



# 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 4<sup>th</sup> July 2002)



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

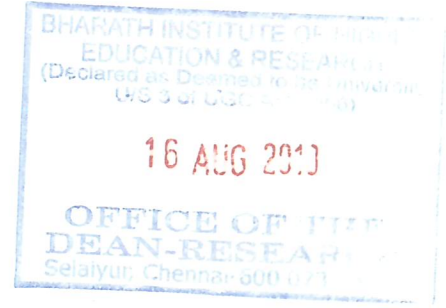
173, Agaram Road, Selaiyur, Tambaram,  
Chennai - 600 073. Tamil Nadu.

Ref. No.SMS-2018-O-03

Date: 16.08.2018

TO

Mr. R. Vijaykumar  
Professor/Physiology  
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: The Relationship between Non-Linear Analysis of Heart Rate Variability, QT c Interval and cardiovascular Risk Factors in Young Individuals with Pre-Diabetes**

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

**Approved on: 06.08.2018**

**Payment details:**

**Voucher No.48**

**Dated: 22.08.2018**

With Regards

Dean-Research

# Bharath University

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

## CASH / PAYMENT VOUCHER

Date 22/08/2018

V.No. 48

Debit \_\_\_\_\_ Amount \_\_\_\_\_

**Rs.**

PAID TO Dr. R. Vijay Kumar

RUPEES One Lakh Only


TOWARDS Seed Money Scheme - 2018



Authorised by 

Finance Manager

Cashier/Accountant



Payee's Signature

## PROPOSAL SUBMISSION

### 1. Details of Principal Investigator

**Name** : Dr.R.Vijayakumar  
**Designation** : Professor  
**Highest Qualifications** : Ph.D.  
**Department** : Physiology  
**E-mail** : sivanviji@gmail.com  
**Contact no** : 9445383846  
**Date of Joining** : 2.1.2012

### 2. Details of Co-Principal Investigator

**Name** : Dr. V. Deepika  
**Designation** : Associate Professor  
**Highest Qualifications** : Ph.D.  
**Department** : Physiology  
**E-mail** : deepy843@gmail.com  
**Contact no** : 9962279360  
**Date of Joining** : 27.07.2013

## Technical details

### 1. Introduction:

In India, 69.1 million individuals have diabetes, making it the Diabetic Capital of the world [1]. The reasons for the alarming increase may be due to rapid socio-economic and nutritional transition, lack of self-awareness, and follow-up programs in the society. As per the “ticking clock hypothesis”, the microvascular disease manifestation appears in the precursor stage, before the expression of full-blown clinical type 2 diabetes mellitus [2]. According to the American Diabetes Association, pre-diabetes is Impaired Fasting Glucose (IFG) ranging from 100–125 mg/dL or Impaired Glucose Tolerance (IGT) of 140–199 mg/dL [3]. Pre-diabetes is related to increased cardiovascular (CV) disease and mortality [4]. Evaluation strategies targeting the younger candidates with increased risk will be a potential boon for the society to plan early interventional strategies.

The autonomic nervous system, with its sympathetic and parasympathetic limbs, orchestrates numerous physiological and pathological cardiovascular responses. The sympathovagal imbalance is an indicator of increased cardiovascular risk. A variety of markers have been provided to reflect autonomic activity and cardiovascular risk, that includes heart rate, heart rate variability (HRV), [5] QT interval lengthening, and QTc (Corrected QT interval) [6]. Early diagnoses of autonomic dysfunction employing the Ewing test battery are outdated. HRV has been widely accepted as a non-invasive marker of autonomic control [5]. HRV represents the variation in time between successive heartbeats. The traditionally employed linear analysis method (time and frequency domain) is prone to interference by ectopic rhythms and assumes that the analyzed R-R segments are stationary, and variations occur in a harmonic fashion. Considering the fact that the cardiovascular system exhibits non-linear dynamics, the newly explored non-linear methods of HRV analysis provide better insights into the autonomic control of the cardiovascular system. Poincare plot is a geometric, semi-quantitative method, used for identifying the non-linear patterns within the electrocardiograph (ECG) data [7]. QT interval is an ECG measurement that represents the duration between ventricular depolarization to ventricular repolarization. It is affected by heart rate, so QTc calculated using Bazett’s square root formula is the accepted gold standard that reflects autonomic activity. With this perspective, the current study was aimed to evaluate the cardiac autonomic status employing Poincare plot and QTc in young pre-diabetic individuals. Also, we sought to identify the cardiovascular risk factors that contribute to autonomic dysfunction.

