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Research article

Reference Values for Six-Minute Walk Test in Apparently Healthy Nigerian Adults

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ABSTRACT

The six-minute walk test (6MWT) is a common utility outcome for evaluating exercise capacity in patients with pulmonary diseases. However, there is no existent reference value for Nigerian older adults. This study is therefore aimed at establishing reference values and equations for 45-70 years old Nigerian adults. We consecutively recruited apparently healthy adults into this cross-sectional survey and used standard protocols for 6MWT and anthropometrics. Regression equations were developed based on demographic and anthropomorphic data. These equations were compared to existing prediction equations. One hundred and four participants completed two 6MWT. The average six-minute walk distance (6MWD) was 378 metres; greater in men than women (p<0.001). The 25th and 75th percentiles were 345.10 and 408.18 metres, respectively. The variables that were significantly associated with 6MWD were sex, age and height. We found two explanatory model equations and the model equation for all participants is 6MWD = 297.96 + 47.41 (sex) – 1.001 (age) + 65.214 (height) where female = 0 and male = 1 with explanatory power of 41.3%. Applying other studies' equations to our population resulted in an underestimation or overestimation of the 6MWD. In conclusion, the average 6MWD in this Nigerian population was 378 metres. Age, height and sex were the most significant predictors of 6MWD and the regression equations explained 41% of the variance in the distance walked. These equations will help to improve evaluation of patients with diseases that affect aerobic capacity.

Keywords: *Six-minute walk test; Six-minute walk distance; Exercise capacity; Reference value; Prediction equation; Nigeria*

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INTRODUCTION

The Six-Minute Walk Test (6MWT) is a simple and objective sub-maximal exercise test, which was initially used to assess aerobic capacity in apparently healthy individuals and patients with chronic obstructive pulmonary disease (Ubuane *et al*., 2018). Due to emergence of various clinical expertise and standardization with specific guidelines, its use has been extended to assessing functional exercise capacity in many other diseases such as musculoskeletal, neuromuscular, metabolic, endocrine and hematologic diseases (Bartels *et al*., 2013). The 6MWT has been shown to be of much importance due to its accurate estimation of maximal oxygen uptake. Its advantages include simplicity, inexpensiveness, and reproducibility (Heresi and Dweik, 2011). As a rehabilitative physical performance assessment tool, the 6MWT has been used to evaluate functional capacity, monitor effectiveness of treatment, and assess progression of functional exercise capacity and to predict prognosis (Casas *et al*., 2005).

Data on the psychometric properties and clinical usefulness of the 6MWT overtime have been generated and have been shown to be a better tolerated test which is more reflective of activities of daily living than other walk test (Pitta *et al*., 2005). Prior to the use of 6MWT, functional capacity was assessed using maximal effort Cardio-Pulmonary Exercise Test (CPET). Balke (1963) developed the 15-minute run test and reported that the test was equivalent to a maximal effort CPET. This was later modified to 12-minute run test (Cooper, 1968) and was eventually changed to 12-minute walk test with an underlying rationale that walking mimic daily activities better than running on a treadmill or cycling on an ergometer; hence distance attained during a walk test would reflect daily functional impairments better than cycling or running (McGavin *et al*., 1976).

The 12-minute walk test thrived as a commonly used field-based functional capacity test until 1982 when Butland *et al*. (1982) proposed 2-minute and 6-minute walk tests in place of 12-minute walk test. These authors eventually came up with 6MWT as a 'sensible compromise' between a rather too long 12-minute walk test and a relatively poorly discriminatory 2-minute walk test with a low ability to detect clinically meaningful change in functional capacity and other parameters (Guyatt *et al*., 1984). The 6MWT has been widely researched to provide evidences of its validity and reliability. A comprehensive guideline standard operating procedure was provided by the American Thoracic Society in 2002. The American Thoracic Society has recommended that there should be an establishment of specific reference values for Six-Minute Walk Distance (6MWD) for each population in various age group (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). Reference values acts as a frame of reference for physicians, other health professionals and are used for clinical interpretation and patient care. Reference values for 6MWD in apparently healthy Americans, Arabians, Asians, Brazilians and North Africans have been generated (Tsang, 2005; Ben Saad *et al*., 2009; Iwama *et al*., 2009; Klepper and Muir, 2011; Bourahli *et al*., 2016). Only two studies have reported reference 6MWD values for Nigerians aged 18 - 67 years. One study documented reference values for young Nigerians aged 18-35 years (Mbada *et al*., 2015) and the other (aged 21 – 67 years) documented a regression equation for predicting 6MWD from age, sex and height (Ajiboye *et al*., 2014). There is therefore, the need to generate reference values of 6MWD for other age groups in Nigeria. The aim of this study was to establish the reference values for 6MWD in apparently healthy Nigerian adults aged 45-70years, determine if sex and anthropometric factors influence its values and compare the equation with previous studies.

