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Research Article

Reference Interval Limits for Serum Biochemistry Analytes for Adult and Geriatric Population of Taita-Taveta County, Kenya.

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Abstract

There are few reference interval limits established for routine serum biochemistry analytes for geriatrics in Africa and none in Kenya. This cross-sectional prospective study involving healthy 304 adults and geriatrics randomly recruited from Taita-Taveta County, Kenya meeting Clinical and Laboratory Standards Institute guidelines were used to establish median and 95% range reference interval limits for thirteen routine serum biochemistry analytes. This study has developed age and sex specific reference interval limits for some of the thirteen serum biochemistry analytes for adults and geriatrics of Taita-Taveta County, Kenya that differ from those previously reported in literature from different parts of the world including those of Caucasians and Africans. Therefore, continued use of Caucasian population reference interval limits for these serum biochemistry analytes from textbooks and refereed journal articles, instruments manuals and reagents insert, may lead to misdiagnosis and mismanagement of diseases associated with abnormalities of these parameters. The developed reference interval limits for these serum biochemistry analytes may be adopted for use in adults and geriatrics of Taita-Taveta County for effective care and management of patients.

Introduction

Reference interval limits for serum biochemistry analytes are developed using referent individuals whose healthy status are confirmed using a clear exclusion and inclusion criteria including physical assessment and laboratory investigation by clinicians. The recommended minimum number of referent individuals to participate in reference interval limits development is 120 and covers 95% of the referent individuals. The most accurate reference interval limits for biological parameters including serum biochemistry analytes are developed using the local population who visit a clinical laboratory as recommended by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and Clinical and Laboratory Standards Institute (CLSI) (Solberg, 1986; NCCLS, 2000; CLSI, 2010; Ozarda, 2016). However, this is not so in many African countries including Kenya who are using reference interval limits developed from European and North American populations which are inappropriate.

Besides, these European and North American reference interval limits were developed with technologies which have been upgraded severally using populations whose lifestyles and diets have also changed. These reference interval limits for serum biochemistry

analytes are affected by factors such as age, sex, dietary habits, lifestyle, environment, estimation method, instrumentation and reagents, geographical location, and inclusion and exclusion criteria used in identifying the referent individual. There are also very few well-developed reference interval limits specific for the geriatrics of world including that of the Kenyan population because most reference interval studies are prioritized and developed for use in clinical trials; therefore, verification of reference interval limits for analytes used in clinical laboratories or development of new reference interval limits for analytes for geriatrics has not been a priority (Achila et al., 2017).

Adult reference interval limits are commonly used in hospitals for geriatric population in Africa including Kenya. Further, many biochemical parameters have been reported to change with age; however, these have not been well documented in geriatrics of the world including that of the Kenyan population. Reference interval limits are used by clinicians for accurate interpretation of laboratory medicine reports, diagnosis of the healthy status of patients, disease treatment and/or management, and monitoring the outcome of a therapeutic regimen and/or treatment. The practice of using inappropriate reference interval limits can result in misdiagnosis, use of unnecessary medical procedures, and unnecessary use of medicines. The aim of this study is therefore, to establish the 95% (double-sided) gender and age specific reference interval limits of serum biochemistry analytes for adults and geriatrics of Taita-Taveta County, Kenya and compare them with those previously reported in medical literature.

Materials and Methods

Study site

This study was carried out in Mwatate, Taveta, Wundanyi and Voi subcounties of in Taita-Taveta County, Kenya between May 2015 and December 2017.

Study population

This study involved 304 healthy adult and geriatrics individuals randomly recruited including 150 males and 154 females of Taita-Taveta County, Kenya who had lived there for over 6 months of age 50-95 years. The study participants were evaluated for any illness in the field via clinical history and physical examination by a qualified physician, in addition to using a self-administered questionnaire. The inclusion criteria used to identify the healthy referent individuals included: male and female individuals of 50-95 years who had voluntarily accepted to participate in the study and had lived in Taita-Taveta County for over 6 months; free from human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), hepatitis B and C virus, syphilis, diabetes mellittus, heart disease, liver and kidney disease, and cancer/malignancies. Those who: had recent transfusion or surgery, were smokers and alcohol consumers, and had recent illness were also excluded. These conditions could affect the developed reference interval limits for serum biochemistry analytes. Individuals who refused to participate in the study were also excluded.

