Reference Interval for Body Mass Index, And Vital Signs for Infants, Children, Adolescents, Adults and Geriatric Population of Taita-Taveta County, Kenya

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***Abstract*:-Vital signs including temperature, pulse and respiratory rate, blood pressure, peripheral oxygen saturation, pain, level of consciousness and urine output are used to assess changes in a patient's condition, and early signs of clinical deterioration so that treatment can be initiated to correct the associated disease. They are affected by factors such as age, sex, dietary habits, lifestyle, geographical location, socioeconomic status, health status, medications, ethnicity, genetics, and environment. The aim of this study was to establish 95% reference intervals for three vital signs for Taita-Taveta County Kenyan population. This cross-sectional study was conducted in the Department of Clinical Chemistry, Moi Subcounty Hospital, Taita-Taveta County, Voi, Kenya between May 2015 and December 2017 and involved 191 males and 317 females for vital signs study, and 125 males and 127 females for BMI study. The age of the referents population was 1-95 years. Vital signs were measured using automatic Mindray monitor and BMI was measured by weighing (kg) each referent individual and taking their height (in metres). Reference intervals were developed using EP28A3c guidelines. Mann-Whitney U test was used to develop reference intervals between males and females, and ANOVA and post-ANOVA test was used to compare the effect of age. Data was analyzed using SPSS software version 20. The developed reference intervals for BMI and the vital signs for Taita-Taveta County Kenyan population were different from those reported in medical literature; thus supporting the need for every clinical chemistry laboratory to develop their own reference intervals using their own population.**

***Key Words*: - Body mass index, Vital signs, Infants and children, Adolescent, Adults, Geriatrics**

I. INTRODUCTION

Vital signs are measurements that reflect the body's basic functions and are part of routine patient assessment. Vital signs are surveillance physiological parameters that are used in the early diagnosis of critically ill patients, early detection of a clinically deteriorating patients, and monitoring changes in the critically ill patient's condition mostly by nurses, and physicians. They include not only the five major vital signs including temperature, pulse rate (heart rate), blood pressure (systolic and diastolic blood pressure), respiration rate (rate of breathing), and oxygen saturation, but also the other three newer vital signs including pain, level of consciousness, and urine output [3]. However, proper interpretation of vital signs requires the use of reliable and accurate reference intervals obtained from referent individuals.

Reference intervals are defined as a set of values for a particular variable that is measured in which 95% of healthy population are included. It is used to compare the observed value of a variable to a reference variable value obtained from a defined population of individuals. The comparison is then used to give meaning to the observed variable value and arriving at the correct condition of the tested individual. Reference interval is the central variable value bounded by a lower and an upper limit defined by a specific designated percentile, for example 95 %. It therefore involves collecting data from healthy individuals fulfilling specific inclusion and exclusion criteria. The minimum number of individuals required to determine a reference interval for a particular variable is 120.

Reference intervals for vital signs developed and used in a particular population are used as observational evidence for generating trigger thresholds and informing physicians on normal and abnormal vital signs values in patients. Reference intervals may also be used for early detection of a deteriorating patient condition and therefore provides a basis for early initiation of treatment and hence the correction of the associated disease condition. In most published literature (medical journal articles and/or medical textbooks), there are few relevant reference intervals of all the eight vital signs for particular populations of different parts of the world. Many African countries including Kenya, lack reference intervals for vital signs that are specific to their population and use reference intervals for vital signs derived from the western population in clinical management of patients which are inappropriate for the local population. In addition, because vital signs are affected by factors such as gender, age, race, environmental factors, exercise tolerance and the overall health of the individual, the International Federation of Clinical Chemists recommends that every clinical laboratory establishes its own reference intervals for vital signs using the local population and not to depend on the published reference intervals for vital signs which are inappropriate. This therefore necessitates the need for the development of Kenyan reference intervals for the four vital signs including body mass index specific to the Taita-Taveta County population for use in the proper management of the critically ill patients.

The aim of this study was therefore to develop gender and age specific reference intervals for body mass index and four major vital signs for the Taita-Taveta County Kenyan population. In addition, the developed reference intervals for body mass index and vital signs were compared with the previously developed and reported medical literature (in text books, refereed research articles and in manufacturers inserts reagents kits) from other parts of the world.

II. MATERIALS AND METHODS

Study site

This study was carried out at the Department of Clinical Chemistry, Moi Subcounty Hospital, Taita-Taveta County, Voi, Kenya, between May 2015 and December 2017.

Study design

This was a cross-sectional prospective study design involving 508 referents for the vital signs study and 252 referents for the body mass index study.

