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)
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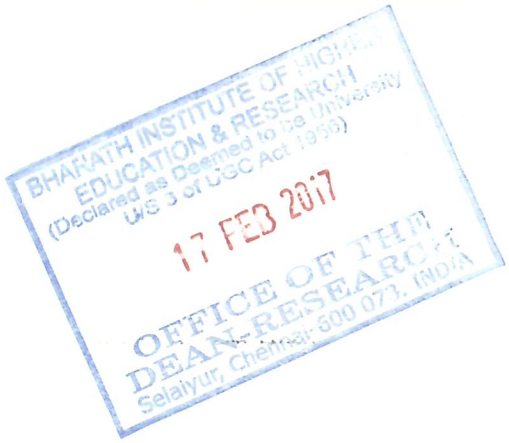
Ref. No.SMS-2015-O-06 Date: 17.02.2017



TO

Mr. B.S. Ravi Kiran
Associate Professor/Biochemistry
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-2015 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: Comparative Study of Nitric Oxide Levels in Metabolic Syndrome and Diabetes Mellitus Patients

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

Approved on: 15.02.2017

Payment details:

Voucher No.27 **Dated: 24.03.2017**

With Regards

Dean-Research

Bharath University

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

CASH / PAYMENT VOUCHER

Date 24/03/2017

V.No. 27

Debit _____ Amount

Rs. 1,00,000/-

PAID TO Dr. B. Sai Ravi Kiran

RUPEES One Lakh only

TOWARDS Seed Money Scheme - 2015

BHARATH UNIVERSITY CHENNAI 600 073. INDIA

Authorised by **Finance Manager** **Cashier/Accountant** **Payee's Signature**

PROPOSAL SUBMISSION

1. **Details of Principal Investigator**

Name	: Dr. Sairavi Kiran Biri
Designation	: Assistant Professor
Highest Qualifications	: Ph.D.
Department	: Biochemistry
E-mail	: bravikiran86@gmail.com
Contact no	: 7708873424
Date of Joining	: 18-04-2011

2. **Details of 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:

The metabolic syndrome (MetS) is considered as the most important public health threat of the 21stcentury, affecting between 10 & 15% of adult populations worldwide. This syndrome is characterized by a cluster of cardiovascular (CV) risk factors including central abdominal obesity, elevated triglycerides, reduced HDL cholesterol, high blood pressure, increased fasting glucose and hyper insulinemia1. Diabetes occurs a decade earlier in Asian population. India has a large and growing population of diabetic patients; its prevalence will reach 350 million by 2025. Diabetes is associated with increased risk for CVD, stroke and other risk factors of metabolic syndrome2. Diabetic mellitus (DM) is a group of metabolic disorder that shares the phenotype of hyperglycemia. Which defects due to reduced insulin secretion, decreased glucose utilization and increased glucose production. Chronic hyperglycemia of diabetics is associated with long term damage, dysfunction, retinopathy, nephropathy and neuropathy. It also predisposes to cardiovascular diseases. DM will be leading cause of morbidity and mortality for the foreseeable future. Majority of the diabetic cases cauterized into type I and type II. Type I (insulin dependent) Type II (insulin independent) because of autosomal immune destruction of β cells of pancreas with consequent insulin deficiency. Additional factors found to increase the risk of Type II DM include aging, high-fat diets, and a less active lifestyle.

Free radical nitric oxide (NO) has emerged as a fundamental signaling device regulating virtually every critical cellular function and is a potent mediator of cellular damage in many conditions3. Endothelium plays a pivotal role in the regulation of vascular tone, controlling tissue blood flow and inflammatory responses and maintaining blood fluidity. These cells produced by vasodilatory substances such as NO. The MetS components, dyslipidaemia, hypertension and type II diabetes are well known CV risk factors and are all associated with impaired endothelial function4.The mechanism by which these risk factors induce endothelial dysfunction. Hyperglycemia may interfere with endothelial function and the NO pathway causing glycation of elastic fibers and failure in smooth muscle relaxation, decrease in NO production (due to a decreased expression of endothelial NO synthase or reduced bioavailability of its cofactor), increase in NO deactivation, and increase in the NO synthase inhibitor5. Hyperglycemia may additionally impair endothelial function by promoting release of free radicals, such as superoxide, which inactivates NO resulting in the production of peroxyinitrite, a potent oxidant that stimulates the production of vasoconstrictor prostanoids

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

Du X, Matsumura T, Edelstein D, Rossetti L, Zsengellér Z, Szabó C, Brownlee M. Inhibition of GAPDH activity by poly (ADP-ribose) polymerase activates three major pathways of hyperglycemic damage in endothelial cells. J Clin Invest. 2003 Oct; 112(7):1049-57.