Study Design

This was a cross-sectional prospective design involving 304 healthy randomly recruited adults and geriatrics population.

Collection of Blood Specimen

Five milliters of blood was drawn from each referent individual between 8-11 am from the vein into plain vacutainer tubes, allowed to clot, and then placed in ice cool boxes and transported to the Department of Clinical Chemistry. Here, the collected blood specimen was centrifuged at 3000 g for five minutes to separate serum which was drawn using a Pasteur pippete and transferred into a vial on which a barcode was used for identification purposes. The vial containing the serum was transferred into a well-calibrated quality controlled Intergra 400 Auto analyzer chemistry machine to run the thirteen serum biochemistry analytes for liver and kidney function tests. Specimen were processed and analysed for serum biochemistry analytes within 2 hours. However, processed serum specimen which could not be analyzed within 2 hours were stored at 2-8^{0}C and analyzed within three days.

Laboratory Analysis

The serum levels for the eight liver function tests including total protein (TP) (a timed endpoint biuret method), albumin (ALB) (a timed endpoint method), alanine aminotransferase (ALT) (an enzymatic kinetic UV rate method), aspartate aminotransferase (AST) (an enzymatic kinetic UV rate method), alkaline phosphatase (ALP) (an enzymatic kinetic UV rate method), gamma-glutamyltransferase (GGT) (an enzymatic kinetic UV rate method), total bilirubin (T-BIL) (a timed endpoint method), and direct bilirubin (D-BIL) (a timed endpoint method), and five kidney function tests including blood urea nitrogen (BUN) (a timed endpoint method), creatinine (CREAT) (a timed endpoint method), sodium (NA) (Ion selective electrode method), potassium (K) (Ion selective electrode method) and chloride (CL) (Ion selective electrode method) were run using a well-calibrated quality controlled Clinical Chemistry AutoAnalyzer (Intergra 400) machine as instructed by the manufacturer using standard operating procedures (SOP). The results were reported in SI units.

Quality Control

The two biochemistry analytes quality control multi-sera material for normal (PNU) and pathological (PPU) levels were run daily to monitor the performance of the Clinical Chemistry

AutoAnalyzer (Intergra 400) machine which was calibrated daily using recommendations of the manufacturer. Results were reported in terms of Levey-Jennings charts.

Data Management and Statistical Analysis

The generated data for each of the measured serum biochemistry parameters was initially recorded in the laboratory notebook, then entered into the spreadsheet, cleaned and exported into SPSS software version 20 for analysis. The descriptive statistics parameters generated from the dataset included mean, variance, standard deviation, median, mode, skewness, standard error of skewness, kurtosis, standard error of kurtosis, range, minimum, maximum, 2.5 percentile and 97.5 percentile. Since the dataset was observed to be mostly non-parametric, it was expressed as median and 95% range. Significance difference between each of the measured parameters for males and females was compared using Mann-Whitney U test with a ρ-value of less than 0.05 considered being significant. Significant differences within and between age categories 50-60, 60-70 and 70-95 years were compared using Kruskal-Wallis H test followed by Mann-Whitney U test with adjusted ρ-value of less than 0.0167 considered being significant. Results were presented in normal tables. Reference interval limits for each of the measured parameters was developed using Clinical and Laboratory Standards Institute (CLSI) guideline EP28 A3c.

Results

Results of the quality control material for serum biochemistry analytes

Results of the quality control material for serum biochemistry analytes are presented in Table 1. These results indicate the assigned quality control values for the measured analytes were similar in terms of coefficient of variation with the measured quality control values of the measured analytes. Thus, the analytical process was working efficiently, and the measured serum biochemistry analyte values are valid and reliable.

Table 1: Internal quality control material for serum biochemistry analytes.