Study population

The study referent population was recruited from four subcounties of Taita Taveta County, which included Mwatate, Taveta, Wundanyi and Voi. The referent subjects recruited and used for the development of the reference interval limits of the five vital signs (systolic and diastolic blood pressure (mmHg), oxygen saturation (SpO_2; %), pulse rate/heart rate (beats per minute), and temperature (^oC)) were 508 while those recruited and used for the development of reference interval limits for body mass index (BMI; kg/m^2) were 252. The referent population involved in vital signs study comprised 191 males (36.9%) and 317 females (63.1%) while those involved in the BMI study comprised 125 males (49.6%) and 127 females (50.4%).

Inclusion criteria

The study population was recruited from Kenyan citizens living in Taita-Taveta County, Kenya of age 1-95 years who were categorized into five groups and were all subjected to age and special requirement as required by the parameters under study. Included in the study were referent adult and geriatric referent individuals who consented to participate by signing the consent form. Also included in the study were infants, children and adolescents whose parents and guardians consented their participation by signing the consent form. A questionnaire was administered to consenting study subjects to gather some socio-demographic data.

Exclusion criteria

Subjects whose blood specimens tested positive results for VDRL, HIV, and HBs-Ag were excluded from the study. Those who did not consent to participate in the study or those whose guardians, and/or parents refused to give consent were excluded from participating in the study. Also excluded from the study were those who were on medication or those involved in excessive exercises.

Ethical approval

This study was approved by Kenyatta University Ethical Committee Ref Number I84/31987/15/ NACOSTI Ref number 16/22096/14531, Taita-Taveta county Medical director.

Measurement of vital signs using Mindray automatic vital monitor

Using a Mindray automatic vital monitor, vital signs were taken using three tubes. For blood pressure measurement, the referent subjects were allowed to sit comfortably with a bare arm at heart level. The brachial artery was palpated just above antecubital fossa and BP cuff was wrapped around the upper arm about 2.5 cm above the brachial artery; the results were given as diastolic and systolic blood pressure. Pulse oximeter sensor was attached to a referent subject's finger for measuring the light absorption of hemoglobin that gave arterial oxygen saturation ($S\rho O_2$), the second tube was clipped on the index finger while the temperature metallic attached to the tube was placed at the axillary (armpit). The machine was then switched on. Upon determining the readings, the results were displayed on the LCD monitor; the displayed results were oxygen concentration in the tissues ($S\rho O_2$), temperatures in degree centigrade (^oC), pulse rate (beats per minute) and systolic and diastolic blood pressure (mmHg). All the results were recorded in the laboratory notebook in addition to age and gender. Quality control by Mindray monitor is ensured by adhering to the set manual procedure and inbuilt quality control that is maintained by servicing it every two years as stated by the manufacture.

Body mass index

Body weight was measured to ± 0.1 kg using electronic scales; standing height was measured to ± 0.001 m using a wall mounted stadiometer and BMI was calculated as weight/height^2 (kg/m^2). Based on WHO criteria, underweight was identified as BMI < 18.5 kg/m^2, overweight as BMI of 25.0-29.9 kg/m^2, and obese as BMI ≥ 30.0 kg/m^2.

Data management and statistical analysis

Data was recorded in the laboratory notebook, entered into Excel Spreadsheet and cleaned for errors. This was then exported to SPSS software version 20 for statistical analysis. The data was subjected to test for normality including measures of Skewness and Kurtosis, Mean, Median, Mode, Shapiro-Wilk test, Kolmogorov-Smirnov (K-S) test, histograms, Box plots, Normal Q-Q plots, and detrended normal Q-Q plots. Results were presented in tabular form. For development of reference interval limits based on gender of the referent individuals of the study population, non-parametric statistics including Mann-Whitney U test was used; here data was expressed as median and range. For the development of reference interval limits based on age and gender, parametric statistics including one way ANOVA and post ANOVA was used; here data was expressed as mean ± standard deviation. $\rho < 0.05$ was considered statistically significant.

III. RESULTS

Established reference interval limits for BMI and selected vital signs for male and female infants, children, adults, and the geriatric population of Taita-Taveta County, Kenya

The established reference interval limits for BMI and selected vital signs for male and female infants, children, adults, and the geriatric population of Taita-Taveta County, Kenya are presented in Table 1. Results indicate that, the established reference intervals for body mass index, and the selected vital signs for male infants, children, adolescents, adults, and the geriatric population of Taita-Taveta County, Kenya for peripheral oxygen saturation (SpO_2) and temperature (Temp) were similar to those of the female infants, children, adolescents, adults, and geriatric population of Taita-Taveta County, Kenya ($\rho > 0.05$). Therefore combined reference interval limits for peripheral oxygen saturation (SpO_2) and temperature (Temp) were established for this population. The established combined reference interval limits for SpO_2 is 99 (86.8-100) % and Temp is 34 (32-35.9) ^oC.

