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Original Research Article

Physical Activity Related Risk Factor Assessment for Altered Drug Pharmacokinetics in Human Population

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ABSTRACT

The study examined the intensity of an individual's physical activity by using self administered International Physical Activity Questionnaire Short Form 7 (IPAQ-SF7) as a measuring tool and assessed its impact on the various body physiological functions likely to alter drug pharmacokinetic processes. The study was conducted in normal, subjects inhabited at different regions in India, with the translated versions of IPAQ-SF7 in Hindi and Tamil languages found the high intensities of vigorous, moderate activities and walking and showed excellent reproducibility as similar as it has been studied in different population worldwide. The resting state systolic and diastolic blood pressures, heart rate and respiratory rate were significantly higher in the subjects. The diaphragmatic breathing pattern was found used by majority of the subjects. The energy utilization of the subjects on their physical activity was obtained in high Metabolic Equivalence of Task (METs) minutes per week. Thus significance in the physiological parameters was strong enough to alter the pharmacokinetics of drugs whose metabolism and elimination are primarily dependent on renal function. This results which will be helpful in optimizing and selecting the drug doses for the people under extreme physical activity with less oxygen consumption in muscles, low level of respiratory rates and high energy utilization in their body.

Introduction

Physical activities (PA) are well known in causing the body physiological functions.Those physiological changes take place during and immediately following the activity or over time as a result of a long-term exercise program. In either way, exercise may affect the way drugs are absorbed, distributed, metabolized, and excreted. Since the physical activity is a multidimensional exposure; it is difficult to find an exact absolute quantitative measure for it. One of the reasons for this is the difficulty in accurately assessing total PA, and its different intensity levels, in day to day life and over extended periods of time [1]. According to existing guidelines, a person who did not meet any of the following three criteria was considered inactive firstly, 3 or more days of vigorous activity during the last week, consisting of at least 20 minutes per day; or secondly, 5 or more days of moderate-intensity activity or walking during the last week, consisting of at least 30 minutes per day; or thirdly, 5 or more days of any combination of walking, moderate or vigorous intensity activities during the last week, achieving a minimum of at least 600 METs minutes per week [2,20,21]. Physical activity may cause increased absorption from an intramuscular or subcutaneous injection site; bioavailability may be increased if drugs injected in to or near to the exercising muscles, resulting in increased appearance of the drug in the systemic circulation [3]. Exercise can affect absorption in two primary ways. Firstly, increased tissue heat during exercise will increase kinetic molecular movement and thus increase diffusion of drug molecules across biological membranes. Secondly, drug

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dispersion away from the drug delivery site can be increased or decreased, depending on whether exercise increases or decreases blood flow to the site of drug administration. Physical exertion causes absorption changes in either way depending on the site of drug administration and blood flow to the site, declined clearance of drugs that undergo extensive hepatic metabolism due to the alteration in blood flow and decreased cardiac output [4]. Absorption of subcutaneously administered drugs may be increased without a concomitant increase in subcutaneous blood flow, suggesting that the exercising tissues may contribute a mechanical or massage-like effect that helps increase drug absorption [5]. The opposite effect may occur if drugs are injected into non-exercising tissues and absorption may be delayed if blood is shunted away from the site of injection and redistributed to more active tissues [6].

The physical exertion such as walking increases the plasma concentration of amoxicillin, an antibiotic as compared to bed rest and sleep [4]. The vigorous physical exertion increases gastrointestinal transit and emptying time these affect oral absorption of orally administered drugs [7]. Physical exertions lower gastric pH and increased membrane permeability and also depend on partition coefficient (pKa) of orally absorbed drugs [9, 10]. Renal clearance decreases for high extraction drugs because physical exertion decreases glomerular filtration rate and renal tubular re absorption. Apart from that it induces increased biliary excretion and clearance of those drugs excreted through biliary route [9]. Exercise induces decreased volume of distribution and elimination especially for low extraction (binding sensitive) drugs because of decreased plasma volume and increased plasma binding consequently of exercise [11]. Drugs most likely affected by physical activity are those that are primarily excreted unchanged in the urine or whose elimination is dependent on liver blood flow or renal function. The drugs that require extra therapeutic monitoring, such as insulin, theophylline and digoxin may be significantly affected by exercise [12]. Therefore, patients taking such drugs should be given under special attention for better therapeutic outcome with reducing possible adverse reactions and avoiding therapy failure. But much of this is still unknown about the interactions that exist between physical exertion and drug therapy.