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

Silva, A.K.; Christofaro, D.G.; Vanderlei, F.M.; Barbosa, M.P.; Garner, D.M.; Vanderlei, L.C. Association of cardiac autonomic modulation with physical and clinical features of young people with type 1 diabetes. *Cardiol. Young* 2017, 27, 37–45

The presence of risk factors is associated with negative modifications in the autonomic behavior in individuals with type 1 diabetes. Colhoun et al. [10] studied 160

adults with type 1 diabetes, and found an inverse association between global variability and several other factors, such as age, disease duration, higher blood pressure, body mass index, waist/hip ratio, triglycerides, HbA 1c, and physical activity. Similar data were also provided by the EURODIAB Prospective Complications Study Group [11], who highlighted HbA 1c, hypertension, distal symmetrical polyneuropathy, and retinopathy as factors capable of predicting the risk of cardiac autonomic dysfunction in type 1 diabetics in a period of 7.3 years

### **2.1. International Status:**

The goals of this study were 1) to evaluate HRV in TODAY participants compared with an obese control group and establish the prevalence of cardiac autonomic dysfunction in the TODAY cohort at follow-up (T2P1); 2) to determine whether prior T2D treatment assignment in TODAY (metformin alone, metformin + rosiglitazone, or metformin + intensive lifestyle intervention) or glycemic control over time are independently associated with impaired HRV; and 3) to assess of the association of cardiac autonomic function with noninvasive measures of arterial stiffness.

### **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**

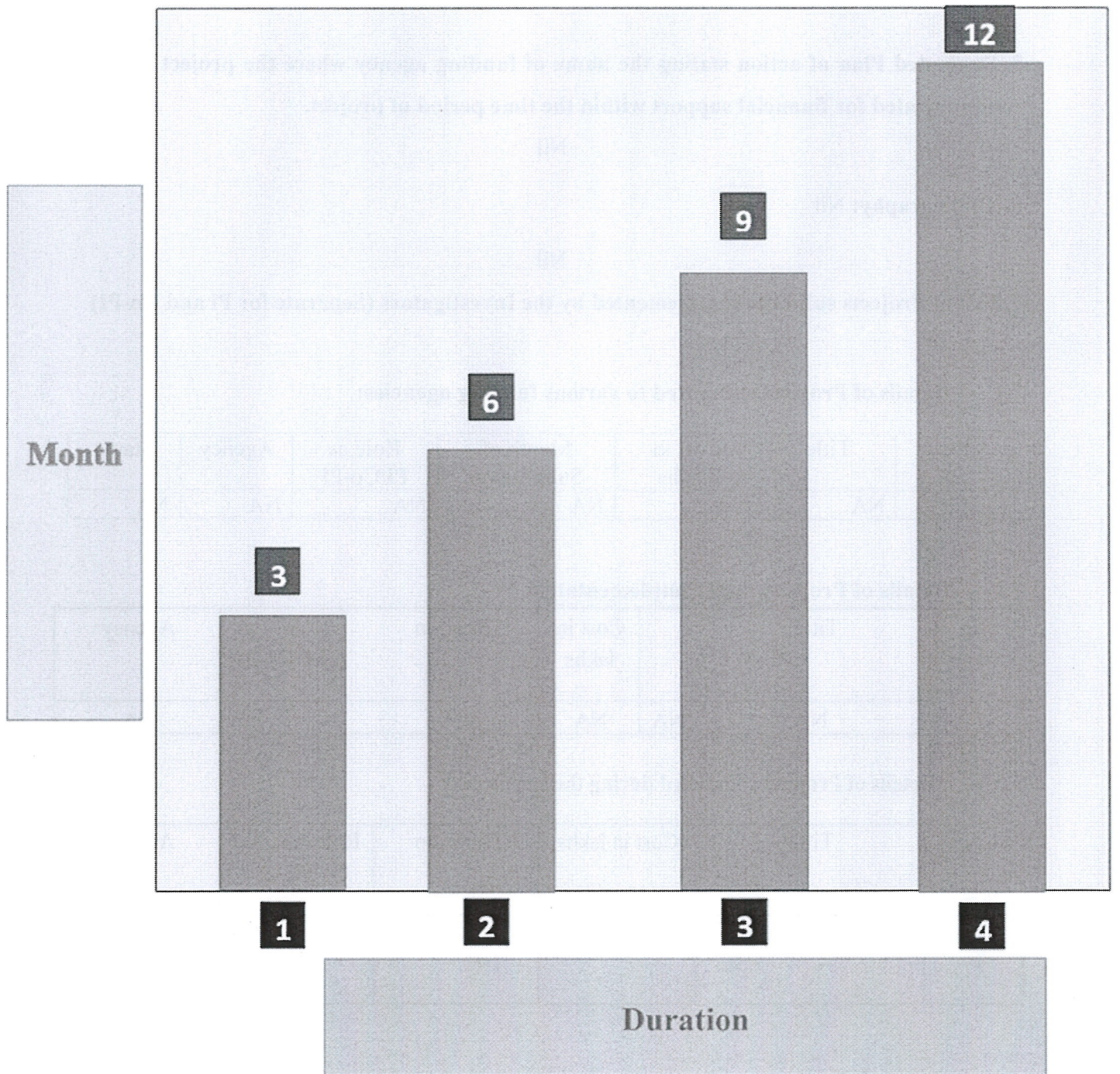
**Study design and patients:** This was a cross-sectional study. Bachelor of Medicine, Bachelor of Surgery students participating in the health check-up program organized by the institution, were the study participants. The study was approved by the Institute Ethics Committee of the Sri Manakula Vinayagar Medical College and Hospital. A total of 403 participants from the 18-25 age group were screened during the medical health check-up program. Sociodemographic details, personal history general examination, systemic examination, family history of diabetes, and blood investigations (fasting blood glucose and lipid profile) were evaluated in all individuals on the day of the health check-up program. Seventy-six participants were excluded due to a history of any medication intake, any form of medical illness, athletes, fasting glucose more than 125mg/dL, or if they reported having cardiovascular diseases. Among the remaining 327 subjects, 32 participants were not willing to participate after hearing the protocol procedures. The remaining 295 subjects were the study participants. Based on their