Analyte (unit)	QC Type	Assigned QC Report			Study QC Report		
		Mean	SD	% CV	Mean	SD	% CV
TP (g/L)	PPU	46	2	4.34	46.6	2.3	4.94
	PNU	68	3.4	5	67.5	3.4	5.03
ALB (g/L)	PPU	29.6	2	6.76	46	2.3	5
	PNU	48.8	2	4.1	102	5	4.9
ALT (U/L)	PPU	139	7	5.04	143.1	2.5	1.75
	PNU	51	3	5.88	49.3	2	4.06
AST (U/L)	PPU	122	6	4.92	145.5	1.9	1.31
	PNU	38	2	5.26	44.8	1.3	2.9
ALP (U/L)	PPU	259	13	5.02	226.8	5.1	2.25
	PNU	102	5	4.9	83.8	2.6	3.1
GGT (U/L)	PPU	259	13	5.02	264	10	3.78
	PNU	53	3	5.66	53	3	5.66
T-BIL (µmol/L)	PPU	66.3	4.9	7.39	93.5	3.1	3.32
	PNU	17.1	1	5.85	21.7	0.9	4.15
D-BIL (µmol/L)	PPU	33.7	2.5	7.42	36.32	0.75	2.06
	PNU	12.7	1.9	14.96	8.52	0.29	3.35
CREAT (µmol/L)	PPU	398	20	5.03	422	20	4.65
	PNU	92	5	5.43	93	5	5.56
BUN (mmol/L)	PPU	26.3	1.3	4.94	22.5	1.9	8.31
	PNU	7.4	0.4	5.4	7	0.3	4.83
K (mmol/L)	PPU	5.2	0.6	3	6.5	0.1	2
	PNU	5.2	0.6	3	4	0.6	1.5
NA (mmol/L)	PPU	144	4	2.8	144	2.5	1.7
	PNU	124.3	2.1	1.7	129	5	3.87
CL (mmol/L)	PPU	116	3	2.6	115.8	2.9	2.5
	PNU	85.3	2.6	3.1	105	5	4.76

Results of the normality statistics of serum biochemistry analytes for adults and geriatrics of Taita-Taveta County, Kenya

Results of the normality statistics of serum biochemistry analytes for adults and geriatrics of Taita-Taveta County, Kenya are presented in Table 2. These results indicate that based on the differences on the values of mean, median, and mode, and the skewness and kurtosis values for the whole sample, and separate males and females (50-95 years), the dataset is generally nonparametric. Significant skewness and kurtosis values were demonstrated by 34/42 (80.95%) and 36/42 (85.71%), respectively, of the measured biochemistry analytes.

Table 2: Results of the normality statistics of serum biochemistry analytes for adults and geriatrics of Taita-Taveta County, Kenya.