MATERIALS AND METHODS

Participants and design: The study was approved by the University of Ibadan/University College Hospital Research Ethics Committee (UI/EC/19/0529). Apparently healthy Nigerians adults aged ≥ 45 years were recruited from the University College Hospital, Ibadan and its neighbouring communities into this cross-sectional survey using the consecutive sampling technique. Prior to data collection, a sample was calculated using linear multiple regression with parameter set at: α=0.05, power=0.95, effect size=0.2, and number of predictors=3(G * Power 3.1 manual, 2020). Minimum sample of 90 was determined to power the study. All participants were ensured free from any form of injury, cardiopulmonary, non-communicable diseases and no one had any previous history of hospitalization prior to the test that may influence their exercise capacity. Prospective participants with physical deformity in the upper limb and or lower limb, individuals with chronic conditions (such as asthma, chronic cough, sickle cell, high blood pressure or being on anti-hypertensive), and those that presented with walking difficulties and obesity were excluded from the study.

This study was carried out between October and December 2019 in the Physiotherapy Department of the University College Hospital, Ibadan. Informed consent was obtained from prospective participants. Participants were also informed of their freedom to refuse to take part in the study and their right to withdraw at any given time. Bio-data such as age and sex were recorded. Standard methods were used to measure blood pressure, heart rate and oxygen saturation at rest and at the end of the six-minute walk test using sphygmomanometer, stopwatch and pulse oximeter, respectively. The BORG rate of perceived exertion scale (RPE) was used immediately after the test to rate how heavy and strenuous the exercise felt. Maximal heart rate (mHR) was estimated using the formula derived for Nigerians (mHR = 207 – 0.62*age in year) (Balogun and Ladipo, 1989). Standard methods were also used to measure weight and height of the participants and the body mass index was estimated. The six-minute walk test was carried out using a 30m straight walk course marked out on a flat surface with a cone placed at both ends of the course and every 3m of it was marked with brightly coloured tape on the floor. The 6MWT was conducted after closing hours (between 4.30 and 6.30 pm) in order to ensure quietness and freedom from human traffic and distraction. The test procedures were explained to each participant before the commencement of the exercise testing. Participants were instructed to stand at the zero mark of the walk course and then walk at his/her own pace, to cover as much ground as possible in a period of six minutes. As soon as the participant were instructed to go, the stop watch was started and stopped when it clocks six minutes. At every minute, the participants were encouraged with the standardized statements such as “You are doing well” or “keep up the good work”. Participants were also informed that they could slow down or rest if necessary. The total walking distance covered during that period were measured and recorded in nearest metres as six-minute walk distance. The test was performed twice in all participants to account for a learning effect. The participants remained at the venue following an uncomplicated first test and were allowed to rest for at least 15-minutes before performing the second walk test on the same day. Since there was no participant that stopped before or during the test, none of the readings were cancelled or paused and no medical attention was given to any participants as regards the safety issues involved in carrying out the test.

Data analysis: Descriptive statistics of mean and standard deviation was used to summarize the variables.

