Indian Pacing and Electrophysiology Journal 21 (2021) 112–119

Contents lists available at ScienceDirect

Indian Pacing and Electrophysiology Journal

journal homepage: www.elsevier.com/locate/IPEJ

Normative data and gender differences in heart rate variability in the healthy young individuals aged 18–30 years, a South Indian cross-sectional study

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ARTICLE INFO

Article history:
Received 20 October 2020
Received in revised form
12 December 2020
Accepted 9 January 2021
Available online 19 January 2021

1. Introduction

The autonomic nervous system (ANS) plays the chief role in heart rate (HR) regulation. Periodic fluctuations of HR occur due to asynchronous firing of sympathetic and parasympathetic components of the ANS to the heart. This fluctuation is called heart rate variability (HRV) and may be recorded with a simple lead II ECG recording, wherein beat-to-beat interval (interbeat interval or RR interval or NN interval) is measured. HRV reflects the functioning of ANS and is now considered standard to measure the same [1]. This in turn allows us to evaluate the neurological state of the organism, its adaptive capacity and the robustness of the regulatory systems.

Several works have highlighted the importance of HRV as a tool for assessing ANS activity in many different conditions and diseases, since the publication of Task force guidelines for standards of measurement, interpretation and use, in 1996. Before this, in 1981, Akselrod *et al.*, had analyzed the power spectrum of HRV [2]. Two frequency domain parameters are widely used: low frequency (LF) power (0.04–0.15 Hz) that represents both sympathetic and parasympathetic influences; high frequency (HF) power (0.15–0.40 Hz) reflecting the modulation of parasympathetic tone, both given in absolute power which is calculated as ms squared divided by cycles per second (ms^2/Hz). In addition, LF/HF ratio indicates the balance between sympathetic and parasympathetic tones. Task Force also put forth other frequency domain parameters such as ultra-low-frequency (ULF) (≤0.003 Hz), very-low-frequency (VLF) (0.0033–0.04 Hz). Global power is measured in terms of Total Power (TP) in absolute units (ms^2). The relative power is also measured in percentage of total HRV power or in normalized units as LF power (nu) and HF power (nu). Further, time domain parameters of HRV are also used, which indicate the variability in interbeat interval (IBI). Some of the common parameters are SDNN (ms), i.e., Standard deviation of NN intervals, RMSSD (ms) (Root mean square of successive RR interval differences), NN50 (number of successive RR intervals that differ by more than 50 ms), and pNN50% (percentage of successive RR intervals that differ by more than 50 ms).

Several cardiac and neural functions change with age. In particular, autonomic functions, and the responses elicited blunt with ageing. To list a few autonomic responses: Orthostatic hypotension occurrence increases with aging [3]; Recovery of heart rate after exercise becomes blunted due to sluggish cardiac vagal response [4]. The two divisions of ANS mature with time, but the degree of the change varies, as they are two different neural pathways. Thus the symaptho-vagal balance also fluctuates with ageing [5]. Reports suggest that HRV reduces with increasing age [6,7]. In fact age is considered as one of the confounding variables in studies related to ANS function [8]. It is thus important to have certain normative standards for each age group, for comparison

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Peer review under responsibility of Indian Heart Rhythm Society.

https://doi.org/10.1016/j.ipej.2021.01.002

against abnormal HRV data.

Another important factor to be considered in HRV analysis is gender differences. Women were found to have higher parasympathetic tone, which reduced after the age of 50 (post-menopausal), while in men, the sympathetic dominance reduced much later in life [9]. However, in both genders, ANS control reduces with age [10]. A few commented on not finding any significant gender related differences in HRV among young healthy individuals [11]. However, gender related differences in cardiac autonomic activity in young healthy subjects is not well established. Therefore, this study was planned to evaluate ANS activity and the influence of gender among young healthy individuals, of a particular age group.

2. Methodology

2.1. Study design

This was a cross-sectional study. A total sample of 288 subjects in the age group of 18–30 years were recruited. Study population was classified based on gender with 125 males and 163 females included. The participants were healthy subjects in age group of 18–30 years, from Bangalore, South India. Recording of HRV of female subjects was during the mid-follicular phase of their menstrual cycle. Informed written consent was obtained from all participants. The study protocol was approved by the institutional scientific committee on human research and ethical review board (Submission reference: MSRMC/EC/2016; Dated: February 11, 2016; MSRMC/EC/2017; Dated: July 25, 2017). The research was conducted as per the Declaration of Helsinki. Participants provided written, informed consent to volunteer for the study. The timeline of data collection was from October 2016 to January 2020.

2.2. Recruitment of subjects - inclusion and exclusion criteria

Healthy subjects aged 18–30 years were invited to participate in the study via advertisements in notice boards of various institutions, social media posts, and posters. Participants who responded to the call were sent an online questionnaire (google form). About 350 responded to the call, of which 322 completed the google form. Inclusion criteria were healthy subjects, aged 18–30 years, of either gender, non-smokers, and alcoholics. Exclusion criteria were any medical disorder (cardiovascular, renal, respiratory, endocrine, hearing problem, psychiatric disorders, stroke, epilepsy), pregnancy; intake of drugs which are known to affect the BP or autonomic status of the individual, including oral contraceptives or hormone replacement therapies. Subjects were screened after taking a detailed medical history and the healthy cardiovascular system of the volunteers was defined by measuring BP, which confirmed their non-hypertensive state, and by measuring baseline HR that confirmed their non-tachycardia state. Follicular phase of menstrual cycles was confirmed by enquiring into their last menstrual period and relevant details.

