



Bharath

INSTITUTE OF HIGHER EDUCATION AND RESEARCH

(Declared as Deemed-to-be University under section 3 of UGC Act, 1956)
(Vide Notification No. F.9-5/2000 - U.3, Ministry of Human Resource Development, Govt. of India, dated 4th July 2002)



Phone : 044-22290742 / 22290125 . Telefax : 044-22293886
Website : www.bharathuniv.ac.in

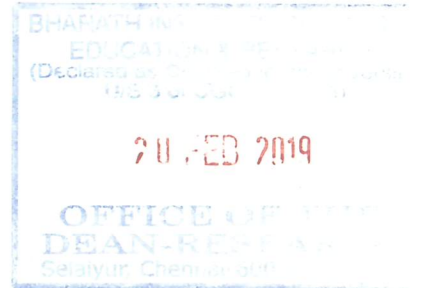
173, Agaram Road, Selaiyur, Tambaram,
Chennai - 600 073. Tamil Nadu.

Ref. No.SMS-2018-O-09

Date: 20.02.2019

TO

Ms. T. Mohanalakshmi
Assoc.Professor/Microbiology,
BIHER.



Thro: Concern Head of the Department

Greetings!!!

We are happy to announce that the Research Advisory Committee has approved your proposal for Seed Money Scheme-2018 which was presented by you. You are requested to complete the proposal and send the progress report to the Dean Research in the prescribed time period.

Title of the Project: A Study of Platelet Indices in Patients with Metabolic Syndrome and Type 2 Diabetes Mellitus

Seed Money Amount: Rs.1, 00,000/- (Rupees One Lakh Only)

Approved on: 05.02.2019

Payment details:

Voucher No.54

Dated: 27.02.2019

With Regards

Dean-Research

Bharath University

SELAIYUR, CHENNAI - 600 073, TAMIL NADU, INDIA.

CASH / PAYMENT VOUCHER

Date 27/02/2019

V.No. 54

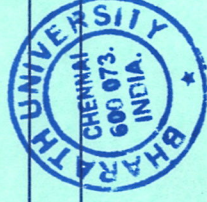
Debit _____ Amount _____

Rs.

PAID TO Dr. T. Probnatalashmi

RUPEES One lakh only

TOWARDS Seed money scheme - 2018



(Handwritten mark)

Authorised by

Finance Manager

Cashier/Accountant

Payee's Signature

(Handwritten signature)

PROPOSAL SUBMISSION

1. Details of Principal Investigator

Name : Dr. T. Mohanalakshmi
Designation : Associate Professor
Highest Qualifications : Ph.D.
Department : Microbiology
E-mail : drpebyreddy@yahoo.com
Contact no : 9849616163
Date of Joining : 10.06.2014

2. Details of Co-Principal Investigator

Name : Dr. E. Prabhakar Reddy
Designation : Professor
Highest Qualifications : Ph.D.
Department : Biochemistry
E-mail : drpebyreddy@gmail.com
Contact no : 9159186879
Date of Joining : 21.10.2009

Technical details

1. Introduction:

Metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM) are the factors of cardiovascular risk. MetS comprises an array of pathogenetically interrelated metabolic and clinical abnormalities (insulin resistance, arterial hypertension, and dyslipidemia) and increases risk of atherosclerotic damage of blood vessels. Metabolic syndrome (MetS) is a combination of abdominal obesity, atherogenic dyslipidemia, elevated blood pressure (BP), and elevated plasma glucose (1). Platelets play a key role in the development of atherothrombosis, a major contributor of cardiovascular events (1). The contribution of platelets to cardiovascular events has been noted for decades. Since then, there have been numerous studies underlying the importance of platelets in thrombotic complications (2). The importance of platelets in cardiovascular disease, medicines aimed at inhibiting platelet activity have been demonstrated to be very effective at decreasing myocardial infarction, stroke. Metabolic syndrome, a precursor to diabetes, is an independent predictor of cardiovascular events (3). Although several measurements of platelet activity have emerged as potential contributors to atherothrombosis, many of these measurements are time-consuming, expensive, use a high sample volume, or require specialty training (4-5). People with diabetes, exhibit increased platelet reactivity. Hyperglycemia contributes to greater platelet reactivity through direct effects and by promoting glycation of platelet proteins. Both insulin resistance and insulin deficiency increase platelet reactivity. Insulin inhibits activation of platelets. Therefore, relative or absolute deficiency of insulin would increase platelet reactivity (6).