50-95 years		N	TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
Mean	M&F	304	73.87	43.23	17.73	24.32	41.98	36.36	6.5	1.91	80.68	4.3	137.6	4.4	97.33	6.05
	M	150	73.46	43.23	20.14	26	40.21	40.98	6.25	2.05	83.93	4.25	137.7	4.25	97.11	6.05
	F	154	74.31	43.23	15.39	22.68	43.66	31.97	6.77	1.76	77.51	4.33	137.7	4.52	97.55	6.05
SEM	M&F	304	0.4	0.25	1.14	0.88	2.92	2.19	0.63	0.09	2.14	0.27	0.38	0.09	0.49	0.11
	M	150	0.52	0.39	2.2	1.45	4	3.48	0.39	0.14	2.64	0.32	0.6	0.05	0.73	0.15
	F	154	0.61	0.32	0.66	1	4.26	2.64	1.18	0.12	3.35	0.43	0.47	0.18	0.66	0.16
Median	M&F	304	74.15	44.1	14.2	20.9	18.95	23.85	4.55	1.6	75	3.68	138	4.28	97	5.5
	M	150	73	44	15	22	19.5	27	5	2	77.5	4	138	4	97	5.7
	F	154	75	44	13.5	20	19	21.5	4	1.5	72	4	138	4	97	5.5
Mode	M&F	304	75.9	44.4	14.2	16.4	0	17.7	2.2	0.9	61	3.2	139.7	4.1	100	4.9
	M	150	72	44	14	16	0	18	4	2	61	4	138	4	104	5.3
	F	154	76	45	10	18	0	18	2	1	65	4	140	4	94	4.9
SD	M&F	304	7.01	4.33	19.91	15.35	50.94	38.16	10.91	1.62	37.34	4.68	6.61	1.64	8.54	1.94
	M	150	6.41	4.79	26.91	17.81	49.01	42.57	4.77	1.74	32.28	3.9	7.35	0.63	8.91	1.7
	F	154	7.61	3.93	8.21	12.35	52.88	32.84	14.63	1.54	41.55	5.35	5.83	2.26	8.24	2.11
Variance	M&F	304	49.16	18.74	396.5	235.7	2595	1456	119.1	2.63	1394	21.94	43.72	2.68	72.87	3.78
	M	150	41.06	22.9	724.05	317.24	2401.9	1811.8	22.75	3.03	1042	15.21	54.05	0.39	79.31	2.89
	F	154	57.95	15.42	64.43	152.39	2796.7	1078.4	214	2.37	1726.4	28.59	33.94	5.11	67.82	4.46
Skewness	M&F	304	-1.22	-1.35	12.01	3.68	1.55	3.02	9.79	3.4	5.9	9.74	-0.5	14.25	0.56	3.65
	M	150	-0.33	-1.2	9.65	3.46	1.93	2.81	1.66	3.44	3.12	6.29	-0.27	0.26	0.57	3.17
	F	154	-1.78	-1.53	1.38	3.52	1.24	3.22	7.99	2.62	7.2	10.69	-0.81	10.62	0.53	3.78
SES	M&F	304	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14	0.14
	M	150	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.198	0.21
	F	154	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.195	0.18
Kurtosis	M&F	304	7.12	2.396	181.43	18.3	4.2	10.43	109.6	20.31	59.13	115.6	5.56	231.8	2.15	20.2
	M	150	2.55	1.77	107.7	14.03	7.96	8.74	2.44	20.72	16.76	46.16	6.74	0.2	3.21	15.3
	F	154	9.69	3.24	1.75	23.47	1.58	12.13	66.75	12.72	73.52	125.28	1.87	124.77	0.79	20.9
SEK	M&F	304	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.279	0.28
	M	150	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.394	0.41
	F	154	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.389	0.36
Range	M&F	304	66.64	25.23	318.4	116.5	340.5	251.5	136	153	500.8	66.56	64	28	64	17.9
	M	150	44	25	318	117	340	248	24	15	279	36	64	3	64	12
	F	154	67	23	42	111	272	211	136	12	501	67	36	28	46	17.5
Minimum	M&F	304	27.36	28.2	3.9	6.3	0	4.6	1	0.1	4.2	0.24	109.5	3	74.7	3.8
	M	150	48	28	4	6	0	8	1	0	28	1	110	3	75	3.8
	F	154	27	28	4	8	0	5	1	0	4	0	114	3	78	4.2
Maximum	M&F	304	94	53.43	322.3	122.8	340.5	256.1	137	15.4	505	66.8	173.5	31	138.7	21.7
	M	150	92	53	322	123	340	256	25	15	307	37	174	6	139	15.8
	F	154	94	51	46	119	272	216	137	12	505	67	150	31	124	21.7

