	150	148	142	139	11	32	32	33	33	1	173	172	172	171	2	45	25	20	32	21	12
59	2	Thamarai, 49/F	168	168	167	1	98	97	97	96	2	36	36	36	36	0	149	148	147	146	3	181	100	81	122	95	27
60	2	Abirami, 36/F	182	182	181	1	182	182	182	181	1	34	34	35	34	0	168	167	165	163	5	55	29	27	39	24	15
61	3	Chandra, 55/F	184	182	180	6	170	162	156	149	21	30	32	33	33	3	148	146	140	138	10	157	70	87	47	8.7	38
62	3	Mahendran, 34/F	166	166	163	5	152	150	148	139	13	34	34	34	36	2	146	146	146	146	0	52	24	28	13	5.9	7
63	3	Jeyakodi, 46/F	160	160	156	6	158	152	152	150	8	30	32	34	34	4	138	133	132	130	8	182	56	126	98	32	66
64	3	Manivannan, 52/	234	233	233	1.4	107	107	106	106	0.9	40	40	41	41	1.6	198	192	188	186	12	56	26	30	15	8.7	6.7
65	3	Chitra, 43/F	236	232	229	11	156	150	148	144	12	39	39	40	41	2	195	194	192	190	5	37	20	17	30	5.1	25
66	3	Thenmozhi, 60/F	210	202	197	18	152	150	146	141	11	31	32	32	33	2	196	195	192	190	6	60	26	34	22	10	12
67	3	Prabakaram, 46/	174	172	170	6	121	117	115	109	12	37	38	38	39	2	159	158	156	156	3	416	123	293	179	68	111
68	3	Anushuya, 46/f	165	164	163	4	93	92	92	91	2	40	40	41	41	1	149	148	148	146	3	64	32	32	32	15	16
69	3	Sivakami, 54/F	202	196	191	13	135	132	127	122	13	36	37	37	39	2.5	168	166	166	165	3	339	120	219	17	9	8.1

S.no	Group	Name	TGL.1	TGL.2	TGL.3	TG.reduction	LDL.0	LDL.1	LDL.2	LDL.3	LDLdecrease	HDL.0	HDL.1	HDL.2	HDL.3	HDLincrease	TCH.0	TCH.1	TCH.2	TCH.3	TC.reduction	RF	RF.12wks	RFreduction	ANTICCP	ANTICCP3	ACCP.reduction
70	3	Savithri, 52/F	176	174	171	7	123	120	118	115	8	36	37	37	38	2	152	151	151	150	2	78	39	39	49	17	32
71	3	Padma, 42/F	170	168	165	7	124	121	119	117	7	34	36	36	37	3	143	142	141	138	5	96	53	43	43	14	29
72	3	Radha krishnan,	166	164	160	8	104	102	99	96	8	39	40	41	41	2	139	138	137	137	2	70	31	39	30	15	15
73	3	Ambika, 49/F	172	170	168	6	121	119	116	114	7	36	37	37	38	2	156	155	155	154	2	28	17	11	32	8.1	24
74	3	Majibhur ghari,	214	210	209	7	150	148	142	139	11	33	34	35	36	3	174	172	172	171	3	311	140	171	48	27	21
75	3	RehmathNisha, 3	185	183	181	9	134	131	127	124	10	32	33	34	34	2	154	153	152	151	3	68	30	38	130	39	91
76	3	Grace mary, 51/	165	163	164	3	129	126	122	118	11	37	38	38	39	1.5	148	147	146	146	2	38	15	23	70	27	43
77	3	Rajarajan, 50/M	190	187	186	7	139	134	130	126	13	34	35	35	36	2	162	162	161	160	2	91	49	42	52	20	32
78	3	Mariyakokila, 5	170	168	166	7	124	124	117	115	9	38	38	39	40	2	152	151	150	150	2	133	66	67	59	27	33
79	3	Muthulakshmi, 4	157	154	153	8	116	112	108	105	11	40	40	41	41	1	147	146	146	145	2	110	61	49	61	25	35
80	3	Narayanan, 52/M	157	156	151	8	120	118	115	110	10	40	40	41	42	2	134	134	133	132	2	44	18	26	55	8.1	47
81	3	G.Chandra, 46/F	174	170	168	12	160	158	156	152	8	32	32	32	34	2	130	126	120	122	8	191	60	131	23	8.1	15
82	3	Malathi, 52/f	175	172	170	7	135	133	130	127	8	34	35	35	36	2	156	155	155	154	2	95	47	48	39	19	20
83	3	Riswan Beevi, 4	154	151	148	8	115	113	112	110	5	41	41	41	42	1	138	138	137	136	2	30	13	17	10	8.1	2.2
84	3	Zaheer hussari,	192	190	186	8	140	137	132	129	11	32	33	33	35	3	165	164	163	162	3	78	33	45	36	19	17
85	3	Neournisha, 38/	150	149	148	4	125	123	120	116	9	38	38	39	40	2	137	137	136	136	1	54	24	30	21	10	11
86	3	Ranjani, 44/F	161	158	155	8	122	120	119	117	5	40	40	40	41	1	142	142	142	140	2	24	11	13	114	59	56
87	3	Sivaraman, 39/M	194	193	191	5	143	141	137	134	9	34	35	36	37	3	165	165	164	163	2	389	46	343	32	19	13
88	3	Rajendran, 50/M	229	225	224	7	167	165	162	158	9	31	32	32	34	3	194	193	193	191	3	173	37	137	81	29	52
89	3	Dheergasumangal	162	159	156	7	115	113	112	109	6	39	40	41	41	2	145	145	143	142	3	144	39	104	98	25	73
90	3	Devarajan, 45/M	169	168	164	7	120	118	115	114	6	37	37	37	38	1	154	154	153	152	2	75	33	43	34	13	21