Recent studies on platelet volume indices in the spectrum of ischemic heart diseases show that all platelet indices—plateletcrit, mean platelet volume (MPV) and platelet distribution width (PDW) were significantly raised in patients who had suffered from acute myocardial ischemia. A key component of vaso-occlusion is believed to be increased platelet activation and reactivity, and thus an increased platelet volume resulting in an elevated PDW. Also, higher concentrations of platelet microparticles have been detected in proinflammatory disorders such as sickle cell anemia. Studies on diabetes mellitus (DM), which too is considered to be a prothrombotic state with enhanced platelet reactivity, found a statistical rise in MPV and PDW, yet very few studies have been carried out regarding platelet indices for MetS patients. MetS patients have been found to be at a greater risk for developing insulin resistance, visceral adiposity, atherogenic dyslipidemia, and endothelial dysfunction. Patients with insulin resistance tend to develop hypertriglyceridemia and are prone for developing atheromas in vascular lumen, leading to an increased incidence of coronary artery disease and stroke.⁸ Hypertriglyceridemia too leads to endothelial dysfunction that predisposes to the development of atherosclerotic depositions along vessel lumina. Visceral adiposity has been implicated in dysregulation of adiponectin levels, which too eventually causes vascular dysfunction. (7) Metabolic abnormalities, associated with insulin resistance syndrome, significantly affect functional activity of platelets. Activation of platelets can play an important role in progression of heart failure due to a formation of the microthrombi in the myocardial microcirculation. Although several measurements of platelet

activity have emerged as potential contributors to atherothrombosis, many of them are time consuming, expensive and use a high sample volume. Alternatively, MPV, PDW and P-LCR can be easily determined on routine automated hemograms available at low cost. Patients with larger platelets can easily be identified during routine haematological analysis and timely treatment could be undertaken. Thus, in multiple recent studies, it has been shown that platelet indices are higher in patients suffering from DM, impaired fasting glucose, and dyslipidemia, as compared with MS. Thus, the aim of this study was to analyze the platelet indices in DM and MetS patients.

To assess various platelet indices in MetS patients including plateletcrit, MPV, and PDW. To correlate platelet indices with other parameters of MetS, including waist circumference, BP, and lipid profile. The study also demonstrated an increase in the mean platelet diameter in T2DM patients. The effects of the pro inflammatory cytokines on functional activity of platelets are studied. The present study compares the hematological parameters between patients with diabetes and MS.

2. Review of status of Research and Development in the subject

Smolenski, A. Novel roles of cAMP / cGMPdependent signaling in platelets. *J. Thromb. Haemost.* 2012; 10,167–176.

Diabetes mellitus (DM) is a complex metabolic disorder of great impact worldwide with a central theme of chronic hyperglycemia arising from insulin deficiency or insulin resistance or both.¹ Type 2 diabetes mellitus is the predominant form of diabetes worldwide, accounting for 90% of cases globally.² Diabetes mellitus has been growing rapidly as a worldwide public health problem. According to International Diabetes Federation (IDF) estimation, as of 2019, 463 million (8.8%) adults had DM worldwide. These global prevalence is estimated to be increased to 700 million (10.9%) by the end of 2045. It is estimated that the middle and low-income countries will bear the brunt of the diabetes epidemic to the extent of 80% of the global burden.³