Further, the established reference interval limits for BMI, Systolic and Diastolic, and Pulse rate for the male infants, children, adolescents, adults, and the geriatric population of Taita-Taveta County, Kenya significantly differed from that of the female infants, children, adolescents, adults, and the geriatric population of the same County ($\rho < 0.05$). The established reference interval limits for infants, children, adolescents, adults, and the geriatric population of Taita-Taveta County, Kenya for BMI is 19.7 (14.48-31.84) kg/m^2 for males and 22.0 (14.14-31.84) kg/m^2 for females; systolic is 119 (88-157) mmHg for males and 133 (84-178.2) mmHg for females; diastolic is 68 (46-100.8) mmHg for males and 74 (49-108) mmHg for females and pulse rate is 84 (62-117.6) for males and 87 (60-129) for females [Table 1]

Table 1 Established reference interval limits for BMI and selected vital signs for male and female infants, children, adults, and the geriatric population of Taita-Taveta County, Kenya

Vital Sign (unit)	Sex	N	Median	Percentile		Reference Interval	IV	Difference between M&F	
				2.5th	97.5th			z-value	Sig
BMI (kg/m^2)	M&F	252	20.3	14.3	38.0	14.3-38	23.7	3.411	**ρ = 0.0006**
	F	**127**	**22.0**	**14.1**	**39.9**	**14.1-39.9**	**25.8**		
	M	**125**	**19.7**	**14.5**	**31.8**	**14.5-31.8**	**17.3**		
Systolic BP (mmHg)	M&F	508	116	84.7	174	84.7-174	89.3	3.135	**ρ = 0.0017**
	F	**317**	**119**	**84**	**178.2**	**84-178.2**	**94.2**		
	M	**191**	**113**	**88**	**157**	**88-157**	**69**		
Diastolic BP (mmHg)	M&F	508	71	49	107	49-107	58	3.246	**ρ = 0.0012**
	F	**317**	**74**	**49**	**108**	**49-108**	**59**		
	M	**191**	**68**	**46**	**100.8**	**46-100.8**	**54.8**		
Pulse rate (beats per minute)	M&F	508	86	60.7	125	61-125	64	2.575	**ρ = 0.01**
	F	**317**	**87**	**60**	**129**	**60-129**	**69**		
	M	**191**	**84**	**62**	**117.6**	**62-117.6**	**55.6**		
Oxygen saturation ($S\rho O_2$) (%)	**M&F**	**508**	**99**	**86.8**	**100**	**86.8-100**	**13.2**	1.031	ρ = 0.3027
	F	317	99	92.9	100	92.9-100	7.1		
	M	191	99	73.9	100	73.9-100	26.1		
Temperature (0^oC)	**M&F**	**508**	**34**	**32**	**35.9**	**32-35.9**	**3.9**	1.557	ρ = 0.1195
	F	317	33.9	31.6	35.7	31.6-35.7	4.1		
	M	191	34.1	32	36.14	32-36.1	4.1		

Results are expressed as Median and range for the number of referent participants in the column labeled N. Statistical comparisons of the median values between male and female referent participants were carried out using Mann-Whitney U test. Differences were considered statistically significant at $\rho < 0.05$.

Effects of age on the developed reference interval limits for BMI and the selected vital signs for male and female population of Taita-Taveta County, Kenya

The effects of age on the developed reference interval limits for BMI and the selected vital signs for infants and children, adolescents, adult, and geriatric male and female population of Taita-Taveta County, Kenya are presented in Table 2. The different age groups were categorized as follows: (a) age category 1 (1-12 years), (b) age category 2 (13-17 years), (c) age category 3 (18-55 years), and (d) age category 4 (56-95 years). The reference interval limits for BMI and the selected vital signs differences across age categories were compared for both males and females using ANOVA and post ANOVA test where ρ-values less than 0.05 was considered statistically significant [Table 2].

Results indicate that infants and children, and adolescents had similar reference interval limits for BMI after which the BMI reference interval limits significantly increased in adults, and then significantly decreased in geriatrics. Further, results indicate that reference interval limits for systolic blood pressure for infants and children were significantly lower than those of adolescents which were significantly lower than those of adults which were significantly lower than those of geriatrics. In addition, results indicate that reference interval limits for diastolic blood pressure for infants and children were significantly lower than those of adolescents which were significantly lower than those of adults, which were similar to those of geriatrics. The pulse rate reference interval limits for infants and children were significantly lower than those of adolescents which were significantly lower than those of adults which were similar to those of geriatrics.

The reference interval limits for temperature and peripheral oxygen saturation were statistically similar for infants and children, adolescents, adults and geriatrics. In summary, there was a statistically significant increase in BMI, systolic and diastolic blood pressure, and pulse rate with advancement of age. Temperature and peripheral oxygen saturation was not significantly altered with advancement of age [Table 2].