The independent t-test was used to compare the mean values of general characteristics (age, BMI, height, weight and six-minute walk test variables) between the male and female participants. Pearson moment correlation was used to test for the association between six-minute walk distance and dependent variables (age, BMI, height, weight and six-minute walk test variables) while Spearman correlation was used to test for the association between six-minute walk distance and sex. Regression analysis was applied to assess factors that predict six-minute walk distance. Statistical Package for Social Sciences (SPSS) version 23 was used to analyzed the data at $p < 0.05$

RESULTS

A total number of 138 apparently healthy adults consented to participate in this study, but only 104 (55 males, 49 females) completed the study; 34 participants declined to repeat the six-minute walk test. The age of the 104 participants ranged from 45 to 70 years and their mean age was 51.4 ± 6.72 years (Table 1). The result showed that the cardiovascular parameters measured pre and post were within the normal range. The mean six-minute walk distance of all the participants for this study was 378.24±42.67 m. The male participants had significant higher mean 6MWD (405.67±26.76 m) compared to the female participants (353.80±39.30 m) (Table 1). The male and female participants reached 45.7% and 47.0% of their maximum predicted heart rate, respectively, at the end of the test.

Table 1:
Characteristics of the participants

Variable		All sample	Male	Female	t-value	p-value
		Mean±SD	Mean±SD	Mean±SD		
Demography	Sex n (%)	104(100)	49(47.1)	55(52.9)		
	Age (year)	51.43±6.72	50.80±5.40	52.00±7.71	0.912	0.364
	Height(m)	1.68±0.09	1.70±0.10	1.65±0.07	-3.043	0.003
	Weight(kg)	69.84±12.16	69.16±10.70	70.44±13.40	0.531	0.596
	BMI (kgm^{-2})	24.95±4.86	23.94±4.04	25.86±5.36	2.038	0.044
6MWT	Pre-Systolic Blood pressure (mmHg)	123.83±12.29	123.78±12.63	123.87±12.09	0.040	0.968
	Pre-Diastolic Blood pressure (mmHg)	79.73±8.31	79.61±8.68	79.84±8.03	0.137	0.892
	post Systolic Blood pressure (mmHg)	129.70±13.12	128.96±14.29	130.36±12.08	0.543	0.588
	post Diastolic Blood Pressure (mmHg)	83.62±7.77	83.39±8.91	83.82±6.67	0.281	0.779
	pre-Heart rate (bpm)	76.01±6.39	74.84±6.35	77.05±6.29	1.787	0.077
	post Heart rate (bpm)	81.20±5.90	80.14±5.47	82.15±6.16	1.745	0.084
	Change in Heart Rate (bpm)	5.19±2.11	5.31±1.86	5.09±2.32	-0.518	0.606
	Pre SpO2	98.27±0.54	98.24±0.52	98.29±0.57	0.429	0.669
	post SPO2	98.95±0.32	98.96±0.20	98.95±0.41	-0.215	0.830
	Change inSPO2	0.68±0.53	0.71±0.50	0.65±0.55	-0.576	0.566
	Rate of perceived exertion	7.11±.23	7.12±0.24	7.10±0.22	-0.494	0.623
	Predicted maximal heart rate	175.11±4.16	175.51±3.35	174.76±4.78	-0.930	0.355
	%mHR	46.39±3.45	45.70±3.50	47.01±3.31	1.953	0.054
	6MWD (m)	378.24±42.67	405.67±26.76	353.80±39.30	-7.770	0.000

Table 2:
6MWD stratified by age range

Age range (year)	Participants; n (%)	6MWD (m) Mean±SD	95% CI	Percentile			
				25th	50th	75th	95th
45- 49	52 (50.0)	378.31±33.65	368.94 - 387.68	350.50	376.80	406.63	440.25
50 - 59	36 (34.6)	387.18±41.60	373.10 - 401.26	345.10	400.50	418.23	450.00
60 - 70	16 (15.4)	357.88±63.07	324.27 - 391.49	303.75	349.75	407.28	
45-70	104 (100)	378.24±42.67	369.94 - 386.53	345.10	386.65	408.18	447.50