DEPARTMENT OF PHARMACOLOGY
EFFECT OF PITAVASTATIN IN PATIENTS WITH ACTIVE
RHEUMATOID ARTHRITIS TREATED WITH AT
A RURAL TERTIARY CARE HOSPITAL

CASE SHEET

Registration no:

Date:

Name:

Age:

Sex:

Address:

Phone no:

Occupation:

Marital Status:

Weight (Kg):

Height (Cm):

BMI:

Complaints:

H/o Present illness:

Past History

Personal History:

Family History:

Treatment History:

General Examination:

Pt conscious: oriented: pallor: cyanosis:
 Clubbing: pedal edema : generalised lymphadenopathy

General Examination	Weight	BMI	Pulse	BP	Morning Stiffness
Day-0					
4 th Week					
8 th week					
12 th Week					

Systemic examination:

Joint Name	Day-0				4 th Week				8 th Week				12 th Week			
	L	R	T	S	L	R	T	S	L	R	T	S	L	R	T	S
Shoulder Joint																
Elbow Joint																
Wrist Joint																
Metacarpo phalangeal Joint																
Proximal inter phalangeal Joint																
Knee Joint																

L- Left
 R- Right
 T- Tender
 S- Swollen

SCORING SYSTEM	Day-0	4 th Week	8 th Week	12 th Week
DAS SCORE				
VAS SCORE				

HEALTH ASSESSMENT QUESTIONNAIRE

	Day-0			4 th Week			8 th Week			12 th Week		
	YES	With Difficulty	NO	YES	With Difficulty	NO	YES	With Difficulty	NO	YES	With Difficulty	NO
Are you able to dress yourself?												
Are you able to stand up from a straight chair?												
Are you able to open a container?												
Are you able to climb up 5 steps?												
Are you able to handle TV remotes?												

Investigation:

Name of the Investigation	Day =0	4 th week	8 th week	12 th week
COMPLETE HAEMOGRAM				
Blood Hb%				
RBC Count				
WBC Count				
Platelet Count				
INFLAMMATORY MARKERS				
ESR				
CRP				

IMMUNOLOGICAL MARKERS				
Rheumatoid Factors				
Anti CCP				
BIOCHEMICAL MARKERS				
Blood Glucose				
LIVER FUNCTION TEST				
SGOT				
SGPT				
Serum alkaline phosphatase				
RENAL FUNCTION TEST				
Blood Urea				
Serum creatinine				
LIPID PROFILE				
Total Cholesterol				
TGL				
LDL				
HDL				

Treatment:

Signature of Investigator.

CONSENT FORM

Name of the participant:

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 I am exercising my free power of choice, hereby give my consent to be included as a participant in the study of **“A STUDY ON THE EFFECT OF PITAVASTATIN IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS TREATED AT A RURAL TERTIARY CARE HOSPITAL”**. The nature and purpose of data is for research work. The procedure has been explained to me in detail in the language understandable to me by the investigator. It has been made clear to me that all personal details like name, place, religion, past history etc., will be kept strictly confidential. I permit the result obtained to be used for academic purpose.

Trichy

Date:

Signature of the patient:

Investigator Certificate:

I certify that all the elements including the nature, purpose and possible risks of the above study as described in this consent document have been fully explained to the subject.

Signature of the investigator:

Date:

Name of the Investigator:

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