Table 2 Effects of age on the developed reference interval limits for BMI and the selected vital signs for male and female population of Taita-Taveta County, Kenya

Parameter (units)	Sex	Changes on the value of body mass index and the measured vital signs with age (years)							
		N	1-12 years	N	13-17 years	N	18-55 years	N	56-95 years
BMI (kg/m^2)	M	55	18.00±4.31	54	19.00±2.41	10	**23.50±5.30^{ab}**	31	**22.00±5.43^{abc}**
	F	55	18.00±3.17	18	20.00±2.01	26	**29.00±6.48^{ab}**	29	**27.00±5.55^{abc}**
Systolic BP (mmHg)	M	59	102.27±10.01	64	**109.88±12.26^{a}**	43	**126.40±18.82^{ab}**	25	**138.0±15.11^{abc}**
	F	92	100.82±13.28	53	**112.38±11.31^{a}**	116	**132.68±22.48^{ab}**	56	**142.64±23.71^{abc}**
Diastolic BP (mmHg)	M	59	61.68±13.28	64	**67.13±9.89^{a}**	43	**77.58±17.30^{ab}**	25	**81.20±12.23^{ab}**
	F	92	61.72±8.80	53	**68.51±10.14^{a}**	116	**80.89±13.34^{ab}**	56	**86.18±22.13^{ab}**
Temperature (^{0}C)	M	59	33.96±0.86	64	34.93±5.07	43	33.89±0.97	25	33.88±0.70
	F	92	33.72±1.22	53	34.25±0.80	116	34.30±6.78	56	34.28±2.78
Pulse rate (beats per minute)	M	59	79.31±10.69	64	**83.45±10.34^{a}**	43	**88.70±14.00^{ab}**	25	**93.32±18.23^{ab}**
	F	92	77.11±11.59	53	**83.08±10.44^{a}**	116	**96.14±15.98^{ab}**	56	**98.71±19.40^{ab}**
Oxygen saturation ($S\rho O_2$) (%)	M	59	98.19±4.47	64	**98.18±4.74^{a}**	43	**95.44±8.41^{ab}**	25	**98.40±1.05^{ab}**
	F	92	98.60±1.82	53	97.94±4.30	116	98.25±2.00	56	96.76±9.00

Results are expressed as Mean ± Standard deviation of the number of subjects indicated in the column labeled N. $^{*}\rho < 0.05$ when male reference interval limits are compared to female reference interval limits per each age category; $^{a}\rho < 0.05$ when reference interval limits in age range 1-12 years is significantly different when compared to reference interval limits in age range 13-17 years; $^{b}\rho < 0.05$ when reference interval limits in age range 1-12 years is significantly different when compared to reference interval limits in age range 18-55 years; $^{c}\rho < 0.05$ when reference interval limits in age range 1-12 years is significantly different when compared to reference interval limits in age range 56-90 years; $^{d}\rho < 0.05$ when reference interval limits in age range 13-17 years is compared to reference interval limits in age range 18-55 years; $^{e}\rho < 0.05$ when reference interval limits in age range 13-17 years is significantly different when compared to reference interval limits in age range 56-95 years; $^{f}\rho < 0.05$ when reference interval limits in age range 18-55 years is significantly different when compared to reference interval limits in age range 56-95 year.

Effects of the hand arm side on the reference interval limits for vital signs for male and female population of Taita Taveta County, Kenya

The effects of the hand arm side on the reference interval limits for vital signs for male and female population of Taita Taveta County, Kenya are presented in Table 3. The established reference interval limits for the selected vital signs for the left hand and right hand arm side diastolic blood pressure and pulse rate for male population of Taita-Taveta County, Kenya were similar to the right hand arm side of the female population of the same county ($\rho > 0.05$). Therefore combined reference interval limits of these parameters for this population were established. The established reference interval limits for the combined left hand arm side diastolic blood pressure (46.8-97.4 mmHg) for male and female population of Taita-Taveta County, Kenya were similar to the combined right hand arm side diastolic blood pressure (45.4-100.7 mmHg) and the combined left hand arm side pulse rate of 58-111.2 mmHg was similar to the combined right hand arm side pulse rate of 58.0-113.8 mmHg. The established reference interval limits for the left hand arm side systolic blood pressure for male population of Taita-Taveta County, Kenya was significantly lower compared to the male population right hand arm side systolic blood pressure of the same County ($\rho < 0.05$). The established reference interval for the left hand arm side systolic blood pressure for the male population (92.2-149.8 mmHg) of Taita-Taveta County, Kenya was significantly higher than that of the female population (85.6-144.4 mmHg) of the same County; the right hand arm side systolic blood pressure of the male population (91-165 mmHg) of Taita-Taveta county, Kenya was significantly higher than that of the female population (90.8-145.2 mmHg) of the same County. The left hand arm side systolic blood pressure for the male population (92.2-149.8 mmHg) of Taita-Taveta County, Kenya was significantly lower than the male right hand arm side systolic blood pressure (91-165 mmHg) [Table].