2.3. Baseline demographic data collection

A pre-tested, pre-designed web-based questionnaire was implemented which contained details such as the subject's name, gender, socio-demographic details, educational background, drug history, present or past history of non-communicable diseases if any, and family history of non-communicable disorders, smoking, and alcohol history. Following the collection of data online, the subjects were invited, for further data collection, to the lab.

2.4. Baseline demographic data recording

On the assessment of the online questionnaire responses, about 25 subjects had to be excluded as questionnaire data was incomplete or self-reported body mass index (BMI) was more than 30 kg/m^2 ($n = 297$). These 297 subjects were invited for further data collection, but $n = 6$ declined from participating further. The rest of subjects ($n = 291$) were explained about the study, the protocol, and co-operation expected from them. They were informed about their rights to withdraw their participation from the study. A general health check-up was done for all subjects. The BMI was calculated and BP in the sitting position was measured twice after 5 min' rest (Sphygmomanometer) in between and was noted (23). Only normotensives were included as per inclusion criteria (3 more subjects excluded based on lab recordings).

2.5. Electrocardiograph recording

After overnight fasting, participants were asked to take a light breakfast and abstain from exhaustive exercise, for the past 24 h and tea, coffee about 2 h prior to the recording. It was ensured no one entered the room once recordings began. All the recordings were carried out between 08:00 a.m. and 10:00 a.m. in an isolated examination room at a stable temperature between 20 and 22 °C, in a noise free atmosphere. During the recording, the subjects lay in a semi-darkened, electrically shielded, sound-attenuated room with their eyes closed (24). The subjects were asked to relax in a bed for about 10 min prior to the tests, when lead II (sample rate of 1000 Hz) attachments for Electro-cardiogram (ECG) was done. They were asked to remain as still as possible to exclude movement induced artifacts, and also refrain from talking, falling asleep, and intentionally altering their respiration during the recording. Subjects were carefully monitored to ensure there were no significant respiratory or postural changes during the session. During the first 10 min, blood pressure (BP) cuff was tied to the left arm of the subjects using standardized digital BP monitor was used (Omron HEM-7130L, Europe), the reliability of which has been established (34). ECG was recorded for the next 10 min, as it is twice the minimum window required for HRV analysis. The recording of the data began in the Power lab 15 T Lab chart hardware & software (AD instruments). At the end of 10 min, digital measurement of BP [systolic (SBP), diastolic BP (DBP) and pulse rate] was recorded. After this the subjects were made to feel comfortable and were relieved.

2.6. HRV analysis

Of the whole recording, the first 1–2 min of each segment of data were excluded in case of any transition or adjustment effect. The series with more than 95% of sinus beats were used for analysis. A minimum of 256 data points is required to perform spectral analysis for which recording duration of 5 min of ECG is ideal. In the current study we had more than 10 min of data recorded for each subject, and thus for all subjects a minimum of 8 min and a maximum of 10 min of ECG was analyzed. A region in the channel that contained data without much variation and ectopics was selected and analyzed. HRV software used a peak detection algorithm (threshold level) to find the "R" wave, which was done at a resampling rate of "4Hz". A threshold value was set to detect the beats (R waves – R component of QRS complex) and it was increased to avoid detection of unwanted peaks or decreased to detect genuine beats that would have been missed. Beats that fall outside of the timing of a normal sinus rhythm were considered ectopics. Ectopics were excluded as they do not represent ANS activity and are not believed to contribute to HRV. Inclusion of

ectopics during analysis results in a falsely higher representation of the HF component of HRV [12,13]. In order to avoid influence of linear trend on low-frequency power it was removed. Poincare plot, where RR interval is plotted against the preceding RR interval, in a scatter plot analysis, has been widely used as a quantitative visual tool for HRV analysis [14–16]. After referring the Poincare plot (for the best possible ellipse) [Fig. 1], RR interval Tachogram, a plot of successive RR interval values against the interval number [Fig. 2], and the spectrum [Fig. 3] for any ectopics and detection of R waves, a report [Fig. 4] was generated by the Lab chart software and results were entered onto an excel sheet and tabulated. Sources of error were minimized by having only one of the investigators perform the recording of ECG and analysis of HRV of the subjects. The parameters analyzed were mean NN interval, HR (Average of 10 min), time-domain parameters - analyzed using fast Fourier transformation (FFT size: 1024) were SDNN, RMSSD, NN50, pNN50, spectral components such as VLF, LF, HF and TP components in absolute values of power (ms^2) [VLF, LF, HF, TP (ms^2)] and in normalized units (nu), [LF nu, HF nu], and LF/HF.