fasting plasma glucose (FPG) and IGT values, the subjects were divided into two groups; Group I (n=198) included subjects who had FPG and IGT in the range of 60-99 mg/dL and >140 mg/dL respectively; Group II (n=97) included subjects with FPG and IGT ranging from 100-125 mg/dL or 140– 199 mg/dL, respectively.

**Cardiovascular autonomic function test: HRV Analysis - Poincare plot:** The study was carried in the Autonomic Laboratory, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, between 07.00 to 8:30 A.M. The Task Force guidelines on HRV were followed. The subject was given rest for 10 minutes, and lead II ECG was obtained using Recorders and Medicare (RMS) polyrite D hardware, version 1.0, India. The sampling rate of 500Hz and bandpass filter of 2Hz to 40Hz was followed. The readings were taken thrice each with a five minutes interval, and the last 5 minutes ECG was performed, digitalized, and stored for HRV analysis. From the ECG reading, the RR series were extracted with maximum amplitude and sharpness. Analysis of the RR series was done using the inland version 1.1 software for HRV (Bio-Signal Analysis Group, University of Kuopio, Finland). The Poincaré plot represents a time series on a cartesian plane. It is a scatter plot of  $RR_n$  vs.  $RR_{n+1}$ . The time between two successive R peaks is represented by  $RR_n$ , and the time between the next two successive R peaks is represented by  $RR_{n+1}$ . Employing the ellipse-fitting technique on the plot, two main indices are depicted: the standard deviation of instantaneous beat-to-beat interval variability (SD1), and the continuous long-term R/R interval variability (SD2). On the Poincaré plot, SD1 is the width and SD2 the length of the ellipse. The line of identity (LOI) is the 45° imaginary diagonal line on the Poincaré plot. SD1 depicts short-term HRV and measures the dispersion of points

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

S. No	Activity/ mile stolon	1 <sup>st</sup> 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

Autonomic dysfunction appears in the pre-diabetic stage, in the form of parasympathetic withdrawal and sympathetic dominance. Gender, BMI, and FPG were reported to show a significant association with SD1, SD2, and QTc. This study emphasizes glucose monitoring and evaluating autonomic functions, in younger individuals to know the extent of alterations caused and to plan early interventional strategies.