Percentiles			TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
2.5	M&F	304	57.4	30.1	5.13	8.3	0	8.8	1	0.26	41	1.84	122.2	3.2	81.8	4.2
	M	150	60.33	29.78	4.78	9	0	9	1	0	44.33	2	119.3	3	79.88	3.93
	F	154	56.88	30.88	5.88	8	0	7.63	1	0	34.13	2	123.75	3	82.88	4.2
97.5	M&F	304	88.5	49.7	44.4	66.5	147.3	174.3	19.7	5.8	144.5	8.6	148.9	5.7	112.3	10.8
	M	150	89	51.23	52	93.8	138.58	186.25	20	6	163.45	11.02	155	5.22	113.15	10.3
	F	154	88.25	49	37	50	160.5	160.5	20	6	134.75	8.38	149-	6	114.38	10.9
70-95 years		N	TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
Mean	M&F	81	73.32	42.95	14.87	24.24	49.86	37.33	7.58	2.02	79.42	3.98	135.5	4.36	97.71	6.13
	M	45	72.93	43.49	15.47	26.29	46.22	41.24	6.24	1.8	87.69	4.07	136.67	4.2	98	6.05
	F	36	73.81	42.25	14.11	21.69	54.44	32.58	9.25	2.19	69.08	3.89	134.14	4.42	97.31	6.19
SEM	M&F	81	0.752	0.429	0.948	1.772	6.527	4.788	1.515	0.204	4.113	0.266	0.826	0.069	1.108	0.18
	M	45	1.041	0.564	1.301	2.876	8.844	7.004	0,658	0.231	6.876	0.405	1.181	0.088	1.491	0.22
	F	36	1.11	0.659	1.39	1.661	9.738	6.3	3.315	0.367	2.679	0.321	1.097	0.122	1.67	0.28
Median	M&F	81	73.2	44	13	20.9	44	21.5	5	1.8	70	3.2	137	4.21	98	6
	M	45	73	44	13	22	44	23	5	2	76	4	138	4	100	6
	F	36	74.5	44	12.5	20	54	21	5	2	65.5	3	135	4	96.5	6
Mode	M&F	81	76	44	10	18	0	21	4	1	61	3	137	4	100	5
	M	45	73	44	13	18	0	17	2	2	54	3	138	4	104	5
	F	36	76	44	10	18	0	21	3	1	59	3	137	4	94	6
SD	M&F	81	6.768	3.858	8.536	15.95	58.74	43.092	13.637	1.833	37.018	2.395	7.434	0.626	9.973	1.31
	M	45	6.982	3.782	8.727	19.292	59.328	46.988	4.417	1.546	46.136	2.717	7.923	0.588	10	1.45
	F	36	6.663	3.952	8.338	9.968	58.425	37.797	19.892	2.202	16.075	1.924	6.582	0.732	10.019	1.54
Variance	M&F	81	45.808	14.88	72.863	254.39	3450.4	1856.9	185.98	3.36	1370.3	5.734	55.27	0.392	99.452	1.71
	M	45	48.745	14.301	76.164	372.17	3519.9	2207.8	19.507	2.391	2128.5	7.382	62.773	0.345	100	2.11
	F	36	44.39	15.621	69.53	99.361	3413.5	1428.7	395.68	4.847	258.421	3.702	43.323	0.536	100.39	2.36
Skewness	M&F	81	-0.395	-1.427	1.445	3.106	2.292	3.083	7.776	2.648	3.541	3.37	-0.742	0.789	0.357	1.29
	M	45	0.226	-1.083	1.253	2.887	2.907	2.831	1.086	1.045	2.855	3.385	-0.739	0.647	0.14	1.24
	F	36	-1.16	-1.308	1.771	0.979	1.615	3.64	5.645	2.886	1.445	2.002	-1.07	1	0.651	1.07
SES	M&F	81	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.267	0.33
	M	45	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.354	0.36
	F	36	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.393	0.36
Kurtosis	M&F	81	2.653	2.295	1.324	11.476	8.302	10.197	66.059	10.575	18.085	16.503	2.337	1.092	0.954	2.35
	M	45	3.132	3.909	0.782	8.245	12.888	8.344	0.489	1.139	11.249	15.479	2.793	1.338	0.821	2.61
	F	36	3.046	1.413	2.692	0.868	4.086	16.004	33.005	10.864	2.946	4.789	1.887	0.363	1.484	1.9
SEK	M&F	81	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.529	0.66
	M	45	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.695	0.7
	F	36	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.768	0.82
Range	M&F	81	40.5	18.12	33.1	92.2	340.5	231.9	122	12	279	17.12	45.2	3	49.5	6.4
	M	45	41	19	32	91	340	227	16	6	279	17	45	3	49	7
	F	36	33	17	33	42	272	211	122	12	75	9	32	3	46	7
Minimum	M&F	81	51	30.39	3.9	8	0	5	1	0	28	1.3	109.5	3	74.7	4.4
	M	45	51	30	4	9	0	10	1	0	28	1	110	3	124	4
	F	36	51	31	4	8	0	5	1	0	49	2	114	3	78	4
Maximum	M&F	81	91.5	48.51	37	100.2	340.5	236.9	123	12	307	18.42	154.7	6	124.2	10.8
	M	45	92	49	36	100	340	237	17	6	307	18	155	6	124	11
	F	36	84	48	37	50	272	216	123	12	124	11	146	6	124	11