2.7. Statistical analysis

Data were analyzed using SPSS software version 18.0 (SPSS Inc. Released in 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.). The continuous variables were analyzed using descriptive statistics using mean and SD. The categorical variables were analyzed using frequency and percentage. The normalcy of the data was checked by applying the Kolmogorov-Smirnov goodness of fit test. The variables of HRV were skewed in distribution and thus, they were also analyzed after logarithmic transformation. The remaining variables were compared after combining the values. Baseline comparisons between the groups were carried out using students' t-test for continuous variables and chi-square test for categorical variables. Data is expressed as mean ± SD. All the variables were compared for interaction with age and gender using two-Way ANOVA. All HRV parameters were studied for correlation (using R Gui software), and correlation matrix plotted. Bonferroni multiple comparisons test (Analysis of variance – Multivariate model - ANCOVA) was used to compute the most important variable that had an effect on the dependant variables (HRV absolute and log converted values), after adjusting for all the confounding variables (age, age group, gender, education level, physical activity, family history of non-communicable disorders, height, weight, BMI, SBP, DBP and pulse rate). Since age was statistically significant on baseline comparison, age was further subgrouped into 2 categories (18–23.9 years, ≥24 up to 30 years) and analyzed for age and age group interaction effects on HRV. P value ≤ 0.05 was considered for statistical significance.

3. Results

A total of 288 subjects' data was analyzed of which 125 males and 163 females was included. All the baseline parameters were comparable between the gender groups, except age, SBP and HR. Males were of slightly higher age group (21.53 ± 2.8 years, $P < 0.0001$), and had higher SBP (114.07 ± 9.92 mm Hg, $P < 0.0001$) compared to females [age 20.31 ± 2.6 years, SBP 103.88 ± 9 mm Hg, who had higher HR (74.47 ± 12.5, $P = 0.004$) (see Table 1).

Significant differences were observed between males and females with respect to mean NN ($P < 0.0001$), mean HR ($P < 0.0001$), absolute value of NN50 ($P = 0.010$), HF ms^2 ($P = 0.013$), log converted values of VLF ms^2 ($P = 0.004$), LF ms^2 ($P = 0.008$), absolute and log converted values of LF nu ($P < 0.0001$), HF nu ($P = 0.001$) and LF/HF ($P < 0.0001$). Significant interaction with gender was observed with mean NN ($P = 0.036$), mean HR ($P = 0.036$), frequency domain parameters such as log converted VLF ms^2 ($P = 0.03$), LF ms^2 ($P = 0.018$), absolute and log converted values of LF nu ($P < 0.0001$), HF nu ($P = 0.004$) and LF/HF ($P < 0.0001$). Age group and age-gender interaction was statistically not significant. Time domain parameters did not show any statistically significant difference, though females had a higher level (see Table 2).

A strong correlation was observed across various HRV

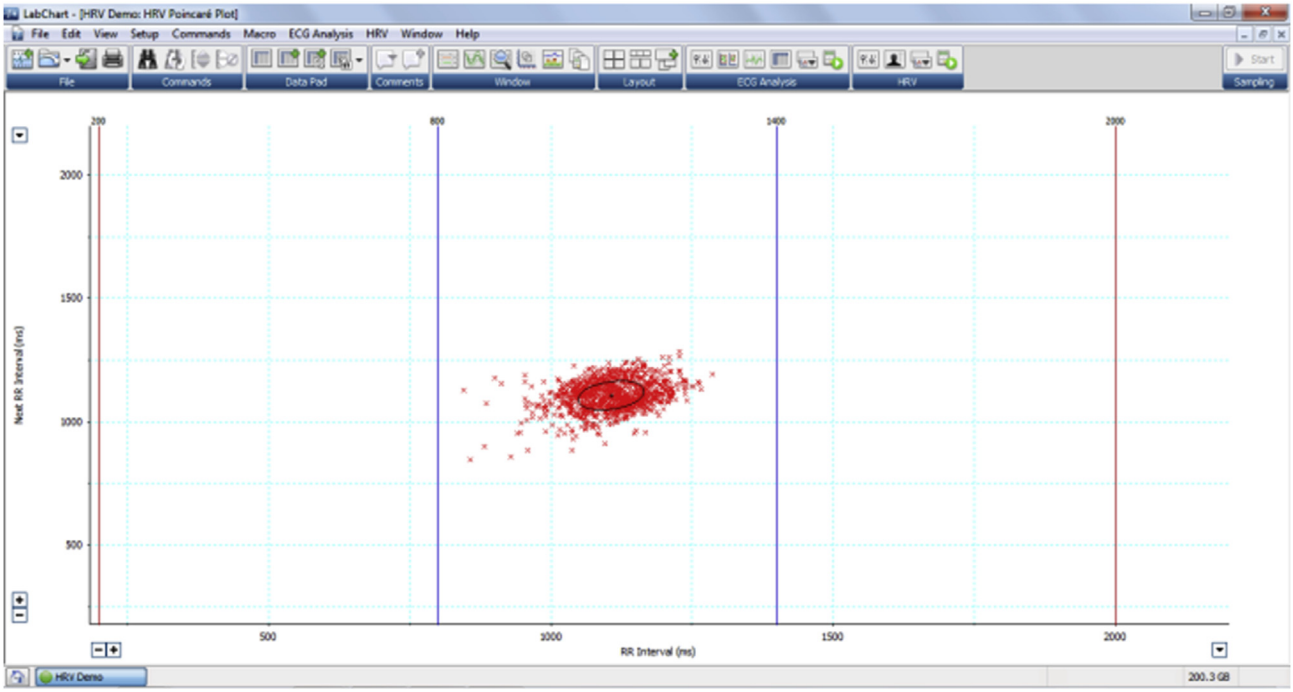

Fig. 1. Poincare plot.