Table 3:
correlation matrixes (r) for 6MWD

Variable	r	p-value
Sex	0.616	0.000*
Age	-0.213	0.030*
Height(m)	0.299	0.002*
Weight(kg)	0.069	0.487
BMI	-0.096	0.330
Pre-Systolic Blood pressure	-0.067	0.499
Pre-Diastolic Blood pressure	0.029	0.772
Post Systolic Blood pressure	-0.028	0.781
Post Diastolic Blood Pressure	-0.026	0.796
Pre-Heart rate	-0.048	0.626
Post Heart rate	-0.051	0.605
Change in Heart Rate	0.003	0.979
Pre SpO2	-0.091	0.360
Post SPO2	-0.068	0.492
Change inSPO2	0.052	0.602
Rate of perceived exertion	-0.006	0.953
Predicted maximal heart rate	0.213	0.030*
%mHR	-0.118	0.233

Table 2 shows the 6MWD for all participants across age groups. Values between the 25th and 75th percentile were considered as the range for reference values. The reference values for all the participants was 345.10 - 408.18 m. Reference values for the different age group are also shown in table 2. Table 3 shows correlation between 6MWD, age, sex, cardiovascular parameters and anthropometric. The 6MWD correlated with the participants' age (r = -0.213, p = 0.03), sex (r = 0.616, p = 0.001), height (r = 0.299, p = <0.002) and predicted maximal heart rate (0.213, p = 0.03).

Table 4:
Regression model for 6MWD**

Parameter		Coefficient	Standard error	p-value
Model 1	Constant	297.960	70.330	0.000
	Sex	47.410	6.830	0.000
	Age (year)	-1.001	.489	0.043
	Height (m)	65.214	39.359	0.101
Model 2	Constant	223.244	66.130	0.001
	Sex*	46.971	6.853	0.000
	Height (m)	69.605	39.439	0.081
	45-49 years	16.783	9.521	0.081
	50-59 years	22.230	10.036	0.029
	60-70 years	0[a]	.	.

**female = 0 and male = 1   [a]This parameter is set to zero because it is redundant.*
**Reference equations of six-minute walking distance (6MWD) are as follows:*
All: 6MWD = 297.96 + 47.41 (sex) – 1.001 (age) + 65.214 (height)
45-46 years: 6MWD = 223.244 + 46.971 (sex) + 69.605 (height) +16.783
50-59 years: 6MWD = 223.244 + 46.971 (sex) + 69.605 (height) +22.23

These four variables were entered into regression model to predict 6MWD. The predicted maximal heart rate was redundant and thus, removed from the model. Table 4 shows the model 1 equation which is for all participants; 6MWD = 297.96 + 47.41 (sex) – 1.001 (age) + 65.214 (height) where female = 0 and male = 1. It has explanatory power of 41.3%. The model 2 equation stratified the participants by age groups. 45-49 years: 6MWD = 223.244 + 46.971 (sex) + 69.605 (height) +16.783 and 50-59 years: 6MWD = 223.244 + 46.971 (sex) + 69.605 (height) +22.23 (where female = 0 and male = 1). The second model has explanatory power of 41.8%.

Comparisons between the measured 6MWD in our participants and predicted 6MWD for the same age ranges using previously established reference equations for Korean(Kim *et al*., 2014), Western Indian(Fernandes *et al*., 2016), Singaporean (Poh *et al*., 2006), Portuguese (Oliveira *et al*., 2019), Brazilian (Britto *et al*., 2013), North African(Ben Saad *et al*., 2009) and Nigerian (Ajiboye *et al*., 2014) populations are shown in Table 5. Walk distance for our cohort was underestimated by five out of seven equations derived from previous populations, including Fernandes *et al*.(Fernandes *et al*., 2016) who underestimated distance walked by our participants by 17.24±27.85m (p<0.001), Poh *et al*.(Poh *et al*., 2006) by 285.84±50.58m (p<0.001), Oliveira *et al*.(Oliveira *et al*., 2019) by 56.02±39.88m (p<0.001) and Britto *et al*.(Britto *et al*., 2013) by 320.58±25.48m (p<0.001). However, walk distance was overestimated by equations derived in African population (Tunisian) by 57.19±82.32 m, p<0.001(Ben Saad *et al*., 2009) and Kim *et al*. (2014) by 8.83±25.94m, p<0.001. The previous equation derived from Nigerian population by Ajiboye *et al*. (2014) also underestimated 6MWD in our sample by 16.78±37.56m.