Percentiles			TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
2.5	M&F	81	51.45	31.04	4.02	8.04	0	9.05	1	0	45.2	1.81	114.2	3.01	78.15	4.4
	M	45	52.65	30.3	4	9.15	0	10.3	1	0	30.55	1.15	111.8	3	76.05	4
	F	36	51	31	4	8	0	5	1	0	49	2	114	3	78	4
97.5	M&F	81	91.28	47.99	36.98	89.1	265.55	214.92	19.86	6.3	193.9	10.9	154.27	6	124.19	10.4
	M	45	76	48.85	18.49	32.96	69	57.5	8.5	2.5	103.65	5.01	141	5.85	104	10.8
	F	36	77.5	45	17.28	25.36	74.75	49.33	18.7	3.06	78.25	4.83	138.75	5	102.75	7
60-70 years		N	TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
Mean	M&F	104	74.04	43.33	18.95	23.41	42.33	33.65	5.97	2.12	76.89	4.05	138.13	4.47	97.53	6.33
	M	58	73.41	42.97	21.95	24.74	38.43	35.12	6.43	2.28	79.59	4.1	138.24	4.19	97.94	6.22
	F	46	74.83	43.78	15.17	21.74	47.24	31.8	5.39	1.91	73.5	3.98	138	4.83	97.26	6.5
SEM	M&F	104	0.582	0.449	3.053	1.69	4.885	2.777	0.489	0.184	2.195	0.291	0.707	0.266	0.794	0.19
	M	58	0.833	0.663	5.395	2.283	5.862	3.667	0.739	0.282	2.76	0.492	1.113	0.087	1.189	0.26
	F	46	0.788	0.577	1.092	2.521	8.226	4.277	0.593	0.217	3.508	0.227	0.78	0.59	1.001	0.31
Median	M&F	104	75	44	14	19.5	17	26.5	4	2	74	4	138	4	98	5.6
	M	58	73	44	14	21.5	15	27.5	4	2	76	3	139	4	97.5	6
	F	46	76	44	14	18	34	23	4	2	70	4	138	4	98	6
Mode	M&F	104	76	44	14	16	0	18	2	2	74	3	138	4	100	4.9
	M	58	72	44	14	16	0	18	3	2	77	3	136	4	94	5
	F	46	76	45	6	18	0	9	2	2	65	4	138	4	100	5
SD	M&F	104	5.938	4.578	31.136	17.238	49.821	28.319	4.986	1.881	22.384	2.97	7.213	2.709	8.096	2.15
	M	58	6.347	5.047	41.084	17.384	44.644	27.927	5.626	2.15	21.02	3.75	8.48	0.661	9.055	2.1
	F	46	5.343	3.915	7.407	17.095	55.791	29.007	4.025	1.473	23.791	1.542	5.287	4.002	6.787	2.39
Variance	M&F	104	35.261	20.96	969.5	297.16	2482.2	801.96	24.863	3.54	501.05	8.823	52.021	7.339	65.553	4.63
	M	58	40.282	25.472	1687.9	302.2	1993.1	779.93	31.653	4.624	441.86	14.059	71.906	0.437	81.985	4.41
	F	46	28.547	15.329	54.858	292.24	3112.6	841.41	16.199	2.17	566	2.377	27.956	16.014	46.064	5.71
Skewness	M&F	104	-0.752	-1.414	9.14	4.047	0.98	2.67	1.823	3.549	0.366	6.679	0.05	9.283	0.962	2.86
	M	58	-0.82	-1.372	7.079	3.958	0.705	2.932	1.778	3.959	1.228	5.992	0.11	0.153	1.216	3.09
	F	46	-0.474	-1.307	1.099	4.405	1.078	2.5	1.494	1.116	-0.27	1.179	-0.41	6.487	0.045	2.37
SES	M&F	104	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.237	0.21
	M	58	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.314	0.29
	F	46	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.35	0.31
Kurtosis	M&F	104	3.087	2.446	89.292	19.194	0.169	8.748	3.188	20.752	2.535	57.124	8.963	91.563	5.985	9.82
	M	58	4.081	1.729	52.306	18.224	-1.031	10.596	2.413	21.337	2.464	41.273	8.291	0.07	7.039	12.5
	F	46	0.338	3.655	1.341	23.802	0.408	7.83	3.013	1.205	2.264	1.331	0.928	43.271	2.264	6.96
SEK	M&F	104	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.469	0.43
	M	58	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.618	0.57
	F	46	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.688	0.61
Range	M&F	104	41	23	318	111	212	166	24	15	150	29	64	28	63	11.7
	M	58	41	23	317	107	137	163	24	15	113	29	64	3	63	12
	F	46	27	22	32	111	212	153	19	6	130	6	27	28	28	12
Minimum	M&F	104	48	28	4	8	0	5	1	0	4	1	110	3	76	4.3
	M	58	48	28	5	12	0	8	1	0	41	1	110	3	76	4
	F	46	59	29	4	8	0	5	1	0	4	2	122	3	84	4
Maximum	M&F	104	89	51	322	119	212	171	25	15	154	30	174	31	139	16
	M	58	89	51	322	119	137	171	25	15	154	30	174	6	139	16
	F	46	86	51	36	119	212	158	20	6	134	8	149	31	112	16
Percentiles			TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
2.5	M&F	104	60.25	28.63	5.63	8	0	8.63	1	0	28.25	2	117.5	3	81	4.4
	M	58	54.18	28	5.48	12	0	9.43	1	0	43.38	1.48	110	3	76	4
	F	46	60.4	30	4.35	8	0	5.7	1	0	4.53	2	123.05	3	84.18	4