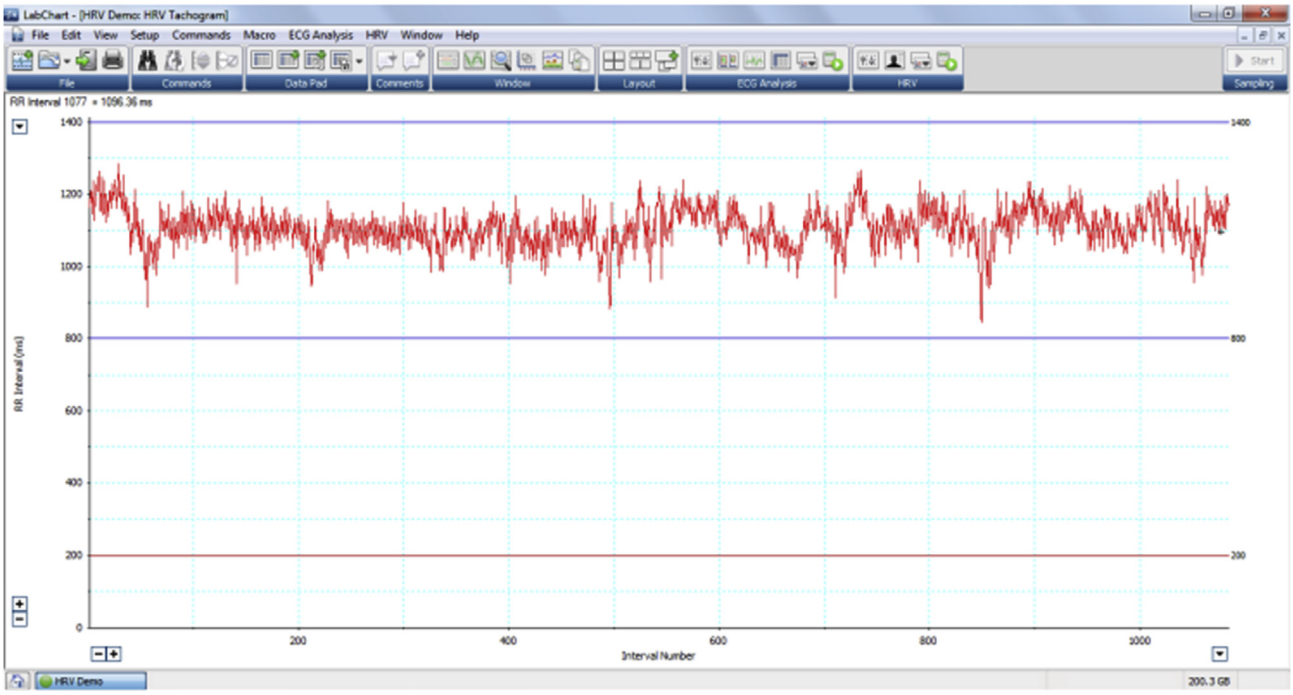

Fig. 2. Tachogram.