2.1. International Status:

Recent studies on platelet volume indices in the spectrum of ischemic heart diseases show that all platelet indices—plateletcrit, mean platelet volume (MPV) and platelet distribution width (PDW)—were significantly raised in patients who had suffered from acute myocardial ischemia. A key component of vaso-occlusion is believed to be increased platelet activation and reactivity, and thus an increased platelet volume resulting in an elevated PDW. Also, higher concentrations of platelet microparticles have been detected in proinflammatory disorders such as sickle cell anemia. Studies on diabetes mellitus (DM), which too is considered to be a prothrombotic state with enhanced platelet reactivity, found a statistical rise in MPV and PDW, yet very few studies have been carried out regarding platelet indices for MetS patients. MetS patients have been found to be at a greater risk for developing insulin resistance, visceral

adiposity, atherogenic dyslipidemia, and endothelial dysfunction. Patients with insulin resistance tend to develop hypertriglyceridemia and are prone for developing atheromas in vascular lumen, leading to an increased incidence of coronary artery disease and stroke.[8] Hypertriglyceridemia too leads to endothelial dysfunction that predisposes to the development of atherosclerotic depositions along vessel lumina. Visceral adiposity has been implicated in dysregulation of adiponectin levels, which too eventually causes vascular dysfunction. [9]

2.2. National Status:

NIL

3. Progress/ achievement so far, if any

- a). Reference papers was collected.
- b). Literature survey was studied.
- c). Materials and methods were designed.