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Table 5:
Measured 6MWD and predicted 6MWD for the same age range from the equations derived in previous studies

Study	Measured (m)	Predicted (m)	Predicted – measured
Kim *et al*. (2014)	598.5±57.92	607.33±2.54	8.83±25.94*
Fernandes *et al*. (2016)	483.36±67.91	466.12±27.85	-17.24±27.85*
Poh *et al*. (2006)	560±105	470.13±74.22	-89.87±74.22*
Oliveira *et al*. (2019)	627.8±73.3	571.78±39.88	-56.02±39.88*
Britto *et al*. (2013)	586±106	265.42±25.48	-320.58±25.48*
Ben Saad *et al*. (2009)	624±111	681.19±82.32	57.19±82.32*
Ajiboye *et al*. (2014)	517.6±72.2	500.82±37.56	-16.78±37.56*
Present study	378.24±42.67	378.22±27.42	-0.02±27.42

*significant at p<0.001 using student t-test

DISCUSSION

This study established the reference values for 6MWD in apparently healthy Nigerian adults aged 45-70years and presented new equations to predict the distance covered during 6MWT. The equations show that 41% of the variance was explained by age, sex and height. To our knowledge, this is the first study in Nigeria to establish 6MWD reference value and equation among older adult population. Participants in the two previous studies from Nigeria are relatively younger than our participants (Ajiboye *et al*., 2014; Mbada *et al*., 2015).

The mean 6MWD in our sample was 378.24±42.67 m. The distance walked by our participants is shorter compared to previous studies among the Asian (Poh *et al*., 2006; Kim *et al*., 2014; Fernandes *et al*., 2016; Zhang *et al*., 2017; Zou *et al*., 2017b, 2020), north and south American (Britto *et al*., 2013; Halliday *et al*., 2020), European (Oliveira *et al*., 2019) and north African (Ben Saad *et al*., 2009) populations. Generally, these previous studies' participants achieved 53% - 73% of their predicted maximum heart rate compared to our samples who achieved 46% of their predicted maximum heart rate. This difference in exercise capacity may be responsible for lower work distance walked by the participants in our study. Another plausible reason could be that Nigerian adults are generally physically inactive compared with these studies' participants. Studies have suggested that distance walked by physically active is longer than distance walked by physically inactive (Zou *et al*., 2017b, 2017a, 2020). The 6MWD in our sample is also shorter than the two previous study from Nigeria (Ajiboye *et al*., 2014; Mbada *et al*., 2015). The participant in our study is relatively older than the previous studies and this could account for the difference. It has been reported that 6MWD decreases with increase in age(Poh *et al*., 2006; Britto *et al*., 2013; Fernandes *et al*., 2016; Zou *et al*., 2017b, 2020; Oliveira *et al*., 2019).

The 6MWD in male participants was significantly longer than that of female participants. This finding was corroborated by previous studies (Ben Saad *et al*., 2009; Ajiboye *et al*., 2014; Kim *et al*., 2014; Mbada *et al*., 2015; Fernandes *et al*., 2016; Zou *et al*., 2017b, 2020; Oliveira *et al*., 2019; Halliday *et al*., 2020). Our data suggest that males are significantly taller than females, a taller height is associated with a longer stride, which generates longer distance (Oliveira *et al*., 2019). It has been reported that men have greater muscle mass than women and this might be another reason for men greater 6MWD (Kim *et al*., 2014; Zou *et al*., 2017b, 2020).

In the univariate analysis of our data, sex, age, height and predicted maximum heart rate were significant correlated with 6MWD. Consistent with previous studies, age was negatively correlated with 6MWD suggesting that 6MWD decreases with increase in age(Poh *et al*., 2006; Britto *et al*., 2013; Ajiboye *et al*., 2014; Fernandes *et al*., 2016; Zou *et al*., 2017b, 2020; Oliveira *et al*., 2019). It has been observed that muscle mass, muscle strength and maximal oxygen uptake gradually decreased with age(Zhang *et al*., 2017; Zou *et al*., 2017b, 2020) and probably responsible for the observation. Height was positively correlated with 6MWD and was the major predicting factors in our model equation, corroborated previous study from Nigeria (Ajiboye *et al*., 2014).