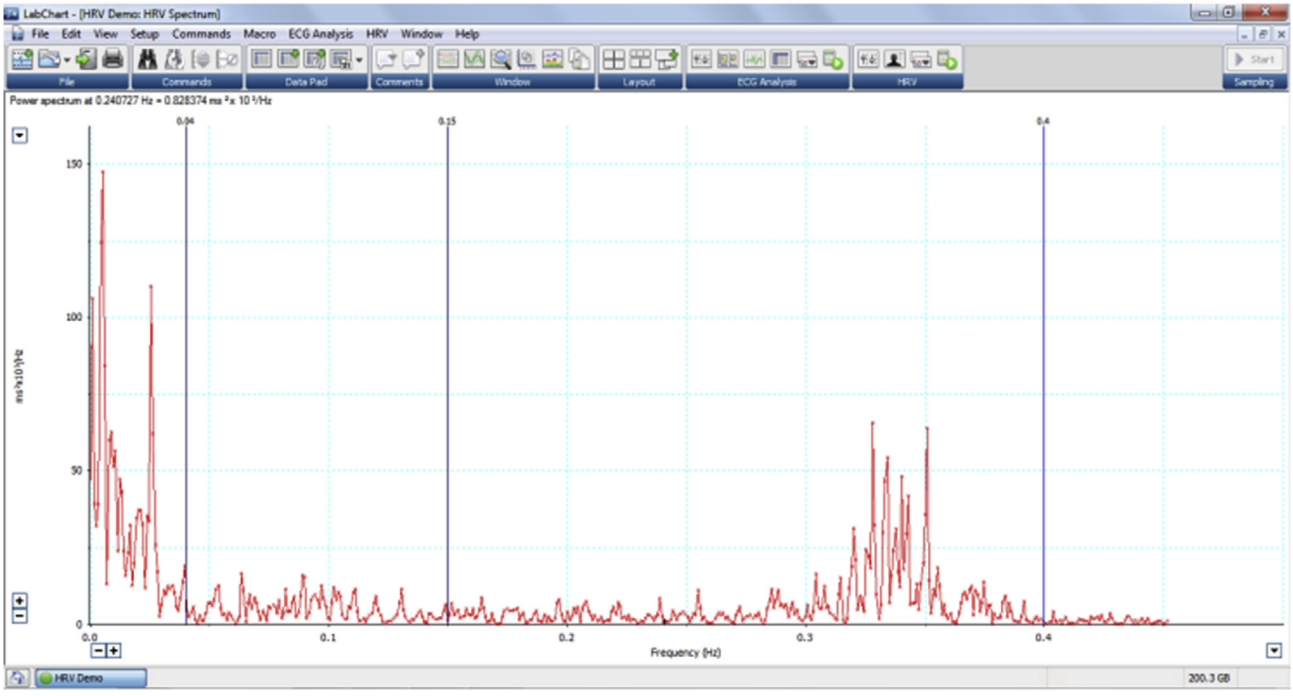

Fig. 3. Frequency distribution spectrum.

parameters (see Supplementary file Table 1 for correlation levels and significance, Fig. 5). The time domain parameters indicate general parasympathetic tone, and was thus negatively correlated with mean HR. Further SDNN and RMSSD strongly correlated with TP ms^2 (with SDNN – r = 0.987, P < 0.0001; and RMSSD – r = 0.909, P < 0.0001) and HF ms^2 (with SDNN – r = 0.918, P < 0.0001; and RMSSD – r = 0.957, P < 0.0001). Strong negative correlation was observed between HF nu and LF nu (r = −0.858, P < 0.0001) and HF nu and LF/HF ratio (r = −0.953, P < 0.0001).

A significant effect of gender was observed on different HRV parameters, after adjusting for covariates (listed in statistical analysis), using multivariate ANCOVA method of analysis (Table 3).

4. Discussion

It is important to create normative data for electrophysiological parameters for each set of population. Effective normative data of HRV is available for other parts of the world [8,17–20], but very few

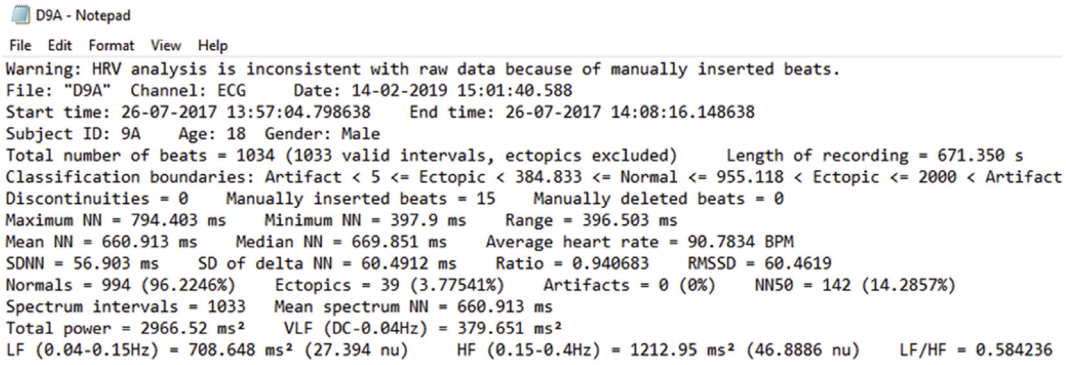

Fig. 4. HRV report.

Table 1
Sociodemographic and baseline data of males and females in the study population.

Parameters	Males (n = 125)	Females (n = 163)	Overall (n = 288)	P*
Age (in years), mean, SD	21.53, 2.79	20.31, 2.33	20.84, 2.61	**<0.0001**
Education level				
Upto graduation	57 (45.6%)	90 (55.2%)	147	0.121
Graduation and above	67 (53.6%)	73 (44.8%)	140	
BMI (kg/m2) mean, SD	23.31, 4.07	22.86, 4.42	23.06, 4.27	0.376
Physical activity involvement				
Yes	73 (58.4%)	85 (52.1%)	158	0.292
No	52 (41.6%)	78 (47.9%)	130	
SBP (mm Hg) mean, SD	114.07, 9.92	103.88, 8.96	108.29, 10.65	**<0.0001**
DBP (mm Hg) mean, SD	70.50, 7.71	69.89, 6.66	70.15, 7.13	0.477
HR (bpm) mean, SD	70.14, 12.22	74.47, 12.46	72.59, 12.52	**0.004**
Family history of non-communicable disorders (Only present indicated)				
HTN	29 (23.2%)	41 (25.2%)	70	0.703
DM	47 (37.6%)	59 (36.2%)	106	0.807
Epilepsy	2 (1.6%)	2 (1.2%)	4	0.790
Cancer	9 (7.2%)	12 (7.4%)	21	0.958
Asthma	7 (5.6%)	13 (8%)	20	0.434