4. Work plan

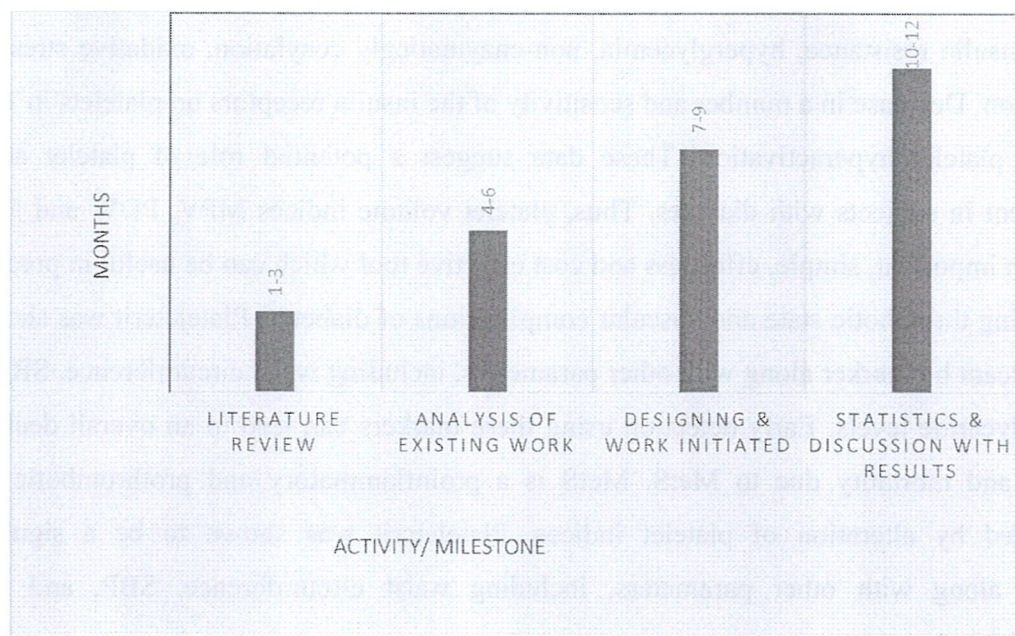
4.1 Methodology

The study was carried between January to December 2019 in Central Laboratory of Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry, India. All the Samples were recruited and collected after informed consent and study was approved by Institutional Ethics Committee approval. Laboratory analysis. The mean platelet volume (MPV), platelet count, and other blood cell indices were measured using a Study participants selected were 100 MetS patients aged between 25 and 60 years, attending the medicine OPD and/ or admitted to the medicine ward/intensive care unit (ICU). A DM, non-MetS participants were chosen. On assessment of waist circumference, BP was the parameter assessed next. Mean SBP, mean DBP On assessment by Student's unpaired t-test, Lipid profile of patients was then assessed. Fasting blood glucose levels of patients was the subsequent parameter taken into consideration. Platelet indices of patients, comprising plateletcrit , MPV, and PDW, were then taken into consideration. The first parameter taken into consideration was the patient's platelets. When mean plateletcrit of the two categories was Compared.

Statistical Analysis: Statistical analyses were carried out using inferential statistics, including chi-square test and Student's t-test. Software used for the analysis was SPSS version 11.5.p < 0.05 being considered as significant.

4.2 Time Schedule of activities giving milestones through BAR diagram. (Maximum of 1/2 pages)

| S. No | Activity/ mile stolen | 1 st Year | | | |
|-------|--|----------------------|-----------|-----------|-------------|
| | | 1-3 month | 4-6 month | 7-9 month | 10-12 month |
| 1 | Literature review | 1-3 month | | | |
| 2 | Analysis of existing work | - | 4-6 month | | |
| 3 | Designing & work initiated | - | - | 7-9 month | |
| 4 | Statistics & Discussion with results | - | - | - | 10-12 month |



4.3 Expected outcome within the time period of See Money Scheme

Platelet activation causes high risk of cardiovascular complications in MetS. T2 DM is associated with the changes in the intra cellular signaling systems regulating platelet functions. Due to the altered NOS expression and activity, platelets increase their prothrombogenic potential. The cGMP-mediated anti aggregational effects of insulin, involving NOS and NO-dependent mechanisms, become abnormal. The effects of aggregation triggering agonists are modulated by the proinflammatory factors. All these mechanisms of changes in platelets aggregation activity in MetS and DM T2 are caused by the metabolic disturbances including insulin resistance, hyperglycemia, and dyslipidemia. Results of our study may lay a foundation for a discovery of new approaches for prevention and treatment of cardiovascular complications in MetS and DM T2 in early stages of metabolic disorders in patients. Patients with metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM) have high risk of micro circulation complications and micro angiopathies. Factors leading to platelet activation in MetS and T2 DM comprise insulin resistance, hyperglycemia, non-enzymaticgly cosylation, oxidative stress, and inflammation. Decrease in a number and sensitivity of the insulin receptors on platelets in T2DM can cause platelet hyperactivation. These data suggest a potential role of platelet activity measurement in subjects with diabetes. Thus, platelet volume indices MPV, PDW and P-LCR provides an important, simple, effortless and cost effective tool which can be useful in predicting an impending thrombotic state and vascular complications of diabetes. Plateletcrit was shown to be a significant biomarker along with other parameters, including waist circumference, SBP, and serum triglyceride levels. Early detection using these markers can lead to an overall decline in morbidity and mortality due to MetS. MetS is a proinflammatory and prothrombotic state, characterized by alteration of platelet indices. Plateletcrit was shown to be a significant biomarker along with other parameters, including waist circumference, SBP, and serum triglyceride levels.

5. Suggested Plan of action stating the name of funding agency where the project will be communicated for financial support within the time period of project.