Table 3 Effects of the hand arm side on the reference interval limits for vital signs for male and female population of Taita Taveta County, Kenya

Vital Sign (unit)	Sex	N	Mean±SD	Percentiles (2.5% and 97.5%)		Reference Interval (RI)	IV	Difference between M&F	
				X-1.96SD	X+1.96SD			t-value	Sig
Left systolic BP (mmHg)	M&F	65	119.1±15.2	89.3	148.9	89.3-148.9	59.6	1.962	ρ = **0.0498**
	F	32	**115.0**±15.0*	**85.6**	**144.4**	**85.6-144.4**	**58.8**		
	M	33	**121.0**±14.7	**92.2**	**149.8**	**92.2-149.8**	**57.6**		
Right systolic BP (mmHg)	M&F	65	123.0±18.4	95.2	167.0	92.0-167.0	**75**	6.821	ρ = **0.0017**
	F	32	**118.0**±13.9*	**90.8**	**145.2**	**90.8-145.2**	**55.5**		
	M	33	**128.0**±18.9[a]	**91.0**	**165.0**	**91.0-165.0**	**73.9**		
Left diastolic BP (mmHg)	M&F	**65**	**72.0±12.9**	**46.8**	**97.4**	**46.8-97.4**	**50.6**	0.0788	ρ = 0.9372
	F	32	71.5±13.9	44.3	98.7	44.3-98.5	54.2		
	M	33	70.0±12.0	46.5	93.5	46.5-93.5	47		
Right diastolic BP (mmHg)	**M&F**	64	**73.0±14.1**	**45.4**	**100.7**	**45.4-100.7**	**54.3**	-0.806	ρ =0.4265
	F	32	71.9±14.3	44.0	99.8	44.0-100.0	56		
	M	33	74.0±14.1	46.3	101.7	46.3-101.7	55.4		
Left pulse rate (beats per minute)	M&F	65	**79.9±12.0**	**58.0**	**113.8**	**58.0-113.8**	55.8	0.525	ρ = 0.5995
	F	32	80.0±13.0	67.0	105.4	67.0-105.4	38.4		
	M	33	79.8±11.1	58.0	101.5	58.0-101.5	43.5		
Right pulse rate (beats per minute)	M&F	65	**79.9±11.4**	**58.0**	**111.2**	**58.0-111.2**	53.2	0.643	ρ = 0.5201
	F	32	80.4±10.1	60.6	100.2	60.6-100.2	39.6		
	M	33	79.3±12.8	54.4	104.3	54.3-104.3	50		

Results are expressed as Mean ± standard deviation (SD) for the number of subjects shown in the column labeled N. M = for male, F = female, M&F = combined male and female values, RI = reference interval limits; $\rho < 0.05$ is considered statistically significant by 2-tailed t-test.

Comparison of the developed reference interval limits for BMI and vital signs for infants, children, adolescents, adults and geriatric population of Taita-Taveta County, Kenya with those reported in medical literature

A comparison of this study's reference interval limits for BMI and the selected vital signs with those reported in medical literature are presented in Table 4. This comparison indicates that: this study's lower reference interval limit for BMI is lower than that of the separate male and female American population, and the upper limit is higher and lower for males and females, respectively. Further, this study's lower reference interval limit is lower than that reported by WHO, while the upper reference interval limit is higher. This study's lower reference interval limit for systolic blood pressure is higher for both gender for American population, while the upper limits are similar and lower for males and females, respectively; diastolic blood pressure lower reference interval limit are lower than that of the American population, while the upper limits are lower[4]. This study's lower reference interval limits for systolic blood pressure is lower and higher than that of male and female Chinese population, respectively, while the upper limit is higher; diastolic lower reference interval limits is lower than that of the Chinese population, and the upper limits are lower. For pulse rate, this study's lower reference interval limits are higher than those of the Americans and Chinese, while the upper reference interval limits are lower [12, 4]. For peripheral oxygen saturation ($S\rho O_2$), this study's combined lower reference interval limits are lower than that reported by WHO, while the upper limits are similar. For axillary body temperature (^{0}C), this study's lower and upper reference interval limits are lower than the combined reference interval limits reported by (6) of 35.01-36.93^{o}C, Marui et al. [13] of 35.54-37.40^{o}C, Gunes and Zaybak [9] of 34.50-36.50^{o}C, and Thomas et al. [23] of 34.62-37.40^{o}C and 33.11-35.67^{o}C for females of 21-36 years and 39-59 years, respectively, for other populations.