Vascular injury in diabetes consequential from hyperglycemia has been associated with oxidative stress that leads to depletion of intracellular glutathione with an augmented plasma extracellular superoxide dismutase which intervenes lipid peroxidation and diabetic complications.[2–4] Elevated concentration of superoxide dismutase causes impairment of

endothelial isoform of nitric oxide synthase (eNOS) by triggering advanced glycation end products and poly (ADP-ribose) polymerase.[5] NO is synthesized as a byproduct of conversion of its physiological precursor l-arginine to l-citrulline. This reaction is catalyzed by a family of enzymes known as NO synthases (NOS).[6] Nitric oxide is produced in endothelial cells from the substrate l-arginine via eNOS. Elevated asymmetric dimethylarginine levels cause eNOS uncoupling, a mechanism which leads to decrease NO bioavailability. The endothelial dysfunction associated with diabetes has been attributed to lack of bioavailable NO due to reduced ability to synthesize NO from l-arginine. New basic research insights provide possible mechanisms underlying the impaired NO bioavailability in type 2 diabetes. So, the nitric oxide is reduced in the course of vascular disease (e.g., diabetes and hypertension). [7–11]

2.1. International Status:

Diabetes mellitus (DM) is a metabolic disease characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both [1], [2]. Depending on the intensity and duration of exposure to hyperglycemia, structural damage may occur in vascular endothelium and nervous tissue, leading to dysfunction, and even failure of different organs and tissues, characterizing the diabetic chronic complications [2]. These complications are divided into macrovascular-(coronary artery disease, peripheral vascular disease and stroke) and microvascular-complications (diabetic kidney disease, diabetic retinopathy and neuropathy), and are associated with high morbidity and mortality rates among diabetic patients [3].

In diabetic patients, hyperglycemia stimulates the production of advanced glycation end products (AGEs), and enhances the polyol, protein kinase C (PKC) and hexosamine pathways, which may lead to oxidative stress [13], [14]. Then, excessive reactive oxygen species (ROS), such as superoxide anion (O2−), react rapidly with NO radicals, forming the peroxynitrite anion, which is a toxic oxidant capable of damaging several biological molecules, leading to tissue injury [15], [16], [17].

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 conducted at SLIMS, Puducherry. The study included 200 diabetic patients, 200 MetS patients and 200 Controls. The study was approved by the institutional ethical committee of Sri Lakhsmi Naryana Institute of Medical Sciences, Puducherry according Helsiniki 1975 human ethical guidelines. All the data were collected in a prescribed perform and obtained informed consent form from studied subjects. Nitricoxide were estimated by Kinetic cadmium reaction. FBS, lipid profile assessed by using standard method using commercial kits. 5 ml of venous blood samples were collected from patients and controls and these samples were collected overnight fasting of 12 hrs. Collected samples centrifuged under 2000 rpm for 20 min and after centrifugation of samples (plasma) used to assess the Nitiricoxide levels.

The diagnosis of diabetes mellitus was based on World Health Organization (WHO) criteria,i.e. a fasting blood glucose (FBG) of 110mg/dL after a minimum 12-hour fast, with symptoms and family history of diabetes. The diagnosis of metabolic syndrome was based waist, BMI, waist-hip ratio, systolic and diastolic blood pressure, Blood glucose levels. NCEP ATP III 2001 CRITERIA FOR METABOLIC SYNDROME: The purpose of ATP III was to identify people at higher long-term risk for cardiovascular diseases (CVDs) who deserved clinical lifestyle intervention to reduce risk. Presence of three of the following five factors is required for diagnosis of metabolic syndrome6. Central obesity: Abdominal waist circumference: Men >102 cm, women >88 cm. Fasting plasma glucose >110 mg/dl or diagnosed type 2 diabetes mellitus (T2DM). Fasting plasma triglyceride >150 mg/dl or medication. Fasting plasma HDL cholesterol: Men <40 mg/dl, women <50 mg/dl or medication. Blood pressure ≥120/80 mm Hg or medication