Nil

6. Bibliography: Nil

Nil

7. List of Projects submitted/implemented by the Investigators (Separate for Pi and Co-PI)

7.1 Details of Projects submitted to various funding agencies:

| S.No | Title | Cost in Lakhs | Month of Submission | Role as PI/Co-PI | Agency | Status |
|------|-------|---------------|---------------------|------------------|--------|--------|
| 1 | NA | NA | NA | NA | NA | NA |

7.2 Details of Projects under implementation

| Sl. No. | Title | Cost in lakhs | Duration | Role as PI/ Co-PI | Agency |
|---------|-------|---------------|----------|-------------------|--------|
| 1 | NA | NA | NA | NA | NA |

7.3 Details of Projects completed during the last 5 years

| Sl. No. | Title | Cost in lakhs | Duration | Role as PI/ Co-PI | Agency |
|---------|-------|---------------|----------|-------------------|--------|
| 1 | NA | NA NA | NA | NA | NA |

8. List of publications published by the Investigators, if any:

a) Principal Investigator

| S. No | Author names | Title of paper | Name of Journal | Vol (Issue) | Page No. | Year |
|-------|---|--|--|-------------|-----------|------|
| 1. | E Prabhakar Reddy1*, T.Mohanalakshmi2 | Role of Immunity: Current Status of COVID-19-A Review | Br J Med Health Res | 7(10) | 24-36 | 2020 |
| 2. | E. Prabhakar Reddy , Mahadeo Mane , T. Mohanalakshmi 1* 2 3 | Triglycerides fasting or non-fasting? Current knowledge in diagnostic values | Asian Journal of Pharmacy and Pharmacology | 5(2) | 218-226 | 2019 |
| 3. | T Mohana Lakshmi1* , BS Ravi Kiran2, P | High Sensitive C – Reactive Protein in Hypertension and | Research Journal of Pharmaceutical, | 7(6)' | 2017-2021 | 2016 |

| | | | | | | |
|----|---|---|---|------|---------------|------|
| | Jayakumar ³ , R Srikumar ⁴ , E Prabhakar Reddy ⁵ . | Metabolic Syndrome. | Biological and Chemical Sciences | | | |
| 4. | T Mohana Lakshmi 1, Chidambaram ² , A Vaithialingam ³ , and E Prabhakar Reddy ⁴ * | Advantages of Stem Cell Research: Role of Medical therapy in India. | Research Journal of Pharmaceutical, Biological and Chemical Sciences | 5(3) | 96-99 | 2014 |
| 5. | E Prabhakar Reddy , T.Mohana Lakshmi , Shankar Manohar Pawar | Antioxidants Status in Haemodialysis Patients | Int J Biol Med Res. | 3(1) | 1466- 1468 | 2012 |

b). Co-Principal Investigator

| S.No | Author names | Title of paper | Name of Journal | Vol (Issue) | Page No. | Year |
|------|---|---|--|----------------|----------|------|
| 1. | M Maney, V Rao, EP Reddy , A Vaithilingam | Prolonged Storage-Induced Changes In Haematology Parameters And Stability At Room Temperature For Counting Red And White Blood Cells And Platelets | Paripex-Indian Journal Of Research | 6 (3) | 46-48 | 2017 |
| 2. | 1B. Sai Ravi Kiran*, 2T. Mohana Lakshmi, 3R. Srikumar, 4E. Prabhakar Reddy | Total Antioxidant Status and Oxidative Stress in Diabetes Mellitus and Metabolic Syndrome | International Journal of Pharmaceutical Sciences Review and Research | 40(1) | 271-277 | 2016 |
| 3. | V Kowsalya, R Vijayakumar, R Chidambaram, R Srikumar, E Prabhakar Reddy , S Latha, I Gayathri Fathima, C Kishor Kumar | A study on knowledge, attitude and practice regarding voluntary blood donation among medical students in Puducherry, India. | Pakistan Journal of Biological Sciences | 16(9) | 439-442 | 2013 |

9. Budget

| SI. No | Head | Amount (Rs.) |
|--------|---|-------------------|
| 1 | BP Apparatus, Stethoscopes, Body weight weighing machine, SPSS version 16 Chicago, IL, USA, ECG machine | 50,000/- |
| 2 | Consumables (gels bottles, cotton, sprit, testing charges, tools, etc.) | 25,000/- |
| 3 | Travel support for the purpose of research work. | 10,000/- |
| 4 | Contingency | 10,000/- |
| 5 | Others consumables | 5,000/- |
| | Total | 1,00,000/- |

*In case of any joint proposal for purchasing a same equipment, each of the associated PLs is also required to give separate budget (without any clubbing) to avoid any ambiguity, if all the associated projects are not awarded by committee.

