International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2015): 6.391

Derivation of Reference Equation for 6-Minute Walk Test in Healthy North Indian Young Adult Males and Females Aged 20-40 Years

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Abstract: ***Background: Six-min walk test (6MWT) is a globally recognised assessment tool for functional capacity. It is a clinical tool to determine the prognosis and effectiveness of any therapeutic/medical intervention. However, previous reference equations for the six-minute walk distance (6MWD) have failed to accurately predict the 6MWD due to variations in population. Objective: The aims of this study were 1) to measure 6MWD in healthy North Indian young adult males and females, 2) to compare the established 6MWD with the previous studies, and 3) to develop a regression equation for healthy north Indian males and females. Material and Method: 200 healthy subjects (males=116, females=84) between 20-40 years of age were enrolled after screening. A standardized 6MWT was administered and distance was measured. Results: The mean (±SD) distance of 6MWT was 626.08±64.49 m. The previous published equation did not correctly predict the distance in north Indian population. Gender, height, age, physical activity score (PAS) and socioeconomic status (SES) showed a significant relationship with the 6MWD which Predicted 6MWD: 160.903 - 1.640*Age (years) + 2.540*Height (cm) – 3.708*BMI (kg/m^2) + 29.098*PAS + 6.931*SES + 34.815*Gender*** *(where female = 1; male = 2)* ***which explained around 62.5% of variance of 6MWD, whereas Gender, height and age Predicted 6MWD: 188.633 – 2.902*Age (years) + 3.257* Height (cm) + 26.780*Gender*** *(where female = 1; male = 2)* ***which explained 54.7% of variance of 6MWD. Conclusion: Published equations are not valid for predicting the 6MWD in healthy north Indian young adult males and females.***

Keywords: Aerobic capacity, Prediction equation, cardiopulmonary fitness

1. Introduction

Walking is an activity we perform as an activity of daily living. The ability to walk for certain distance is a quick, easy, inexpensive and better tolerated tool to measure the physical functional capacity. It can also be performed by any elderly and severely limited patient who cannot be tested with other expensive or standard tests like treadmill or cycle ergometer. The distance walked in 6 minutes is reduced in several diseases like obstructive and interstitial lung disease, heart failure, arthritis and neuromuscular diseases [1]. So, assessment of the functional capacity is important to understand the impact of diseases [2].Several studies have been conducted across the world to establish a reference data for 6MWT, and multiple reference equations have been developed to predict the distance walked in 6-minutes for a healthy population. The regression equations published in the literature for the 6MWT exhibit great variability in their results. In fact, a large number of studies have reported differences in the normal predicted 6MWD with the differences in population [2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. Ethnic, geographic and anthropometric variations have been the reported responsible factors for discrepancies in 6MWD [2]. Among the most popular equations are the ones developed by Enright and Sherrill [3] and by Troosters et.al [2]. To the best of our knowledge, there are only two previous studies that have developed reference equations for 6MWT in the Indian population. The study by Vaish H et al, recruited older adults aged 40-60 years. The study by Ramanathan RP et al., was done on subjects aged 25-80 years which is a very wide range across which the physiology of an adult undergoes significant changes. This might pose a threat to its validity in a younger population and warrant further investigation. Therefore, the purpose of this study was i) to determine the normal 6-MWD in healthy, young adults, ii) to compare it with the predictions of previous available equations, iii)to derive new reference equation for the 6-MWD.

2. Material and Method

Participants

A total of 200 healthy subjects between 20-40 years of age participated in the study. All subjects were recruited from National Institute of Tuberculosis and Respiratory Disease, New Delhi from among the patients' attendants, people visiting the Institute and from the nearby community. The study was approved by the research and ethical committees of the National Institute of Tuberculosis and Respiratory Diseases, New Delhi. All participants provided written informed consent prior to the study. Healthy, north Indian, young males and females aged 20-40 years, with body mass index (BMI) range of 18.5–29.9 kg /m^2 and absence of any acute disease in the six-weeks preceding the study were included. Subjects included were asymptomatic with a normal health status described as being asymptomatic with stable vital signs blood pressure (BP) <139/89 mmHg, resting heart rate (HR) <100 beats per/min), normal chest X-ray, normal electrocardiogram (ECG) and normal spirometry values (forced vital capacity (FVC]) > lower limit of normal (LLN) of predicted; forced expiratory volume in 1 sec (FEV1) > LLN of predicted; FEV1/FVC > LLN of percentage predicted [12].