(i)Data expressed as mean ± SD.
(ii)*Between males and females.
(iii)SBP: Systolic blood pressure (mm of Hg).
(iv)DBP: Diastolic blood pressure (mm of Hg).
(v)BMI: Body Mass Index (kg/m^2), HTN: Hypertension, DM: Diabetes mellitus.

researchers have tried to establish a normative data for Indian population [21–23]. The aim of the current study was to establish normative short-term HRV data (time domain and frequency domain) among young adults aged 18–30 years, with specific reference to gender differences. This study provides HRV data measured over 5–10 min, among a group of 288 young adults, residents of South India.

Short-term HRV measurements (~5 min) is the most commonly employed and published HRV data over past many years. In the normative data given by Task force, wherein 24-h data was used to compute time domain parameters, the mean (SD) of SDNN was 141 (39) and RMSSD was 27 (12). In the current study we observed a lower level of SDNN [64.43 (1.64)] and higher level of RMSSD [61.64 (2.33)], which could be due to short-term HRV data analysis or employment of free breathing technique or due to the age group included in comparison to that commented in Task Force, where 24-h recording of ECG and HRV of healthy subjects aged 40–70 years were analyzed [1,7]. In contrast, most of the frequency domain parameters levels matched with the normative data given by Task Force, except HF (ms^2 and nu) levels, which was higher in the present study, indicating higher parasympathetic tone in younger adults. Nunan et al. [24], commented that the HRV values varied according to breathing (free or paced, sex, and method of spectral power analysis, autoregressive (AR) or FFT. In the current study we followed free breathing technique. Gender differences were noted and FFT was used to analyze the HRV parameters. The normative data [mean(SD)] given by them of SDNN 50 (16), RMSSD 42 (15), LF ms^2 591 (291), LF nu 52 (10), HF ms^2 657 (777), HF nu 40 (10), LF/HF 2.8 (2.6) [16], was almost similar to our overall group results, except for LF ms^2 [1227.43(74.97)] which was higher in our data. Compared to a South Indian study, the TP 1158 (124), HF 585 (69) and LF 573 (65) in ms^2 were much higher in the current study [TP 4712.86 (271.2), HF 1858.39 (149.2) and LF 1227.43 (74.97)], probably due to mean age range used for young adults in that study (29–30 years) compared to the current study (20–21 years) [21]. Further, this South Indian study did not include time domain or other frequency domain parameters to compare.

In the current study we further evaluated the gender differences in cardiac ANS function among young adults. The mean NN interval was low among females compared to males, while mean HR was higher in females compared to males, the difference being statistically significant ($P < 0.0001$). This said, however, the time domain parameters, such as RMSSD, NN50 and pNN50 were higher among females with difference in absolute values of NN50 being statistically significant ($P = 0.010$). These time domain parameters are said to be indicators of parasympathetic activity, or high frequency variations in HR. However, it is important to note that a 24-h recording of HRV is considered better for time domain analysis.

Table 2
Gender differences in HRV and age, gender interaction.

Parameters	Gender		Overall	P*	P value**		
	Males	Females			Between age groups	Between gender	Between age and gender
Mean NN Interval (ms)	876.84, 11.27 (2.94, 0.06)	822.12, 9.87 (2.91, 0.07)	845.87, 7.59 (2.92, 0.07)	**<0.0001**	0.721	**0.036**	0.354
Mean HR (bpm)	69.82, 0.89 (1.84, 0.06)	74.68, 0.89 (1.87, 0.07)	72.57, 0.65 (1.86, 0.07)	**<0.0001**	0.722	**0.036**	0.354
SDNN	64.44, 2.05 (1.78, 0.16)	64.42, 2.44 (1.76, 0.20)	64.43, 1.64 (1.77, 0.18)	0.406	0.393	0.415	0.830
RMSSD	57.36, 2.56 (1.70, 0.23)	64.93, 3.60 (1.72, 0.28)	61.64, 2.33 (1.71, 0.26)	0.562	0.385	0.605	0.781
NN50	207.19, 13.14 (2.17, 0.41)	258.44, 14.59 (2.20, 0.59)	236.19, 10.13 (2.19, 0.52)	0.644	0.513	0.498	0.530
pNN50	30.42, 1.89 (1.33, 0.44)	32.38, 1.83 (1.29, 0.60)	31.53, 1.32 (1.31, 0.54)	0.550	0.543	0.890	0.603
TP ms^2	4423.07, 277.04 (3.54, 0.32)	4935.08, 429.48 (3.50, 0.41)	4712.86, 271.19 (3.52, 0.37)	0.390	0.327	0.406	0.849
VLF ms^2	1460.47, 110.22 (3.04, 0.34)	1181.10, 101.87 (2.92, 0.37)	1302.35, 75.24 (2.97, 0.36)	**0.004**	0.809	**0.03**	0.935
LF ms^2	1314.84, 94.36 (2.99, 0.35)	1160.40, 110.92 (2.87, 0.40)	1227.43, 74.97 (2.92, 0.38)	**0.008**	0.397	**0.018**	0.581
LF nu	47.37, 1.42 (1.65, 0.17)	37.52, 1.15 (1.54, 0.19)	41.80, 0.94 (1.58, 0.19)	**<0.0001**	0.415	**<0.0001**	0.396
HF ms^2	1471.35, 116.15 (2.98, 0.44)	2155.20, 245.93 (3.03, 0.53)	1858.39, 149.17 (3.00, 0.50)	0.416	0.247	0.545	0.846
HF nu	45.99, 1.38 (1.64, 0.16)	52.12, 1.15 (1.70, 0.14)	49.46, 0.90 (1.67, 0.15)	**0.001**	0.423	**0.003**	0.381
LF/HF	1.34, 0.10 (0.01, 0.32)	0.88, 0.05 (−0.16, 0.31)	1.08, 0.05 (−0.09, 0.32)	**<0.0001**	0.394	**<0.0001**	0.349