10. Name of at least two subject experts from the Institute and one from the outside Institute with their contact details:


| | |
|--|--|
| <p>1. Dr. Praveen Kumar. V Associate Professor in Microbiology, Chalmedha Anand Rao Institute of Medical Sciences, Karimnagar, Telanagana Mobile No: 8332063265 E-mail id: vpraveenkumar4@gmail.com</p> | <p>2. Dr. Patta Appa Rao Professor in Microbiology NRI Medical College, Vishakapattinam Mobile No: 9848766293 E-mail id: pattaapparao@yahoo.com</p> |
|--|--|

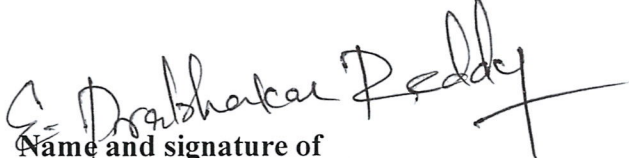
CERTIFICATE FROM THE INVESTIGATOR

Project Title: A Study of Platelet Indices in Patients with Metabolic Syndrome and Type 2 Diabetes Mellitus

It is certified that

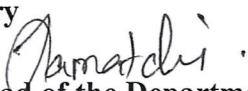
1. I do hereby agree to submit a complete proposal for financial support to the external funding agency within the time period of SMS-2018.
2. I undertake that spare time on equipment procured in the project will be made available to other users.
3. I agree to submit a certificate from Institutional Biosafety Committee, if the project involves the utilization of genetically engineered organisms. I also declare that while conducting experiments, the Biosafety Guidelines of Department of Biotechnology, Department of Health Research, GOI would be followed in to.
4. I agree to submit ethical clearance certificate from the concerned ethical committee, if the project involved field trails/experiments/exchange of specimens, human & animal materials etc.
5. I agree to abide by the terms and conditions of SMS-2018, BIHER, and Chennai.


**Name and signature of
Principal Investigator**



**Name and signature of
Co-Principal Investigator**

Date: 23.01.2019

Place: Pondicherry


Forwarded by Head of the Department

Signature of the Head


DEAN
SRI LAKSHMI NARAYANA INSTITUTE OF MEDICAL SCIENCES
OSUDU, AGARAM VILLAGE,
KODAPAKKAM POST,
PUDUCHERRY - 605 502

PROJECT EVALUATION FORMAT

Recommendation sheet

| | |
|---|--|
| Name of the Principal Investigator | Dr. T. Mohanalakshmi |
| Name of the Co-Principal Investigator | Dr. E. Prabhakar Reddy |
| Name of the Department | Microbiology |
| Title of project | A Study of Platelet Indices in Patients with Metabolic Syndrome and Type 2 Diabetes Mellitus |
| Recommendation of the evaluation committee (Recommended/Revision/Not Recommended) | Recommended - |
| Financial allocation recommended | Rs. 1,00,000/- |

| SI. No. | Head | Amount |
|---------|---|-------------------|
| 1 | BP Apparatus, Stethoscopes, Body weight weighing machine, SPSS version 16 Chicago, IL, USA, ECG machine | 50,000/- |
| 2 | Consumables- Gel bottles, cotton, sprit, testing charges, tools, etc. | 25,000/- |
| 3 | Travel support for the purpose of research work. | 10,000/- |
| 4 | Contingency | 10,000/- |
| 5 | Others consumables | 5,000/- |
| | Total | 1,00,000/- |

Name and Signature of the Research Advisory Committee members with date.



[Signature]
(Dr. G. Jayalakshmi)