Exclusion criteria were any of the health problem or use of any kind of medication that might interfere with the ability to perform physical activity (such as impaired cognition, metabolic, cardiac, neuromuscular and musculoskeletal disease), use of walking aids, past or current smokers, sensory deficits, pregnancy, history of DM-2, hypertension or any history of heart or lung surgery.

All participants were enrolled after screening at the National Institute of Tuberculosis and Respiratory Diseases. Height was recorded using a height scale (Avery Healthcare, UK), body weight was recorded using a beam balance scale (Equinox, India) and BMI was calculated using the formula kg /m^2. Spirometry was performed using Transfer Test Model (P K Morgan Private Limited, Hertford, UK) to determine FVC, FEV1 and FEV1/FVC according to the American Thoracic Society (ATS) and European Respiratory Society guidelines for spirometery. The results were reported as percentage of predicted values [12]. Subject's pre-systolic and diastolic blood pressure were measured by Digital Sphygmomanometer (Omron, HEM-7113, JAPAN), peripheral blood saturation and heart rate were measured by Pulse - oximeter (NONIN-model 9570, USA), physical activity score were also recorded [13], socioeconomic status was also recorded by using kuppuswame scale [14], then 6MWT was performed by the subjects according to the ATS [15] guidelines and post measurements were taken.

6MWT procedure

The 6MWT was administered according to a standardised protocol, as prescribed by ATS guidelines [15]. The subjects were made to sit in a chair located near the starting position for at least 10 min before the test. During this time, HR and oxy-haemoglobin saturation and systolic and diastolic blood pressures by digital sphygmomanometer were recorded. Subjects were asked to walk as far as possible for 6 minutes in indoor hospital corridor. While walking round on the 30m corridor was demonstrated by primary investigator prior to the subjects walk. Standardised verbal encouragement was provided. Subjects were allowed to stop if they developed symptoms of dyspnoea, dizziness, chest pain, or leg cramps, but were encouraged to continue walking as soon as they could. At the end of test, each subject's HR, BP, SPo2, RPE (Borg value) and the distance covered in 6 minutes was measured.

Statistical Analysis

This study aimed to determine the 6MWD of healthy north Indian young adults and to compare this value with previously reported regression equations [5, 6, 7, 8, 9, 10, 11, 16, 17] and if found a significant difference then to develop a regression equation. To the best of our knowledge, this is the first study to predict 6MWD, particularly among the young adult males and females age 20 - 40 years those living in North India. The 6MWD reference value determined in the study was found to be underestimated by previously reported values of Ramanathan's reference equation[11], by a mean of the actual distance walked by the north Indian subjects was 626.08±64.49 and the predicted distance according to the south Indian Ramanathan's equation was 567.21±31.74 m and difference of 58.87 ± 50.68 m. This discrepancies in the distance walked may be due to geographic [12] and ethnic variations. Similar like the previously reported equations 6MWT was done using a single test protocol, which was strictly adhered to the ATS [15]guidelines. We Statistical analyses were performed using SPSS software, version 21 (Statistical Package for the Social Sciences Inc, Chicago, IL, USA). Following tests performed as follows: Correlations were estimated using Pearson's coefficient of correlation for parametric data. Comparisons between measured and predicted 6MWD also included paired t-test. Stepwise multiple regression analysis was used to develop the reference equation for 6MWD and $p< 0.05$ was considered significant.

3. Results

The baseline characteristics of the study population and results of 6MWT are summarised in Table 1. The mean (±SD) distance of present population 6MWT was 626.08±64.49. 6MWD was 566.2±75.9 (m) [5], 593±57 (m)[6], 409± 51(m)[7], 409.09 ± 83.85 (m)[11] which was underestimating the distance walked by the present population, where was taken $P<0.05$. There was significant correlation between 6MWD and age (Figure 1), height (Figure 2), PAS (Figure 3) and SES (Figure 4). The previous published equation did not correctly predict the distance in north Indian population. Multiple regression analysis showed that Gender, height, age, SES and physical activity were independent predictors for the 6MWD: 160.903 - 1.640*Age (year) + 2.540*Height (cm) – 3.708*BMI (kg/m2) + 29.098*PAS + 6.931*SES + 34.815*Gender (where female = 1; male = 2) explained the 62.5% of variance of 6MWD, whereas Gender, height and age Predicted 6MWD: 188.633 – 2.902*Age (year) + 3.257* Height (cm) + 26.780*Gender (where female = 1; male = 2) explained 54.7 % variance of 6MWD.