Note:
1All values given as absolute values - Mean, SD (Log10 mean, SD).
2*Between males and females; **Calculated using two-way anova.
3P value retained for only log converted HRV parameters.
4.Age groups (18–23.9 years, ≥24 up to 30 years).

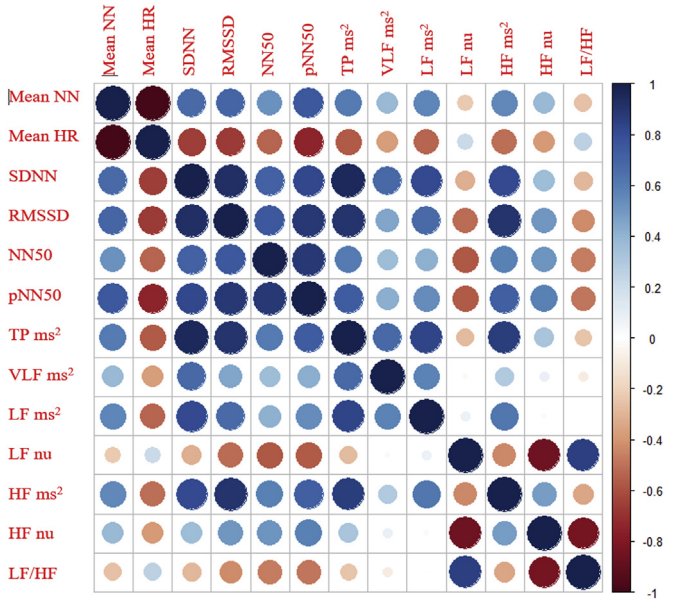

Fig. 5. Correlation matrix of HRV parameters (absolute levels).
a) Positive correlations are displayed in blue and negative correlations in red color. Color intensity and the size of the circle are proportional to the correlation coefficients. In the right side of the correlogram, the legend color shows the correlation coefficients and the corresponding colors.
b) SDNN (ms), i.e., Standard deviation of NN intervals; RMSSD (ms) (Root mean square of successive RR interval differences); NN50 (number of successive RR intervals that differ by more than 50 ms); and pNN50% (percentage of successive RR intervals that differ by more than 50 ms); Low frequency (LF) power (0.04–0.15 Hz); high frequency (HF) power (0.15–0.40 Hz) given in absolute power (ms^2/Hz); very-low-frequency (VLF) (0.0033–0.04 Hz); in normalized units - LF power (nu); HF power (nu); LF/HF ration – LF.HF.

Among the frequency domain parameters, TP ms^2, HF ms^2 (P = 0.013), HF nu (P = 0.001) was high among females compared to males, indicating or reconfirming better parasympathetic tone among females in this age group. Among males, VLF ms^2, LF ms^2 and LF/HF were higher, in that, log converted level of VLF ms^2 (P = 0.004) and LF ms^2 (P = 0.008) was statistically significant. Absolute and log converted levels of LF/HF were statistically significant as well (P < 0.0001). Significant interaction effects of the HRV parameters with gender was also observed [mean NN, mean HR, log converted VLF ms^2 (P = 0.03), LF ms^2, absolute and log converted values of LF nu, HF nu and LF/HF]. Normalized powers are said to be better at detecting the effect of gender differences in HRV and ANS balance [9].

On correlation analysis, it the mean HR was inversely correlated to all the time domain parameters. Further SDNN and RMSSD strongly correlated with TP ms^2 and HF ms^2, similar to other studies [25]. Strong negative correlation was observed between HF nu and LF nu and HF nu and LF/HF ratio, clearly demarcating the sympathovagal balance differences [16]. Gender had a significant influence on the HRV parameters, such as RMSSD, NN50, pNN50, LF nu, HF ms^2, HF nu, LF/HF, log converted RMSSD, LF nu, HF nu and LF/

Table 3
ANCOVA results after controlling for the confounding variables.