Table 4 Comparison of the developed reference interval limits for BMI and vital signs for infants, children, adolescents, adults and geriatric population of Taita-Taveta County, Kenya with those reported in literature

Parameter	Gender	This study RI	WHO	Foppa et al., 2016	King et al., 2006
BMI (kg/m^2)	M	14.5-31.8	18.5-24.9	20.5-36.5	
	F	14.1-39.9		16.7-37.9	
Systolic BP (mmHg)	M	88.0-157.0		94.6-157.4	91.5-138.2
	F	84.0-178.2		88.7-159.3	80.7-116.0
Diastolic BP (mmHg)	M	46.0-100.8		58.4-93.6	55.5-83.4
	F	49.0-108.0		54.4-89.6	53.0-74.6
Pulse Rate (heart beats per minute)	M	62.0-117.6		39.5-86.5	48.2-88.6
	F	60.0-129.0		46.4-85.6	52.6-90.6
Oxygen saturation (SpO_2) (%)	M	86.8-100	95-100		
	F	86.8-100			
Temperature (0^oC)	M	32.0-35.9			
	F	32.0-35.9			

Chinese population studied by King et al. [12], American population studied by Foppa et al. [4].

IV. DISCUSSION

Body mass index

Results of this study indicating significantly increased established reference interval for body mass index (BMI) for females (22.0 [14.1-39.9] kg/m^2) compared to that of males (19.7 [14.5-31.8] kg/m^2) of Taita-Taveta population indicates that BMI is gender dependent for this population. This difference could be attributed to the greater body fat content in females compared to males of similar age. These established BMI reference intervals for the Taita-Taveta population are different from those reported in literature (WHO BMI) of 18.5-24.9 kg/m^2 indicating that the use of international WHO BMI reference interval for the Taita-Taveta population is inappropriate. This difference of the established BMI reference interval for the Taita-Taveta County, Kenya population from the WHO BMI reference interval may be attributed to genetic factors, ethnicity, lifestyle, influence of altitude adaptation, or other environmental factors. However, while this BMI reference interval gender difference was also reported by Foppa et al. (4), the males (20.5-36.5 kg/m^2) in their study demonstrated a higher BMI reference interval than the females (16.7-37.9 kg/m^2) suggesting that their male population had a higher body fat content than females, an observation contradicting expectation. Results indicating significantly increasing body mass index (BMI) reference interval for both the males and females of Taita-Taveta County, Kenya population with age indicates that this parameter is age dependent for this population. This finding is in agreement with that reported by Peter et al. [15] indicating increasing BMI with age in an Austrian population. This increase of BMI with age could be attributed to the increase in body fat content with age caused by lifestyle changes. Merrill et al. [14] also demonstrated increasing BMI with age. Buffa et al. [1] reported that body fat mass increases as one ages during adulthood for both gender because of reduced overall energy expenditure. Shimokata et al. [18] demonstrated increasing upper and central body fat deposition with advancing age. Silawat et al. [19] demonstrated increasing body fat content in males with advancing age. Roberts & Dallal [17] demonstrated increasing body fat content in males and females with advancing age.

Temperature

Results of this study indicating similar reference interval limits for temperature (32.0-35.9 ^{o}C) for both females and males of Taita-Taveta population suggests that temperature is gender independent for this population. This observation is in contrast to previous earlier reports indicating that females have a higher body temperature than males because of their thicker layer of subcutaneous fat which insulates their bodies from faster heat loss resulting in higher body temperatures [21]. Normally, females have a higher body temperature than males when they are ovulating due to raised progesterone levels. This observation may therefore suggest that the females who participated in this reference interval limits development study were not in the ovulation stage of their menstrual cycle. This established reference interval limits for temperature for the Taita-Taveta County, Kenya population is lower than the previously reported literature normal body temperature of 36.6-37.2 ^{o}C. It also contrasts with the axillary (armpit) temperature reference interval limits reported by Geneva et al.[6] of 35.01-36.93^{o}C for males and females, Marui et al. [13] of 35.54-37.40^{o}C for Japanese males and females of mean age 20.7 years, Hasan et al. [10] of 35.61-37.50^{o}C for males and females of mean age 34 years, Gunes and Zaybak et al. [9] of 34.50-36.50^{o}C for males and females of 65-90 years, and Thomas et al. (23) of 34.62-37.40^{o}C and 33.11-35.67^{o}C for females of 21-36 years and 39-59 years, respectively. The difference in the established reference interval limits for temperature for this study relative to the previously reported literature temperature reference interval limits may be due to genetic and environmental factors of the population used in the development of the reference intervals.