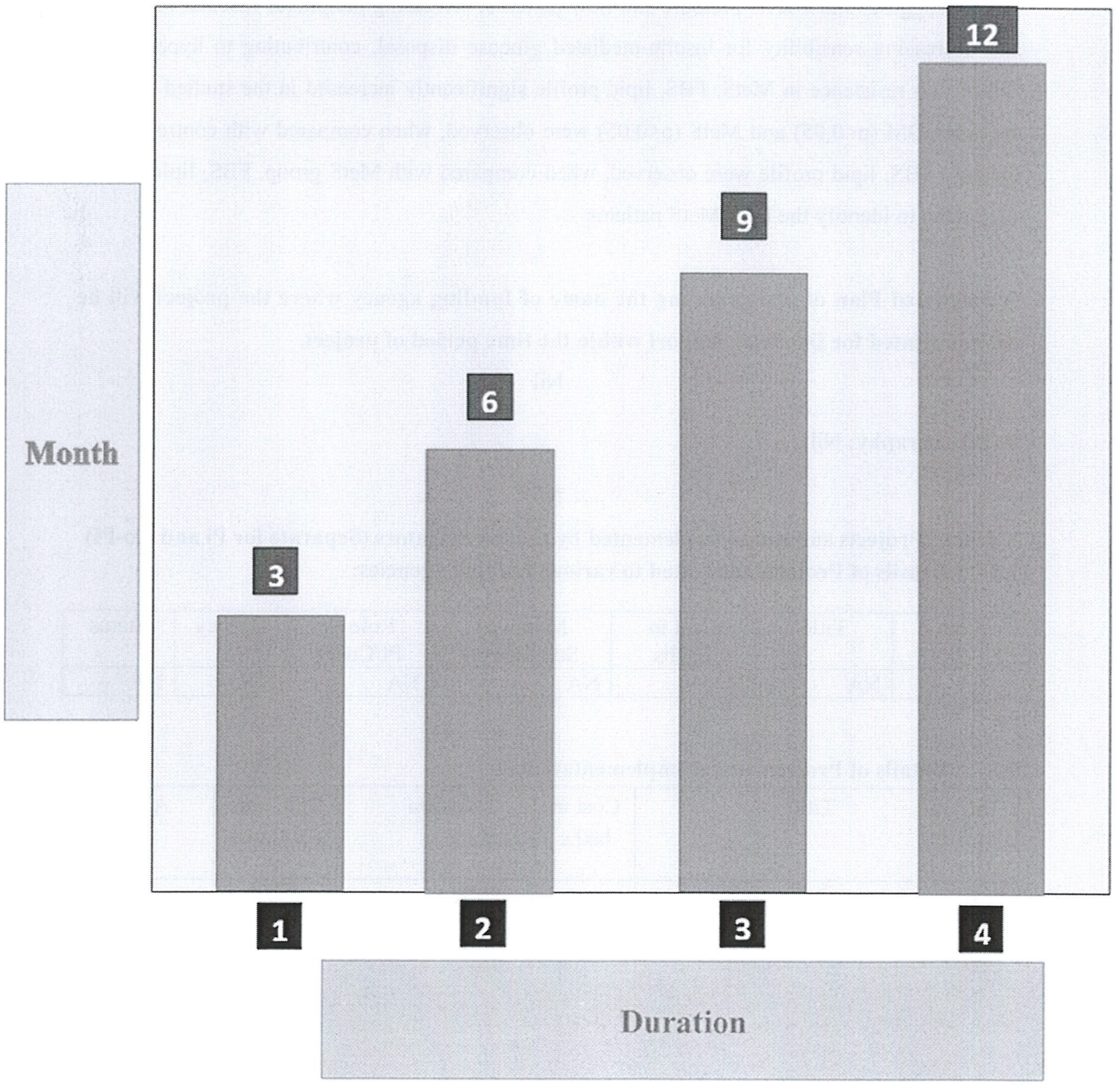
Statistical Analysis

All results were summarized as mean ± SEM. The statistical analysis was done using SPSS 11.5 (SPSS, Inc.,Chicago)., and the comparison between patients and control was done by using Anova. A P-value less than 0.05 were considered statistically significant. The statistical significance was kept of P value <0.001 is comparatively highly significant.