Reference equation for healthy individual North Indian (20-40 years)

160.903 - 1.640*Age (year) + 2.540*Height (cm) – 3.708*BMI (kg/m2) + 29.098*PAS + 6.931*SES + 34.815*Gender (where female = 1; male = 2)

4. Discussion

took 200 males and females subjects aged 20–40 years and compared it with the Ramanathan's reference equation who took 125 males and females subjects of age group 25-80 years which was on south Indian population. Pulmonary function test (spirometry) of all the subjects of the present study was normal using European predicted values, as North Indian values were not available. It has been shown by some researches that ethnicity influences physical fitness test performance [18, 19]. Subjects were enrolled by convenience sampling in both the studies.

The possibility of differences in 6MWD due to the level of sub-maximal effort exerted by the subjects is low, as in the present study subjects reached an average of 60±11.33% for Females and 61.67% for males of their maximal percentage of predicted heart rate which was calculated by using the formula: 220 – age (years), while subjects in the other previous studies ranged from 44% - 74 % of their maximal predicted heart rate as in Chetta[6] et. al., Alameri[7]et. al., Osses[9] A. et. al., Soares [20] et. al.,

Other contributing factors may be habitual walking habits, mood of the subject, cognitive status, psychological factors and level of motivation.

In the present study, the correlation between age and 6MWD was negative, which is consistent with previous studies [3, 5, 6, 7, 9, 11, 20]. The shorter distance walked as age increased can be explained by decreases in muscle mass, muscle strength and maximum oxygen consumption due to aging [21-23]. On the contrary, the positive correlation of 6MWD and age of less than 20 years is the result of higher degree of maturation among adolescents when compared with children [24]. In present study height found to be positively correlated with 6MWD and also found to in consistent with the previous studies. Previous reports have attributed the relationship between height and walked distance to increased leg length, which generates a longer stride and a more efficient gait [4, 6, 7, 8, 18]. In present study, weight was found insignificant correlation with 6MWD (for females, r = -.085, p = .442), (for males, r = .105, p = 0.261) was not represented in the final regression equation. The reason might be that present study involved only healthy subjects in the BMI range of 18.5kg/m^2 – 29.9 kg/m^2. It is found in consistent with a study on healthy subjects older than 20 years [3]. As few studies found weight to be a strong predictor of 6MWD in population older than 40 years [2, 3, 10, 25]. Previous studies reported the relationship between weight and 6MWD have been inconsistent as many studies reported either no relation or positive relation of weight with 6 MWD [6, 7, 9, 10, 16].Most of the studies involving adult and elderly participants presented mean BMI values that were representative of overweight. A value of BMI > 30kg/m^2 as the thresh hold value for shorter 6MWD in healthy Caucasians [3]. Few studies used BMI > 35kg/m^2 as exclusion criteria [2, 3, 7] whereas few studies included the BMI up to 39.9 kg/m^2[7, 24]. In present study Physical activity has also attributed the positive correlation between physical activity and 6MWD (r = .427**, p = 0.000). This is found consistent El-Sobkey et. al [26]. Physical inactivity usually leads to altered or decreased muscle metabolism, decreased muscle mass and decreased physical capacity [7].

The results of the present study revealed a significant positive correlation of socioeconomic status with 6MWD (r = .328, p = .000) which is consistent with Saad et. al [27]. They found that the 6MWD was 132 m longer in individuals with higher level of schooling and 129 and 30 m longer in better socioeconomic status. Proposed model equation for the total sample: 6MWD (m) = 12.49*FEV1 - 145.42*gender - 4.58*age - 5.27 *BMI + 2.30*physical activity score + 12.78*SEL (low: 0/high: 1) + 1051.58.