The established reference interval limits for temperature of the Taita-Taveta population was not affected by the age of the referent individual indicating that temperature is age independent for this population. This age independence of the established reference interval limits for temperature is in contrast with what is reported in literature; infants and children have a higher body temperature than adults because their hearts are immature and have faster and irregular heart beats per minute which generate more heat and therefore raises the body temperature. Adults have mature hearts with slower but regular heart beats per minute and therefore generate less heat resulting in lowered temperature.

Systolic and diastolic blood pressure (mmHg)

The results of this study indicating significantly higher systolic and lower diastolic blood pressure reference interval limits in males (88-157 mmHg [69 mmHg]/46-100.8 mmHg [54.8 mmHg]) compared to females (84-178.2 mmHg [94.2 mmHg]/49-108 mmHg [59 mmHg]) of Taita-Taveta County population implies that these parameters are gender dependent with females having a lower systolic and a higher diastolic reference interval limits than males. These findings are in agreement with those previously reported by King et al. [12] on the Chinese population who demonstrated gender differences in systolic and diastolic pressure of males (91.5-138.2 mmHg [46.7 mmHg]/55.5-83.4 mmHg [27.5 mmHg]) and females (80.7-116.0 mmHg [35.3 mmHg]/53-74.6mmHg [21.6 mmHg]), respectively, with males having significantly higher systolic and diastolic reference interval limits than females. Foppa et al. [4] also demonstrated a higher reference interval limits for both systolic and diastolic blood pressure for males (94.6-157.4 mmHg/58.4-93.6 mmHg) compared to females (88.7-159.3mmHg/54.4-89.6mmHg). However, while diastolic reference interval gender difference was demonstrated in this study, females had a significantly higher diastolic reference interval limits than males. The difference in the reference interval limits of the results of this study and those reported by King et al. [12] and Foppa et al. [4] could be due to ethnicity, genetic and environmental factors. Ethnic differences in diastolic blood pressure (mmHg), and the right ventricular measurements such as end diastolic volume (mL) and ejection fraction (%) are higher in nonwhite's compared to white's population as demonstrated by Kawut et al. [11]. The observed higher systolic reference interval limits in males compared to females could be due to the higher body mass index [kg/m^2], body surface area [m^2], and right ventricular measurements such as end systolic volume [mL], end diastolic volume [mL], stroke volume [mL], and cardiac output [L/min] in males compared to females as demonstrated by Foppa et al. [4]. Results indicating increasing systolic, and diastolic (age category 1-12 < 13-17 < 18-55 ≈ 56-100 years) blood pressure (mmHg) and pulse rate (beats per minute) (age category 1-12 < 13-17 < 18-55 ≈ 56-100 years) with advancement of age in this Taita-Taveta County, Kenyan population could be due to the decrease in the right ventricular measurements (end systolic volume [mL], end diastolic volume [mL], stroke volume [mL], cardiac output [L/min]) with advancement in age as demonstrated by Foppa et al. [4]. Kawut et al. [11] also reported higher right ventricular measurements (end systolic volume [mL], end diastolic volume [mL], stroke volume [mL], and cardiac output [L/min]) and mass, and a lower ejection fraction (%) in males compared to females. This could also be due to reduction of expansion and contraction of blood vessels with advancing age resulting in increasing systolic and diastolic blood pressure. Further this could relate to the size of the cavity or space (lumen) within the blood vessels and the amount/volume of blood flowing through it. As a person advances in age, body fat increases [19] resulting in deposition of the increased cholesterol in the lumen of blood vessels making their diameter narrower thus increasing resistance to blood flow resulting in increasing systolic and diastolic blood pressure.

In contrast, Silawat et al. [19] demonstrated a nonsignificant increase of systolic and diastolic blood pressure of males with advancing age. Results indicating significantly higher right hand arm side systolic reference interval limits in males compared to the left hand arm-side reference interval limits indicate that this parameter is dependent on the hand arm-side. This could be attributed to the higher right hand arm-side heart rate variability measurements (that is fluctuations in cardiac rate or rhythms) (time domain:

maximum beat to beat interval (ms), minimum beat to beat interval (ms), mean beat to beat interval (ms), standard deviation of beat to beat interval calculated in the entire recording session (ms), standard deviation of beat to beat intervals calculated on 5 minute segment (ms), square root of the mean squared difference of successive beat to beat intervals (ms), percentage of adjacent beat to beat intervals that differ by more than 50 ms (%), frequency domain: very low frequency range (0.003-0.04Hz), low frequency range (0.04-0.15Hz), and high frequency range (0.15-0.40Hz) (representing parasympathetic and sympathetic control, respectively) compared to the left hand arm-side heart rate variability measurements as demonstrated by Yüksel et al. [24]. Results indicating statistically similar diastolic blood pressure reference interval limits for males and females right and left hand arm side suggest that this parameter is independent of the hand arm-side used.