The International Physical Activity Questionnaire (IPAQ) was developed as an instrument for cross-national assessment of physical activity and for standardizing measures of health related physical activity behaviors of population in many countries and in different socio cultural contexts also have acceptable measurement properties for monitoring population levels of physical activity among 18 to 65 years old adults in diverse settings and has been validated in 12 countries [13]. The IPAQ-SF7 has been recommended for population prevalence studies, where time is limited, because it is easier and more feasible to complete than the long Form. The reliability and validity of the IPAQ-SF7 has been tested in more than 12 countries [12, 14]. The background of the present study is that physical activity is considered as a stressor in human being working at various occupations. Physical activity has the ability to cause many changes in the human physiological functions such as heart rate, respiratory rate, blood pressure, cardiac output, and blood flow to muscles, major metabolizing organ liver and the major excretory organ kidney. Since the process of pharmacokinetics is a physiology dependent, these factors could play a significant role in alteration of body physiological functions and thereby affecting drug pharmacokinetics lead to therapy failure. Based on this hypothesis, the present study aims to measure the intensity of physical activity in people inhabited at two places where the day to day life supporting facilities are significantly different and also find the changes in physiological markers and vital parameters. The resultant values can be correlated and interpreted to the major factors which are studied to alter drug pharmacokinetics without any invasive procedures in study subjects. The international Physical Activity Questionnaire 7 Short Form (IPAQ-SF7) and Long Form (IPAQ-LF7) have been used for many purposes including the studies which were done for checking physical inactivity in Asian population also [15].

The major objective of the present study is to use the translated version of IPAQ-SF7 in two different languages to measure people's physical activity by its frequency (days/week) duration, intensity (minutes/day) or to multiply total time with intensity and energy expenditure achieved by expressing the intensity variable as a METs minutes per week value i.e, 1 METs represents the metabolic rate of an individual at rest and equals approximately 1 kcal/kg/h. An activity with an intensity of 5 METs would require 5 times the resting metabolic rate [16]. The data generated by this study will help in assessing the associated changes in body physiological functions which are prone to alter drug pharmacokinetic processes when they are under extreme physical activity as the part of routine life. The study also aims to check the reliability and reproducibility of both Tamil and Hindi language versions questionnaires in the current population in measuring their physical activity.

Methods

There are no general criteria for the selection of sample size in a questionnaire validation study. Hence, in the present study sample size was calculated on the basis of the general recommendation by Roscoe [16] is that minimum at least 30 and not be larger than 500 because at 500 sample error will not exceed 10 % of the standard deviation about 98 % of the time. Within this range of 30 to 500 it is appropriate that the sample should be 10 % of a parent population [17]. Here, the selected sample size is more than 10 % of the studies which have been conducted on IPAQ-SF7. Over a period of 6 months from October 2013 to March 2014, a total of 256 participants were recruited from different locations of India such as Ooty and Coonoor from Tamil Nadu; Bhupal and Sagar and Kota from Rajasthan and New Delhi so that a sample size of 128

subjects was participated in each language versions of IPAQ-SF7.

The enrollment was in the approach that every people in the society like government employees, workers on daily wages, factory workers, people working at construction site as part time and full time, students, teaching staff of professional colleges, housekeeping staff, salesmen, small scale business running people, corporate employees, security persons etc. A total of 256 subjects were participated in the study from four different regions of India of which the both Hindi and Tamil versions of IPAQ-SF7 self Administered is used. In this study, the IPAQ was administered in face to face interviews. It takes approximately 8 to10 minutes to complete each IPAQ. Inclusion criteria for the participation of subjects were Men and Women of age 20 to 60 years, Body Mass Index (BMI) in normal range and Waist Hip Ratio (WHR) in normal range. Exclusion criteria was according to existing guidelines, a person who did not meet any of the following three criteria was considered inactive or low active:

- 3 or more days of vigorous activity during the last week, consisting of at least 20 minutes per day; or
- 5 or more days of moderate-intensity activity or walking during the last week, consisting of at least 30 minutes per day; or
- 5 or more days of any combination of walking, moderate-, or vigorous-intensity activities during the last week, achieving a minimum of at least 600 METs minutes per week.