#### 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.	R. Yuvaraj1, <b>R. Vijayakumar1*</b> , G. Bupesh2, S. Vasanth2	Effect of Saraswatarishta on sleep deprivation induced behavioral changes in mice	Drug Invention Today	12 (8)	1741-1744	2019
2.	Velusami Deepika 1,2, <b>Raman Vijayakumar3</b>	Impact of Body Mass Index on Arterial Stiffness in Young Prehypertensives: A Cross Sectional Study	Journal of Research in Health Sciences	18(1): e00402	1-6	2018
3.	Deepika.V1, <b>R.R.Vijaya Kumar2*</b> , S. Latha Vijaya Kumar3 And Dr.R.Srikumar4	Impact of body mass index on corrected QT Interval in prehypertensives	International Journal of Pharma and Bio Sciences	8(1): (B)	266-270	2017
4.	S Latha, <b>R Vijaya Kumar</b> , BR Senthil Kumar, G Bupesh, TSV Kumar	Acute and repeated oral toxicity of antidiabetic polyherbal formulation flax seed, Fenugreek and Jamun seeds in Wistar albino rat	Journal of Diabetes & Metabolism	7(3)	1-7	2016
5.	<b>Vijaya kumar R</b> , Kishor kumar.C, Christy A, Sasikala C	Prevalence of Prehypertension among school students in Puducherry	Research Journal of Pharmaceutical, Biological and Chemical Sciences	6(1)	631-637	2015

**b). Co-Principal Investigator**

S. No	Author names	Title of paper	Name of Journal	Vol (Issue)	Page No.	Year
1.	<b>Deepika Veluswami</b> , B Ambigai Meena, S Latha, I Gayathri Fathima, K Soundariya, K Senthamil Selvi	A study on prevalence of phenyl thiocarbamide (PTC) taste blindness among obese individuals	Journal of clinical and diagnostic research: JCDR	9(5)	<b>CC04</b>	2015

2.	SP Venkatesh, K Soundariya, V <b>Deepika</b>	A study on attitude of medical students towards learning of communication skills	J of Evolution of Med and Dent Sci	3(27)	7567-7573	2014
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## 9. Budget

SI. No	Head	Amount (Rs.)
1	BP Apparatus, Stethoscopes, Body weight weighing machine, SPSS version 16 Chicago, IL, USA, ECG machine	45000
2	Consumables (gels bottles, cotton, sprit, testing charges, tools, etc.)	10000
3	Travel support for the purpose of research work.	10000
4	Contingency	25000
5	Others consumables	10000
	<b>Total</b>	<b>1,00,000</b>

\*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:

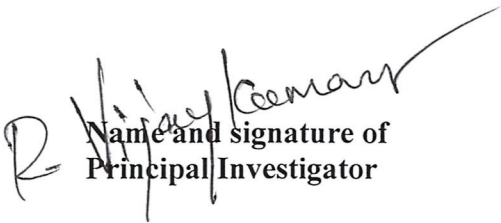
<p>1. <b>Dr. R. Ravindran,</b> Professor in Physiology IBMS, Chennai <b>Mobile No:</b> 9444145990 <b>E-mail id:</b> ravindran89@gmail.com</p>	<p>2. <b>Dr. Vasuki,</b> Associate Professor in Physiology, Priyadharshini Dental College, Thiruvallur <b>Mobile No:</b> 9443793114 <b>E-mail id:</b> vasukiphysio@gmail.com</p>
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## CERTIFICATE FROM THE INVESTIGATOR

**Project Title:** The Relationship between Non-Linear Analysis of Heart Rate Variability, QTc Interval and Cardiovascular Risk Factors in Young Individuals with Pre-Diabetes

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:** 18.07.2018

**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.R.Vijayakumar
Name of the Co-Principal Investigator	Dr. V. Deepika
Name of the Department	Physiology
Title of project	The Relationship between Non-Linear Analysis of Heart Rate Variability, QTc Interval and Cardiovascular Risk Factors in Young Individuals with Pre-Diabetes
Recommendation of the evaluation committee (Recommended/Revision/Not Recommended)	<i>Recommended</i>
Financial allocation recommended	<i>Rs. 1,00,000/-</i>

SI. No.	Head	Amount
1	BP Apparatus, Stethoscopes, Body weight weighing machine, SPSS version 16 Chicago, IL, USA, ECG machine	45000
2	Consumables- Gel bottles, cotton, sprit, testing charges, tools, etc.	10000
3	Travel support for the purpose of research work.	10000
4	Contingency	25000
5	Others consumables	10000
	<b>Total</b>	<b>1,00,000</b>

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



*[Signature]*  
(Dr. G. Jayalakshmi)