Demographic factors of age and sex, and anthropometric factor of height predicted the 6MWD in our sample and it's accounted for 41.3% of variance. Several demographic and anthropometric factors have been shown to influence the 6MWT performance in healthy participants, showing 19.6−78% of the variance in the 6MWD(Poh *et al*., 2006; Britto *et al*., 2013; Ajiboye *et al*., 2014; Kim *et al*., 2014; Fernandes *et al*., 2016; Zou *et al*., 2017b, 2020; Oliveira *et al*., 2019; Halliday *et al*., 2020). Age, height, weight, BMI and sex were the most common variables used to predict 6MWD among these studies. Predicting 6MWD with age, sex and height or BMI accounted for 30% - 46% variance in the 6MWD similar to our finding (Britto *et al*., 2013; Ajiboye *et al*., 2014; Oliveira *et al*., 2019; Zou *et al*., 2020). Height was the predominant predictor of 6MWD in our sample which was similar to a previous study which found only height as predicting factors of 6MWD (Kim *et al*., 2014). A taller height is associated with a longer stride, which generates a longer distance (Poh *et al*., 2006; Kim *et al*., 2014; Oliveira *et al*., 2019).

In the present study, we derived two equations using sex, height and age or age group. Both equations accounted for 41% of variance of 6MWD. The use of predictive equations for 6MWD created for populations other than the one studied, was associated with underestimation or overestimation of the predicted distances in consonant with previous study(Britto *et al*., 2013; Ajiboye *et al*., 2014; Kim *et al*., 2014; Fernandes *et al*., 2016; Oliveira *et al*., 2019; Zou *et al*., 2020). The previous predicted equations underestimated 6MWD in our sample (Poh *et al*., 2006; Britto *et al*., 2013; Fernandes *et al*., 2016; Oliveira *et al*., 2019). The difference may be attributed to anthropometric variation and differences in methodology employed in various studies. This is corroborated by our data, the participants of a study with minimum underestimation of 6MWD (17metres) are shorter than our sample (Fernandes *et al*., 2016). However, a study which used the same methodology as ours and with similar height underestimated 6MWD in our sample by 56 meters (Oliveira *et al*., 2019). Even, the only study from North Africa overestimated our sample's 6MWD (Ben Saad *et al*., 2009). This is call for caution using foreign 6MWD reference value for interpretation of Nigerian adults' population. Using previous equations, our data suggest that walked distance can vary as up to 320 metres. This is of great clinical importance if we consider the minimally significant difference already established in several adult populations, such as 25 metres for coronary artery disease (Gremeaux *et al*., 2011), 30 metres for chronic pulmonary obstructive disease (Polkey *et al*., 2013) and 32 metres for heart failure(Shoemaker *et al*., 2013). These differences also highlight the importance of developing reference values or equations for the 6MWD for specific populations. In view of differences between measured and predicted 6MWD using previous equation from Nigeria population, it is also important to establish reference value for specific age range. The previous equation from Nigeria population underestimated our sample 6MWD because our sample are relatively older (Ajiboye *et al*., 2014). The mean age of our sample is 51 years while previous study was 36 years, as distance walked decreases with age (Zou *et al*., 2017b, 2020).

In interpreting the results of our study, some limitations have to be borne in mind. Most of the participants in this study were drawn from members of staff of one tertiary health institution and thus, may not be representative of whole Nigerian adult population. In addition, participants were volunteers and were not randomly selected. However, in the absence of national reference for 6MWD for aged 45-70 years, the reference values and equations derived may be found useful in Nigeria clinical setting.

In conclusion, we have established reference values and equations for 6MWD for 45-70 years old Nigerian population. The average 6MWD in this Nigerian population was 378 metres. Age, height and sex were the most significant predictors of 6MWD and the regression equations explained 41% of the variance in the distance walked. These equations will help to improve evaluation of patients with diseases that affect exercise capacity.

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