Also participants have any kind of diseases or under treatment for various illness conditions, hypertension, diabetes, risks for cardiovascular and metabolic disorders and who are practicing Yoga or meditation as their routine. The persons have physical disability were excluded before starting the study. Similarly, incomplete questionnaires were also excluded after the completion of data collection. All the participants were given a written Informed Consent Form (ICF) contains about the aim and objective, purpose of the study, relevance to the society, risks, benefits etc. ICF has been translated in Hindi and Tamil before administering in to participants. A copy of signed ICF was given to each participant. Since the IPAQ-SF7 is an open access for research purpose, the proposal designed for the study has presented in the meeting of Institutional Review Board (IRB) and approval was obtained. The questionnaires have been translated, back translated and validated in Tamil, the languages which the majority people speak in locations of Tamil Nadu and Hindi languages which the majority people speak in north zone of India includes Madhya Pradesh, Rajasthan and New Delhi for better understanding and conveying the ideas between populations and researcher. The method of face to face interview was used in questionnaire administration because it enables transparency in conveying the true meaning of each question. Also it encourages the participant to ask doubts and clarifications related to questions and in the other way this method of interview assures more productivity of outcome. For the success filling of questionnaire, daily 3 to 5 participants were asked to gather in a room received the questionnaire with filling instructions and there was no time limit given for the task. We also ensured that, during the time of questionnaire filling, the participants had no communication with each other, in the attempt of avoiding possible undesirable interferences in their responses and ultimately in the final outcome.

The Metabolic Equivalence of Task (METs) minutes per week data was calculated in order to categorize the participants in High, Moderate and Low physical activity. The MET values were derived from work undertaken during the IPAQ Reliability Study undertaken in 2000-2013. Using the Ainsworth [18, 19] shows, an average METs score was derived for each type of activity. All types of walking were included and an average METs value for moderate intensity, vigorous intensity and walking was created.

The METs values to be used for the analysis of IPAQ data:
Walking = 3.3 METs,
Moderate PA = 4.0 METs and
Vigorous PA = 8.0 METs.

The METs calculation was done as follows:

- Walking METs minutes/week = 3.3 X walking minutes X walking days
- Moderate METs minutes/week = 4.0 X moderate-intensity activity minutes X moderate days
- Vigorous METs minutes/week = 8.0 X vigorous-intensity activity minutes X vigorous-intensity days

So that, Total physical activity METs minutes/week = the sum of Walking + Moderate + Vigorous METs minutes per week scores. The collected data analysis was done according to the IPAQ Guidelines scoring protocol revised 2005 [20, 21]. The physical activity duration data collected in hours was converted into minutes; the results reported as a weekly frequency were converted into an average daily time. The guidelines instruct the application of Truncation Rule in to the analyzed data because of it does have the important effect of preventing misclassification among the categories. The analyzed data was subjected to Truncation Rule in such a way that the data containing all Walking, Moderate and Vigorous time variables exceeding 3 hours or 180 minutes are recoded also in the same time. The participants worked for up to 10 minutes were counted as Zero minutes. Similarly, the sums of Walking, Moderate and Vigorous activities > 960 minutes were excluded from the data sheet. The incomplete questionnaires and questionnaires answered ‘do not know’, ‘not sure’ and left blank were excluded. From the finally selected data, the time spent for each activity was converted in minutes per day and minutes per week [22, 23]. The estimates are valuable in relative terms and can be used to rank individuals or groups of subjects within a population from the least, moderate to the most active. The total days spent for Walking, Moderate and Vigorous activities have been calculated to assess the categorical data on the days spent for each activity per last seven days.

The cross validation studies, assessment of test reliability is important in studies where questionnaires are used as a tool of measurement and this interval should not be too brief in order to prevent participants remembering what they previously answered, and should not be too long either, as participants' scores may have actually changed. A period of 1 to 2 weeks is often recommended, however, there may be reasons for Shortening or lengthening this time [23]. The questionnaire's reproducibility was obtained by means of a second application on the 50 persons (>20% of the total participants) of the 256 subjects who have participated in the study from each language zone, same subjects within 14 days interval using the same procedures used in the first application. The objective was to measure whether the same questionnaire answered at the times of second administration have any significant difference from the first time administration or not. A few participants who did not show up at the day for the questionnaire's reply filling were excluded.

Results

Descriptive Characteristics (Table 1) of the each 128 subjects participated in IPAQ Tamil version and Hindi version, 92 were men (71.8%) and 36 were women (28.2%). The mean age for men and women were 35.73 ±10.57 and 37.25±11.2 respectively. Social habits (Table 2) data show higher count in male smokers (n=47) and alcoholics (n=24). The occupational status shows majority were employed in daily wages work areas of which 86 were men and 26 were women, 43 men and 18 women were working in private sectors. The 18 unemployed women were housemaid, 9 men were running their own business and 15 were unemployed.