Peripheral oxygen saturation ($S\rho O_2$) (%)

The results of this study indicating a similar peripheral oxygen saturation ($S\rho O_2$) reference interval limits for Taita-Taveta County, Kenya population of 86.8-100 % implies that this parameter is gender independent. This is similar to the normal peripheral oxygen saturation ($S\rho O_2$) of 95-100 % reported in medical literature. For this population, bronchodilation and oxygen treatment may be initiated in patients with peripheral oxygen saturation ($S\rho O_2$) below 86.8 %.

Pulse rate

The results of this study indicating a significantly higher pulse rate reference interval in females (87 [60-129] beats per minute) compared to males (84 [62-117.6] beats per minute) of the Taita-Taveta population implies that this parameter is gender dependent. These results are in agreement with those reported by Foppa et al. [4] demonstrating females (46.4-85.6 beats per minute) having a higher pulse rate compared to males (39.5-86.5 beats per minute) of similar age. However, they contrast results reported by King et al. [12] who demonstrated a statistically similar pulse rate for both males (48.2-88.6 beats per minute) and females (52.6-90.6 beats per minute) of Chinese origin. This reduced pulse rate in males compared to females of the Taita-Taveta population may imply that the males of this coastal region have a more efficient circulatory system similar to that of athletes and physically fit persons who have lower pulse rates than females who may be having a poorer circulatory system. It may also be possible that females are involved in more intense activity requiring more oxygen for muscles which fastens their heart beats per minute than that of males with reduced activity which requires less oxygen resulting with slower heart beats per minute [22]. These two possible causes of the observed results were not investigated in this study. In addition, results of this study demonstrating a significantly increasing pulse rate for this Taita-Taveta population with advancing age suggesting that pulse rate is age dependent. This observation contrasts reports in literature indicating that as age increases, pulse rate decreases since infants and children have a faster pulse rate than adults. They also contrast the findings reported by Silawat et al. [19] demonstrating similar pulse rate of males with advancing age.

The decrease of pulse rate with age is based on the fact that for a normal person pulse rate is proportionate to body size. Infants and children have small bodies whose temperature homeostasis is maintained by their heart beats per minute which is faster than those of adults. This results in a greater loss of the generated heat in infants and children than adults who have bigger bodies with lower heart beats per minute resulting with less heat generation but a longer retention time to compensate for their size [22]. Results indicating a statistically similar pulse rates regardless of whether it is measured from the left or the right hand arm side suggests that the measurement of pulse rate is independent of the hand arm side used. These results may indicate that the Taita-Taveta population have no gender based left-right hand dominant arm side normally contributed by the greater muscle mass of the individual. The predominant left or right hand arm side of either gender would have produced a greater pulse rate.

The observed similarity in pulse rate regardless of the hand arm side used may suggest that the Taita-Taveta population has similar blood vessels hardness/elasticity for both the right and the left hand arm side. The right hand arm side has normally harder blood vessels than the left hand arm side for males and the left hand arm side has harder blood vessels for females than the right hand arm side. These observations agree with those reported by King et al. [12] who demonstrated similar pulse rates for both gender.

This study had several limitations including first, this study generated BMI and vital signs reference interval limits for the male and female population of Taita-Taveta County, Kenya which may not be generalized for other populations of Kenya. Secondly, the recommended sample size for each age subclass was below 120 referent individuals recommended by EP28 A3c guideline (CLSI, 2010). Thirdly, the pulse rate was only taken for the awake population but not for the sleeping population. Sleeping and awakeful state may interfere with the pulse rate value. Fourthly, the axillary (armpit) temperature taking time which has an impact in temperature measurement accuracy was not fixed to 6-7 minutes. Fifth, the reference intervals for respiratory rate, and oral, tympanic (ear), and rectal temperature which differ from axillary (armpit) temperature for the Taita-Taveta County, Kenya population were not developed.

In conclusion, this study has developed age and gender specific reference interval limits for body mass index (kg/m^2), and vital signs temperature (^0C), systolic and diastolic blood pressure (mmHg), peripheral oxygen saturation ($S\rho O_2$) (%), and pulse rate (beats per minute) for male and female population of Taita-Taveta County, Kenya which are different from those reported in medical literature for other populations. This difference in the developed reference intervals for BMI and four vital signs for the Taita-

Taveta County, Kenya population from those reported in medical literature supports the need for use of locally developed reference interval limits for these parameters to allow early accurate clinical detection, management and/or treatment, and monitoring the performance of therapeutic treatment regimens on recovery or deterioration of the acutely ill patients.

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