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

S. No	Activity/ mile stolen	1st Year			
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

To sum up, serum NO was observed a significant increase ($p<0.001$) in nitric oxide among MetS and diabetes group and significant difference ($p<0.001$) between DM and MetS groups being higher in MetS group along with difference in other biochemical parameters. No is reduced in the course of vascular disease in DM. Increased production of superioxide anion on OS to reduce plasma NO levels. Endothelial cells secrete different mediators such as vasodilators i.e.,NO, and vasoconstrictors i.e., endothelin-1. Hyperglycaemia and other metabolic changes may lead to impairment of NO production .When compared to controls, It was found a significant increase ($p<0.001$) in nitric oxide among MetS and diabetes group and significant difference ($p<0.001$) between DM and MetS groups being higher in MetS group. This finding suggests that affects pressure and flow patterns, increasing peripheral vascular resistance and decreasing sensibility for insulin-mediated glucose disposal, contributing to hypertension and insulin resistance in MetS. FBS, lipid profile significantly increased in the studied subjects such that DM ($p<0.05$) and MetS ($p<0.05$) were observed, when compared with control group. Increase FBS, lipid profile were observed, when compared with MetS group. FBS, lipid profile were done to identify the DM, MetS patients

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	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 Name	Title paper	Name of journal	Volume & Issue	Year
1.	**Sai Ravi Kiran B,** Mohana Lakshmi T, Srikumar R, Prabhakar Reddy E.	F2 Isoprostanes levels in metabolic syndrome	International Journal of Research in Pharmaceutical Sciences	8(3); 459-462	2017
2.	**B.Sai Ravi Kiran,** T.Mohana Lakshmi, SLV.Sankeerthi.Ch, G.Surya Prakash, V.Seshadri Reddy, S.Arul Murugan, E.Prabhakar Reddy	Evaluation of Oxidative Stress Presented in Patients with Diabetes Mellitus and Metabolic Syndrome.	Journal of Current Trends in Clinical Medicine & Laboratory Biochemistry	2(1): pp 33-38.	2014
3.	E.Prabhakar Reddy, **B.Sai Ravi Kiran** et al,	Green Tea Consumption on Serum Lipids and Blood Sugar Levels in Puducherry Subjects	Current Research in Microbiology and Biotechnology	2(4):pp 422-425	2014
4.	T.Mohana Lakshmi, **B.Sai Ravi Kiran,** E.Prabhakar Reddy et al.,	Comprehensive Review on Diabetes, Hypertension and Metabolic Syndrome	Journal of Current Trends in Clinical Medicine & Laboratory Biochemistry	2(3): pp 1-11.	2014
5.	Sreeramadasu Ramaiah, Ganesh Rathod, **B.S.Ravi Kiran,** Prabhakar Reddy	Lipids and Oxidized LDL in Metabolic Syndrome.	Journal of Current Trends in Clinical Medicine & Laboratory Biochemistry	2(4): pp 17-28.	2014

6.	E. Prabhakar Reddy, Shankar Manohar Pawar, **B. Sai Ravi Kiran**	A Review of green tea- health benefits and effects.	Journal of Current Trends in Clinical Medicine and Laboratory Biochemistry	Vol 1: Issue 3:1-11	2013
7.	Sudhakar, Venugopal, **B. Sai Ravi Kiran**	Ratios of age & sex with blood group prevalence in dengue fever	Journal of Current Trends in Clinical Medicine and Laboratory Biochemistry	1 (2); 24-27	2013
8.	Sandhya rani T, Balasubramanian, B. Sai Ravi Kiran, Jayarani. K, Naveen Kumar. C	Incidence of malaria and typhoid in acute fever in tertiary care hospital around pondicherry	International journal of recent scientific research	6 (6) ; 4378-4381	2015
9.	Sandhyarani. T, Jayarani. K, Sai Ravikiran. B, Naveen Kumar C	Microbiological profile and spectrum of drug susceptibility in asymptomatic bacteriuria among antenatal women	Universal research journal of medical sciences	1 (1); 13-16.	2014
10	S.L.V.Sankeerthi CH,,A.Vaithalinga m, T.Sandhya Rani, **B.Sai Ravikiran,** T.MohanaLakshmi, E. Prabhakar Reddy	Evaluation of Clinical Utility of Serum Enzymes, Lipid Profile, Homocysteine in Early Stages of Acute Myocardial Infarction.	Research Journal of Pharmaceutical, Biological and Chemical Sciences	5(2): 755-759.	2014
10	T Vijhaya Priya, CV Baba, Rathinakumar, S Arul Murugan, B **Sai Ravi Kiran,** E Prabhakar Reddy.	Evaluation of Safety and Efficacy of Laser Assisted Insitu keratomileusis for Correction of High Myopia - A Retrospective Study.	Research Journal of Pharmaceutical, Biological and Chemical Sciences	5(3):100-116.	2014
11	T Mohanalakshmi, Sandhya Rani T, Sankeerthi.CH, B. **Sai Ravi Kiran,** V.Sreenivasulu	A report on extended spectrum beta lactamases producing Escherichia coli isolated from clinical samples	Current research in microbiology & biotechnology	2 (2); 347-350	2014