Table 1: Descriptive characteristics

Particulars	IPAQ Short Form 7 TAMIL		IPAQ Short Form 7 HINDI	
Gender	Men	Women	Men	Women
No. of subjects	92	36	74	54
Mean Age (SD)	35.73±11.87	37.25±11.75	39.12±11.1	43.89±10.02
Resting BP Systolic (SD)	136.16±6.6	130.5±3.9	132.32±9.1	125.5±7.9
Resting BP Diastolic (SD)	84.34±6.4	86.48±3.4	82.12±8.1	82.75±7.5
Heart Rate (SD)	74.48±1.5	73.6±2.8	74.98±3.1	73.41±2.9
Respiratory Rate (SD)	24.42±1.5	22.14±1.8	22.63±2.5	22.41±2.2
Body Temperature (SD)	98.74±1.5	98.55±1.2	98.51±0.5	98.53±0.15

Table 2: Social Habits

Social Habits	IPAQ Short Form 7 TAMIL	IPAQ Short Form 7 HINDI
Smoker	47	43
Alcoholic	24	28

The vital Parameters (Table 1), resting systolic Blood Pressure of men inhabited in hill areas was 136.16 ±6.6 which was comparatively high than in women 130.5±3.9 But the resting diastolic blood pressure was higher in both men and women; 84.34±6.4 and 86.48±3.4 respectively.

Heart Rate at resting state found in both kind of population was normal. Respiratory rate were 24.42 ±1.5 in men and 22.41±2.2 in women subjects participated in IPAQ-SF7 Hindi version. Body Temperature was 98.74 ±1.5 in men and 98.55±1.2 in women in hill areas. Here the standard deviation (SD) calculated shows the possible temperature fluctuations due to the cold climatic conditions and associated oxygen concentrations in hill areas. But body temperature reading were not changed in subjects participated from other non hill areas, even though period of the data collection was done in cold sessions. The breathing pattern (Table 3) of all the participants shows prominent number of subjects who have found using abdominal breathing (diaphragmatic breathing) along with chest. The numbers of subjects found using abdominal breathing in both set of people in both sexes were approximately between 40 to 52 % to chest breathing.

Table 3: Breathing Pattern

Particulars	IPAQ Short Form 7 TAMIL		IPAQ Short Form 7 HINDI	
Gender	Men	Women	Men	Women
Breathing Pattern- Chest	92	36	74	54
Breathing Pattern- Abdomen	41	19	32	22
% Abdominal Breathing	45.21	52.77	43.24	40.74

The categorical analysis (Table 4) was done using the scores in three levels of physical activity (low, moderate and high) as proposed in IPAQ-SF Scoring Protocol. Low activity represented individuals who do not meet the criteria for moderate and vigorous intensity categories and total of <599 METs minutes per week. Moderate activity represented moderate or vigorous intensity activities achieving a minimum of at least 600 METs minutes per week. High activity represented achieving a minimum of a least 3000 METs min per week.

Table 4: Categorical score classification of physical activities according to revised IPAQ guidelines [21]

Category of Physical Activity	Criteria for Selection
Category 1 Low	The subjects who do meet criteria for physical inactivity[2,20,21] and/or do not meet criteria 2 and 3 physical activity category
Category 2 Moderate	The subjects who meet at least one of the below: a) 3 or more days vigorous intensity activity for at least 20 minutes per day or, b) 5 or more days moderate intensity activity and /or walking at least 30 minutes per day or, c) 5 or more days any combination of vigorous, moderate and walking activity achieving at least a total physical activity 600METs minutes per week.
Category 3 High	The subjects meet at least one of the below: a) Vigorous intensity activity 3days per week achieving a total of 1500METs minutes per week or, b) 7 or more days of any combination of vigorous, moderate and walking achieving a total of 3000 METs minutes per week.

Psychometric properties [24] defined as the elements that contribute to the statistical adequacy of the instrument in terms of reliability and validity of IPAQ-SF7 Tamil version (Table 5) shows majority of the participants 47 men and 14 women were under category 2 where the subjects have undergone 3 or more days of vigorous activity of at least 20 minutes per day or 5 or more days of moderate-intensity activity and/or walking of at least 30 minutes per day or 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 METs minutes per week. The least number of participants only 9 men and women in Category 3 where the subjects have showed Vigorous-intensity activity on at least 3 days and accumulating at least 1500 METs minutes per week or 7 or more days of any combination of walking, moderate or vigorous-intensity activities accumulating at least 3000 METs minutes per week. The number of subjects in Category 1 where the subjects have showed no physical activity or any activity is reported which is not enough to meet Categories 2 or 3 were16 men and 5 women.