Dependent variables (HRV)	F statistic	P
RMSSD	5.619	0.018
NN50	8.423	0.004
pNN50	4.511	0.035
LF nu	11.138	0.001
HF ms^2	5.266	0.023
HF nu	4.293	0.039
LF/HF	7.642	0.006

Note:
a) Bonferroni multiple comparisons test (Analysis of variance – Multivariate model – ANCOVA) was used to compute the most important variable that had an effect on the dependant variables (HRV values), after adjusting for all the confounding variables (age, age group, education level, physical activity, family history of non-communicable disorders, height, weight, BMI, SBP, DBP and pulse rate). Note that only significant results are shown.
b) Insignificant findings were for HRV parameters SDNN, TP, VLF (ms^2), LF (ms^2).

HF, after adjusting for confounding variables such as age, age group, education level, physical activity, family history of non-communicable disorders, height, weight, BMI, SBP, DBP and pulse rate.

The gender difference in autonomic balance is said to begin during adolescence [26]. In a previous study, all the HRV parameters were shown to be lower among women aged lesser than 30 years, which reduced beyond this age and disappeared beyond 50 years [27]. After the age of 50 years, the gender-related difference in parasympathetic regulation is shown to reduce. In this study, it was also shown that women in age group of 40–49 years had a higher HF than men [9]. In one study where 30 college going males and females HRV was studied on a day to day basis, no significant difference in HRV was observed between gender subgroups [11]. In the study conducted in India, gender-related difference was observed with HF (nu) and HF/LF ratio being significantly higher among females, and LF (nu) and absolute values were significantly lower in females [21]. Gender difference was specifically observed among adolescent and adult age groups in the study. In contrast, this gender difference in HRV was not seen among children (6–16 years old) [28]. Importantly a recent meta-analysis looking into influence of gender on HRV, studied 63,612 participants (31,970 females), wherein it was seen that females had a significantly lower mean RR interval, SDNN, TP, LF power, LF/HF ratio but higher HF power. And similar to the current study, it was reported that although women had a greater mean HR, they had higher parasympathetic control as evidenced by HF power [29]. In another study, conducted among 255 participants, observed a significant effect of HR on HRV indices than age or gender. Influence of gender was seen only among younger adolescents and young adults, and the authors commented that this lack of gender influence in late adolescence was probably due to incomplete maturity of the ANS [30].

The fact of lower sympathetic activity among females, and the resulting protection from cardiovascular morbidities is well put forth by various researchers [21,22,31]. The mechanism accounting for the gender difference in autonomic balance is well reviewed by Dart et al. [32], wherein a few prenatal influences (neuropeptides in brain, acetylcholinesterase activity and ganglionic neurons in brain), sex hormones acting across different brain regions and a few peripheral effects of gonadal hormones, have been propounded.

The strength if the present study is that for the first time it has tried to establish a normative time domain and frequency domain HRV data for young adults in age group of 18–30 years, in South India, with specific reference to gender differences. After adjusting for the various confounding variables, gender differences in HRV persisted. The sample size was adequate for drawing sufficient evidences. The group was homogenous, with respect to education level, place of residence, physical activity and general health. Standardized equipment, lab conditions and statistical measures were used for data collection and analysis. Most of the data matched with the existing normative data literature, further confirming the universality of the HRV data. The limitations were that the other age groups were not studied, breathing was free, and not paced and 24-h data of HRV was also not included. This study is important as, to the best of our knowledge, there is no normative data available for South Indian population and many recent studies focus on HRV as one of the important technique for ANS functioning. This will be the baseline HRV data on which further studies may be developed. It is also imporatnt to understand population dynamics for the evaluation and treatment of patients with ANS disorders in South India and to compare normal data against abnormal ones. Future research may include to further investigate other age groups, using 24-h HRV data and conduct other HRV parameters analysis and further strengthen the existing literature of normative data of HRV. In this study we have established the normative data of HRV among young adults and also observed that gender has a significant effect on various HRV parameters, implying role of gonadal hormones on ANS balance.

Authors declaration

All authors of this manuscript have approved the final version of the manuscript. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Clinical trials identifier

NCT02691585, NCT03790462 (full trial protocols can be accessed from clinicaltrials.gov.in).

Funding

The above project was funded by Rajiv Gandhi University of Health Sciences (RGUHS), Government of Karnataka, India (Unique ID: 15M009) and Indian council for Medical research, Government of India, India (ICMR) (2017-0174/F1).

CRediT authorship contribution statement

Kirthana Kunikullaya U: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - original draft, Visualization, Supervision, Funding acquisition. **Radhika Kunnavil:** Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Visualization, Funding acquisition, Writing - review & editing. **Vijayadas:** Methodology, Resources, Visualization. **Jaisri Goturu:** Methodology, Validation, Formal analysis, Data curation, Visualization, Funding acquisition, Writing - review & editing, Supervision. **Vadagenahalli S. Prakash:** Methodology, Validation, Formal analysis, Data curation, Visualization, Funding acquisition, Writing - review & editing, Supervision. **Nandagudi Srinivasa Murthy:** Methodology, Validation, Formal analysis, Data curation, Visualization, Funding acquisition, Writing - review & editing, Supervision.

Declaration of competing interest

Authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ipej.2021.01.002.

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