The present study also demonstrated significant positive correlations between 6MWD and FEV1, FVC and FEV1/FVC, but was not represented in the final regression equation. This correlation is likely as all subjects in present study were healthy, non-smokers, and were free of any infection or chronic illnesses. There are several studies which mention that a practice test before the 6MWT was performed for the first time [5, 8, 17, 27]. ATS [15] guidelines do not necessarily recommend a practice test in most clinical settings. So, only single 6MWT was performed in the present study as performance may improve when a second test is performed. Repetition may be important for pre - post evaluations and cardiopulmonary rehabilitation programmes, where it is important to familiarise patients with the test [7]. The findings of one earlier study conducted in India [11] are not in perfect agreement with the results of the present study. It may be because it was conducted in the southern region of India, whereas the present study was conducted in North India. It has been found that the Lung function correlates with functional capacity, and studies on lung function in India have demonstrated differences in lung function on the basis of regional variations [28]. This study was limited by several factors. The 6MWT has clinical utility in several diseases such as obstructive and restrictive lung diseases, which occurs in different age group, and normal values for the north Indian population are not available for this age group. Finally, we did not assess other potential variables that may have limitations such as peripheral muscle strength, cognitive status, lean body mass, leg length, dietary habits and psychological factors. This study was limited by several factors. The participants were not a random sample from the population of young adult males and females. The sample of convenience was taken. Prospective validity of the developed reference equation has not been checked. Subjects included in study were not collected in equal number from all states of north India.

5. Conclusion

This study described the differences in 6MWD as derived from previous predictive equations. Thus, the application of these reference equations to predict the 6MWD in healthy north Indian young adults might not be valid. Our findings showed that not only age, height, gender, weight and BMI are the independent predictors of 6MWD but other factors such as physical activity and socioeconomic status maybe important determinants and examiners must account for their effect.

Acknowledgements

The authors thank the staff of the N.I.R.T.D. New Delhi, India and also to all the participants for their assistance. There is no conflict of interest.

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Table 1: *Correlation of demographic characteristics with 6MWD*

	Females (n=84)			Males (n=116)		
Variables	Mean± SD	R	p-value	Mean± SD	R	p-value
Age (years)	27.42 ± 6.56	-.649	<0.001*	26.38 ± 5.51	-.349	<0.001*
Height (cm)	153.80 ± 6.31	0.46	<0.001*	166.14 ± 6.10	.474	<0.001*
Weight (Kg)	56.62 ± 8.63	_	†	66.19 ± 11.77	_	†
BMI (kg/m^2)	23.93 ± 3.12	-.385	<0.001*	23.65 ± 2.53	_	†
PAS	2.31 ± 7.05	.450	<0.001*	2.35 ± .54	.502	<0.001*
SES	4.64 ± 1.20	.498	<0.001*	6.94 ± 1.16	.392	<0.001*

6MWT: 6-minute walk test; BMI: Body Mass Index; PAS: Physical activity Status; SES: Socio-economic status; SD: standard deviation. *Significant difference at $p < 0.05$.

Table 2: Vitals at rest and following *6MWT*

	Females (n=84)			Males (n=116)		
Characteristics	Mean± SD	R	p-value	Mean± SD	R	p-value
RHR(bpm)	82.21 ± 11.33	_	_	76.92 ± 10.70	.207	.026*
PHR(bpm)	117.01 ± 22.24	_	_	119.28 ± 23.26	.308	.001*
RSBP(mmHg)	118.20 ± 10.23	_	_	129.72 ± 7.71	_	†
PSBP(mmHg)	134.48 ± 15.05	_	_	146.09 ± 13.27	_	†
RDBP(mmHg)	78.26 ± 7.63	_	_	83.06 ± 6.40	_	†
PDBP(mmHg)	85.83 ± 10.86	_	_	91.95 ± 10.06	_	†

6MWT: 6-minute walk test; R: correlation coefficient with respect to 6MWD; RHR: resting heart rate; PHR: post-6MWT heart rate, RSBP: resting systolic blood pressure; RDBP: resting diastolic blood pressure; PSBP: post-6MWTsystolic blood pressure; PDBP: post diastolic blood pressure; SD: standard deviation. *Significant difference at $p < 0.05$.