Table 5: Physical activity measures in the participants of IPAQ 7 Tamil version

Level of Physical Activity	Categories of Physical Activity	Men	Women
		Average Physical Activity (SD)	**Average Physical Activity (SD)**
Vigorous PA	Category 1	133.0 ±20.14	192.0±21.12
	Category 2	489.95±84.97	339.82±69.71
	Category 3	1357.33±74.81	1533.11±97.39
Moderate PA	Category 1	135.05±25.57	152.16±56.17
	Category 2	730.14±89.27	929.14±739.05
	Category 3	1466.66±98.92	1626.66±78.02
Walking	Category 1	152.46±32.46	165.0±27.42
	Category 2	657.30±45.46	650.57±451.17
	Category 3	704.33±51.30	1056.0±67.04
Total PA	Category 1	400.54±44.67	509.16±57.84
	Category 2	1736.53±64.12	1919.54±125.01
	Category 3	3528.33±139.49	4215.77±315.99

The psychometric properties of IPAQ Hindi version (Table 6) show more number of subjects in Category 1 because the participants were the employed in the private corporate sectors where the physical activities are lesser than others. The number of subjects in the category 1 was 43 men and 13 women, followed by 24 men and 11 women were in Category 2 and only 4 men and 2 women were in Category 3 where the extreme physical activity is measured. The average physical activity in the each category of both language versions of IPAQ has been analyzed. Table shows the average physical activity.

measured in each category with standard deviations.

Table 6: Physical activity measures in the participants of IPAQ7 Hindi version

Level of Physical Activity	Categories of Physical Activity	Men	Women
		Average Physical Activity (SD)	**Average Physical Activity (SD)**
Vigorous PA	Category 1	181.39±17.64	121.5±81.01
	Category 2	371.66±81.48	390.54±25.94
	Category 3	2640.0±126.54	240.0±27.21
Moderate PA	Category 1	221.23±18.15	250.66±18.77
	Category 2	830.87±84.52	840.0±82.24
	Category 3	1860.0±93.62	3120.0±148.1
Walking	Category 1	94.54±12.74	126.84±18.22
	Category 2	304.56±289.76	152.1±15.01
	Category 3	643.5±37.73	981.0±38.05
Total PA	Category 1	492.03±21.73	483.34±17.01
	Category 2	1507.06±125.24	1382.64±118.64
	Category 3	4423.5±156.44	4251.0±164.71

The overall physical activity was found much higher in the people who are inhabited in the rural hill areas than the urban population shown in Graph 1. Men were more exposed to the vigorous physical activities than women. Walking activity was more prevalent in women in the rural hill areas whereas moderate physical activity was found predominant in both set of population.

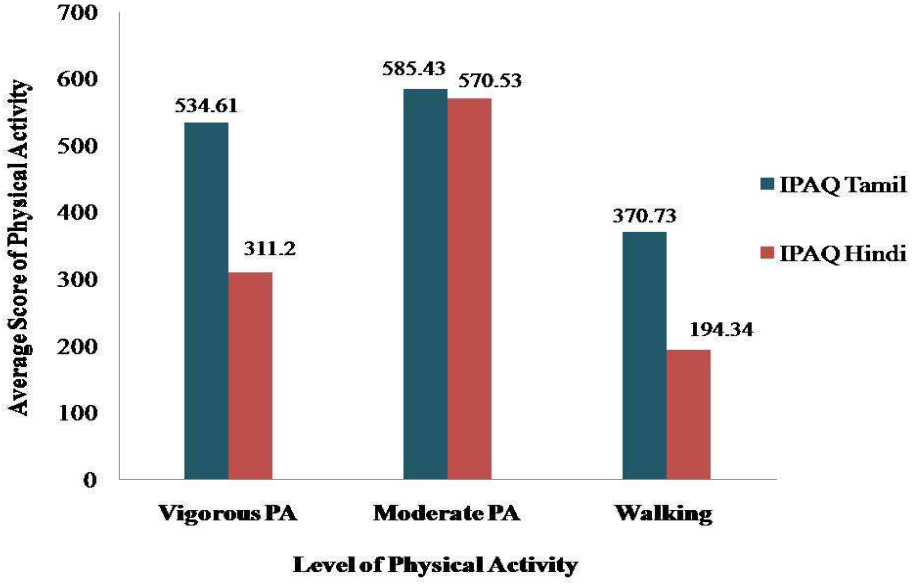

Fig 1: Summary of the intensity of physical activity in both IPAQ-SF7 Tamil and Hindi versions