	Reddy,E. Prabhakar Reddy				
12	Ravi Babu, B.Venugopal, K.Sabitha, **B.Sai Ravikiran,** E.Prabhakar Reddy	Comparative Study of Liver and Kidney Biochemical Parameters in Normal and Pre-Eclamptic Gestation.	Journal of Current Trends in Clinical Medicine and Laboratory Biochemistry	Vol 1, Issue 3: pages 26-30	2013
13	T.Sandhya Rani, T.Mohana Lakshmi, Ch.S.L.V.Sankeerthi,, **B.Sai Ravikiran,**	Distribution of Staphylococcus aureus and Pseudomonas aeruginosa in Chronic wounds	Journal of Current Trends in Clinical Medicine and Laboratory Biochemistry	Vol 1, Issue 2: pages 15-19.	2013
14	Ayarin Glorida Stephen.J, E. Prabhakar Reddy, T.Mohana Lakshmi, **B.Sai Ravi kiran**	Laboratory Errors-In routine Biochemical Investigations..	Journal of Pharmaceutical and Biomedical Sciences	Vol 22(27) : 1-2.	2012.
15	K.Srinivasa Rao, B.L.Kudagi, P.Ram Mohan, R.Prema, **B.Sai Ravi Kiran**	Comparison of The Efficacy And Safety of Penicillins and Cephalosporins In Treatment of Pediatric Patients With Lower Respiratory Tract Infections.	Journal of Current Trends in Clinical Medicine and Laboratory Biochemistry	V0l 2, Issue 1: Pages 26-32	2014

b). Co-Principal Investigator

S. No	Author names	Title of paper	Name of Journal	Vol (Issue)	Page No.	Year
1.	Kalpana Thalava1, ***E Prabhakar Reddy2**, and A Vaithilingam3.	HCG and CA-125 Levels In Pregnancy And Abortion Patients.	Research Journal of Pharmaceutical, Biological and Chemical Sciences	8(2)	2745-2749	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	60,000
2	Consumables (gels bottles, cotton, sprit, testing charges, tools, etc.)	25000
3	Travel support for the purpose of research work.	5000
4	Contingency	5000
5	Others consumables	5000
	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:

1. **Dr. Lokesh,** Associate Professor, Dept of General Medicine, Mahatma Gandhi Medical College and Research Institute, Pondicherry, **Mobile No**: 9791360480 **E-mail id:** lokeshdr@gmail.com	2. **Dr. Sudhakar T,** Professor and HOD, Department of Biochemistry, Chalmedha Anand Rao Institute of Medical Sciences, Karimnagar, Telanagana **Mobile No**: 9849573192 **E-mail id:** manoharmanohar44@gmail.com

CERTIFICATE FROM THE INVESTIGATOR

Project Title: Comparative Study of Nitric Oxide Levels in Metabolic Syndrome and Diabetes Mellitus Patients

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-2015.
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-2015, BIHER, and Chennai.

Name and signature of Principal Investigator

Name and signature of Co-Principal Investigator

Date: 05.01.2017
Place: Pondicherry

Forwarded by Head of the Department

Signature of the Head

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

PROJECT EVALUATION FORMAT

Recommendation sheet

Name of the Principal Investigator	Mr. SAIRAVI KIRAN BIRI
Name of the Co-Principal Investigator	Dr. E. Prabhakar Reddy
Name of the Department	Biochemistry
Title of project	Comparative Study of Nitric Oxide Levels in Metabolic Syndrome and Diabetes Mellitus Patients
Recommendation of the evaluation committee (Recommended/Revision/Not Recommended)	Recommended
Financial allocation recommended	Rs. 100000/-

SI. No.	Head	Amount
1	BP Apparatus, Stethoscopes, Body weight weighing machine, SPSS version 16 Chicago, IL, USA, ECG machine	60,000
2	Consumables- Gel bottles, cotton, sprit, testing charges, tools, etc.	25000
3	Travel support for the purpose of research work.	5000
4	Contingency	5000
5	Others consumables	5000
	Total	**1,00,000**

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

Internal Quality Assurance Cell IQAC Pondicherry-02 SLIMS

Dr. G. Jayalakshmi