Figure Legends

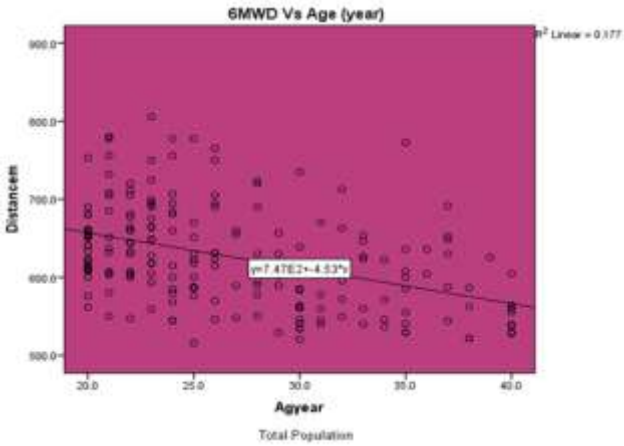

Figure 1: Correlation between 6MWD and age.

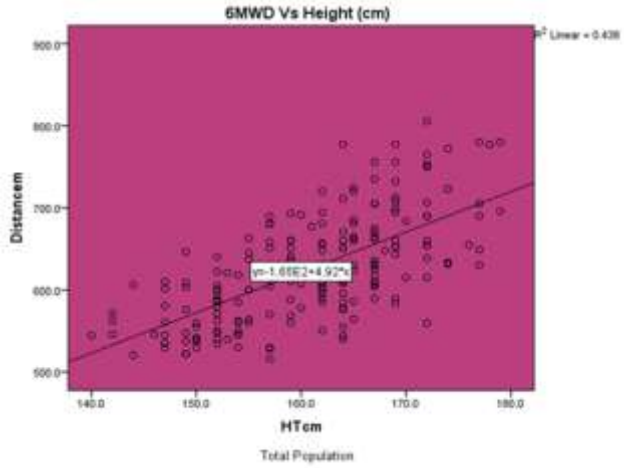

Figure 2: Correlation between 6MWD and height

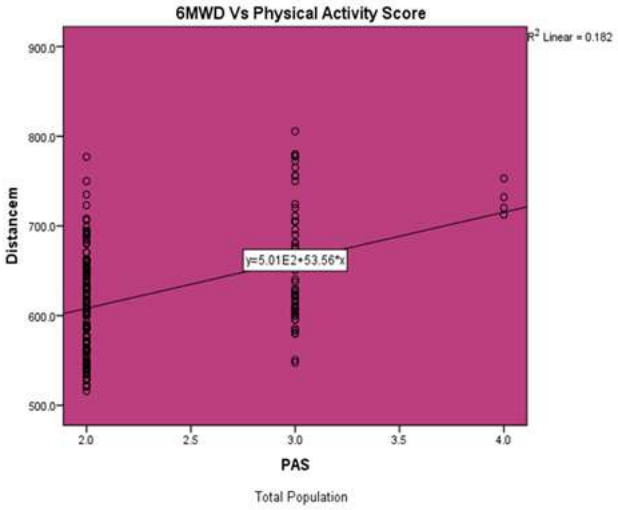

Figure 3: Correlation between 6MWD and PAS

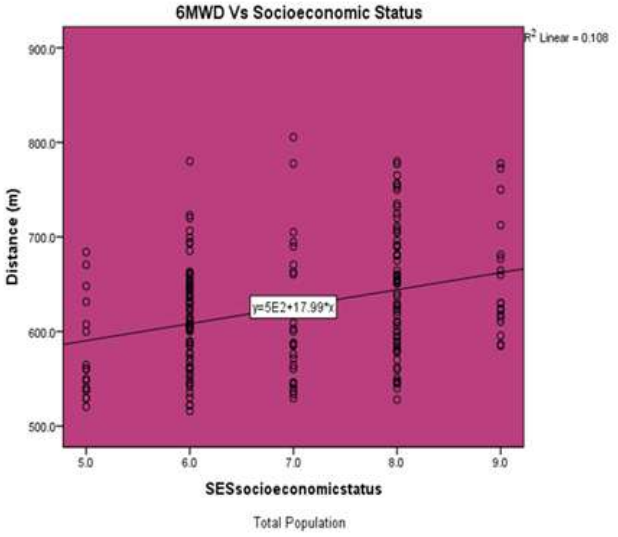

Figure 4: Correlation between 6MWD and SES