The Maximum Oxygen uptake (VO_{2max}) is considered to be a valid indicator of the function of respiratory, cardiovascular and muscular systems working together [25]. The maximal oxygen uptake (VO_{2max}) values were obtained from the both set of people (Table 7) according to their age by using the study which has been done based on maximum and resting heart rates in humans.

The Formula is: VO_{2max}= 15X HR_{max} divided by HR_{rest}. This equation uses maximum heart rate (HR_{max}) and resting heart rate (HR_{rest}) to estimate $VO_{2\ max}$ in ml/ (kg/min) are compared with normal $VO_{2\ max}$ values. There are many protocols for estimating $VO_{2\ max}$ have been developed for whom a traditional $VO_{2\ max}$ test (Graded exercise test either using a treadmill or a cycle ergometer) would be too risky [26]. These generally are similar to a $VO_{2\ max}$ test, but do not reach the maximum of the respiratory and cardiovascular systems and are called sub maximal tests.

Table 7: $VO_{2\ max}$ (Maximum Oxygen uptake) data of the subject participated in IPAQ 7 Short Form Tamil version according to the calculation developed by Niels [26]. (The values expressed as the number of subjects found in each category and the mean score of VO_{2max} calculated inside bracket)

Age (years)	Poor		Fair		Good		Excellent		Superior	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
20 – 29	14 (43.44)	7 (38.12)	9 (43.54)	1 (42.87)	0	1 (46.02)	0	0	0	0
30 – 39	21 (38.24)	2 (35.55)	2 (42.11)	5 (39.14)	0	1 (43.44)	0	0	0	0
40 – 49	24 (36.74)	0	4 (39.55)	4 (37.51)	0	1 (40.75)	0	0	0	0
50 – 59	15 (32.21)	0	3 (36.24)	4 (37.44)	0	2 (33.01)	0	0	0	0
60 – 69	0	0	0	0	0	0	0	0	0	0

Table 8: VO_{2max} (Maximum Oxygen uptake) data of the subject participated in IPAQ 7 Short Form Hindi version according to the calculation developed by Niels [26]. (The values expressed as the number of subjects found in each category and the mean score of VO_{2max} calculated inside bracket)

Age (years)	Category of VO2max Values [n (score)]									
	Poor		Fair		Good		Excellent		Superior	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
20 - 29	18	7	3	5	0	0	0	0	0	0
	38.55	41.52	42.5	39.85						
30 - 39	12	14	0	7	0	0	0	0	0	0
	37.8	36.68		38.04						
40 - 49	13	9	10	8	0	0	0	0	0	0
	35.85	32.68	39.07	38.67						
50 - 59	9	0	9	0	0	2	0	1	0	0
	33.59		35.6			33.44		36.55		
60 - 69	0	0	4	0	0	1	0	0	0	0
			33.65			33.41				

VO_2 rest is dependent on and increases with the individual's body mass Niels suggest that, relative to body mass, resting VO_2 equals about 3.5 $ml.min^{-1}.kg.^{-1}$ i.e. one METs [26]. The factors affecting VO_2 are often divided into supply and demand [18]. Supply is the transport of oxygen from the lungs to the mitochondria (including lung diffusion, stroke volume, blood volume and capillary density of the skeletal muscle) while demand is the rate at which the mitochondria can reduce oxygen in the process of oxidative phosphorylation [27]. Of these, the supply factor is often considered to be the limiting one [28] age, sex, training, changes in altitude, and action of the ventilator muscles [29].

In IPAQ analysis, majority of the subjects are under category 2 as compared to category 1 and 3 and 94 men and 32 women were under category 2 whereas 20 women were in category 3

beside to 14 men. Category 1 has only 14 men and 4 women. The mean age of the women in all three categories were high (category1: 42.16±9.2, category2: 39.28±11.65 and category3: 39.75±15.41) when compared to men of either of the categories. Women in category 3 were found in working more time (METs per week) than men. The breathing pattern of the subjects reveals the fact that stress related conditions associated abdominal breathing (diaphragmatic) along with normal chest breathing. Generally, people are primarily chest, or thoracic, breathers. Chest breathers tend to take shallower breathes. Diaphragmatic, or abdominal, breathing involves the abdominal muscles to facilitate deeper breathing. There may be a linear relationship with the matter of abdominal (diaphragmatic) breathing which has observed. The 64 men and 18 women in the study population have used diaphragmatic breathing. The vital parameter such as heart rate (HR), respiratory rate (RR) and blood pressure values at resting state have shown quite significant increase from the normal level in the subjects working at high altitude areas, where the Tamil language version of IPAQ was administered shown in Table 1

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The comparatively higher respiratory rate found in the people of mountain areas (24.42 ±1.5 in men and 22.28±1.04 in women) shows their high to extreme physical activity in regular life than inhabitants of highly developed urban areas 22.63±2.5 in men and 22.41±2.9 in women. Heart rate of the men participants was (74.48±1.5) seemed increased despite of their social habits is believed to have a role. The increased heart rate in women is also shows the less impact of smoking and alcohol habits those play in altering the physiological markers. Cardiac output is the volume of blood pumped by the heart every minute and is a function of heart rate and stroke volume. During exercise, the demand of the tissues for oxygen increases [30] and increase in muscle blood flow (MBF) is anticipated in view of increased muscular workload during exercise [31]. The Heart Rate was found increased about 17-32% but only a 1-17% increase in MBF when heat was applied during exercise [32, 33]. Normal human body temperature is 98.6±0.9 °F with lower temperatures in the morning and the higher temperatures in the late afternoon and evening, as the body's needs and activities change. The observed body temperatures 98.74±1.12 °F in men and 98.55±1.02 °F in women were not altered as the stress associated conditions causes heat conductance through skin. Another physiological or cardiac marker systolic and diastolic blood pressure has increased in both men and women subjects. Though, the age related changes in systolic and diastolic blood pressure is a fact especially, in women their mean age was 40.5±11.2 in this study. The Cronbach's Alpha values of the both language version of questionnaires have been obtained by using SPSS 20 version. The values were 0.84 for Tamil version and 0.85 for Hindi version.

Discussion

Questionnaires represent the most accessible instrument for the usual physical activity evaluation above all in epidemiological nature studies due to the easiness of being applied to large groups low cost for allowing collecting information with relation to the type and context in which they are performed. The present study examined the physical activity of healthy, normally working individuals from various parts of India. The ages of the participants were selected aged 20 to 60 years, similar to the population for whom the IPAQ instrument was designed. The IPAQ especially focuses on investigation of total time of physical activity energy expenditure (METs minutes^{-1}) to evaluate the validity of physical activity questionnaire often include selected samples of volunteers also IPAQ itself [14]. The Tamil language version of IPAQ-SF7 was administered in healthy individuals who are working at various occupational areas such as construction sites, people working in tea cultivating farms etc. The Hindi language version of IPAQ-SF7 was administered in healthy individuals who are working at various private, corporate sectors, government offices, small scale businessmen etc.

Maximal Oxygen uptakes were generally comparable to age specific normal values [34]. It has been known for thousands of years that breathing has a powerful influence over our physiological and psychological well being and diaphragmatic breathing is considered by many to be the simplest and most effective Form of controlled respiration in the reduction of excessive stress. Studies have shown that practicing this style of diaphragmatic breathing reduces muscle tension and anxiety levels within 60 seconds. Abdominal slow breathing stimulates the Parasympathetic (the relaxation) branch of the Autonomic Nervous System. The breathing switches from slow, abdominal, diaphragmatic breathing to mainly chest breathing that is fast and shallow, when people become upset and chest breathing stimulates the Sympathetic mechanism (the fight and flight) branch of the Autonomic Nervous System. Chest breathing causes an upset in the oxygen and carbon dioxide levels in the body resulting in increased heart rate, dizziness, muscle tension and other physical sensations [35]. Chest to abdominal breathing pattern observed in the present study says the subjects have found using abdominal breathing ranges from 40 to 52 % of the basic chest breathing.

Here the role of chest and abdominal breathing in stress conditions reveal the selection of these parameters as an indicator of stress perception in human population. Validity and reliability are two fundamental elements in the evaluation of a measurement instruments used for conventional knowledge, skill or attitude tests, clinical simulations, survey questionnaires, concepts, psychomotor skills or affective values. Validity is concerned with the extent to which an instrument measures what it is intended to measure. Reliability is the fact that an analysis scale should consistently reflect the construct it is measuring. Reliability is concerned with the ability of an instrument to measure consistently [36]. The reliability ranged between vigorous, moderate and walking to

fair for moderate activity. The assessed test-retest reliability of four physical activity measures used in population studies and one of them was the IPAQ-SF7 [37].

Cronbach's Alpha was developed by Lee Cronbach in 1951 to provide a measure of the internal consistency of a test or scale; it is expressed as a number between 0 and 1. The internal consistency describes the extent to which all the items in a test measure the same concept or construct and hence it is connected to the inter relatedness of the items within the test [38]. There are different reports about the acceptable values of alpha, ranging from 0.70 to 0.90 [39-40]. A low value of alpha could be due to a low number of questions, poor inter-relatedness between items or heterogeneous constructs. If alpha is too high it may suggest that some items are redundant as they are testing the same question but in a different guise. A maximum alpha value of 0.90 has been recommended [41]. A high value of alpha (> 0.90) may suggest redundancies and show that the test length should be shortened [42].

The IPAQ-SF7 has been recommended for population prevalence studies, where time is limited, because it is easier and more feasible to complete than the IPAQ-LF7 measures vigorous, moderate and walking activity in the last seven consecutive day period. These activity categories may be treated separately to obtain the specific activity patterns or multiplied by their estimated value in Metabolic Equivalent of Tasks (METs) and summed to gain an overall estimate of physical activity in a week. One METs represents the energy expended while sitting quietly at rest and is equivalent to 3.5 ml/kg/min of $VO_{2\ max}$. The METs intensity values used to score IPAQ questions in this study were vigorous (8 METs), moderate (4 METs) and walking (3.3 METs) [43]. Physical Activity (PA) data from the questionnaire were transformed into energy expenditure estimates as METs using published values [17] to calculate the weekly physical activity (METs hours week), the number of hours dedicated to each activity class was multiplied by the specific METs score for that activity [14].

Conclusion

The strong association between physical activity and its impact on human body physiological functions were well studied in previous studies. The intensity of vigorous, moderate and walking physical activities in the present population were measured in our study. The associated physiological changes were also measured. The vital physiological parameters such as blood pressure, heart rate, respiratory rate had shown significantly increased in both men and women participants. Approximately half of the study subjects have found abdominal breathing along with chest breathing. Maximum Oxygen consumption (VO_{2max}) or Oxygen uptake in men were poor than in women. This could be a marker of oxygen demand to consumption in muscles, high muscle work load, and social habit like smoking, comparatively high intensity of walking to vigorous activity in the hill areas. The significant markers which have been found in the study like poor oxygen consumption by muscles, incidence of high abdominal breathing, increased blood pressure, and heart rate will have the ability to make significant alteration in the processes associated to drug pharmacokinetics inside body such as decreased cardiac output lead to decrease in blood flow to the drug metabolizing organs. These changes are thought to be normal at rest but significantly decrease during exercise so that the resultant reduced blood flow to liver, kidney and thereby affects drug metabolism and excretion [44].

The IPAQ-SF7 Self Administered version was found to be effective in measuring vigorous, moderate and walking physical activities. The measured physical activity was converted to energy expenditure by using Metabolic Equivalence of Task (METs). The IPAQ-SF7 was found easy to convey to participants and easy to complete within 30 minutes. The reliability and reproducibility of both IPAQ Long From and Short Form have studied worldwide and proved in various ethnic populations. The Cronbach's alpha values which have obtained from the translated Tamil and Hindi language versions of IPAQ-SF7 shows its excellent reproducibility in the present population.

Several physiological changes occur as a result of exercise take place during and immediately following the physical activity and other changes occur over time as a result of a long term exercise program. In either case, exercise will affect the way drugs are absorbed, distributed, metabolized, and excreted. Some drugs such as oral anticoagulants, warfarin and digoxin which have narrow therapeutics index, insulin preparations whose bioavailability depends on muscle blood flow, antiviral, antifungal drugs predominantly metabolized by liver as well as excreted by kidney like aspirin, antibiotics etc. should require to be monitored in individuals under their occupational physical activity. Hence, the efforts of this study will be new innovational steps for the researchers towards adjusting the doses of such drugs in presence of the factors causing drug-exercise interactions.

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Conflict of interest statement

We declare that we have no conflict of interest.

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