97.5	M&F	104	87.13	50.38	45.25	102.13	160	135.5	20	6	134.75	8	151.25	6	110.75	15.7
	M	58	89	50.53	194.7	106.18	129.88	147.73	22.63	10.73	145.45	19.55	164.98	5.53	125.23	16
	F	46	85.48	50.65	35.83	106.93	202.9	149.95	19.3	6	131.55	8	149	26.62	111.65	16
50-60 years		N	TP	ALB	ALT	AST	ALP	GGT	T-BIL	D-BIL	CREAT	BUN	NA	K	CL	RBS
Mean	M&F	119	74.14	43.34	18.62	25.16	36.25	38.17	6.25	1.66	84.84	4.71	138.72	4.38	96.92	5.75
	M	47	74.02	43.3	22.38	27.28	36.66	47.96	6.02	2	85.68	4.6	137.89	4.38	95.49	5.82
	F	72	74.2	43.41	16.16	23.73	36.52	31.73	6.41	1.49	84.3	4.79	139.23	4.34	97.82	5.71
SEM	M&F	119	0.738	0.413	0.974	1.204	4.189	3.855	1.15	0.108	4.283	0.611	0.459	0.062	0.731	0.17
	M	47	0.873	0.783	1.788	2.498	6.344	7.576	0.578	0.187	3.998	0.723	0.722	0.089	1.089	0.22
	F	72	1.08	0.455	1.019	1.125	5.634	3.884	1.866	0.118	6.605	0.894	0.59	0.072	0.959	0.24
Median	M&F	119	74	44	16	24	4	24	5	2	80	4	140	4	96	5.2
	M	47	74	44	18	24	16	27	5	2	88	4	139	4	96	6
	F	72	74.9	44.3	14.1	22.8	1.4	22.4	4.1	1.4	76	3.9	139.8	4.37	96.55	5
Mode	M&F	119	72	44	15	17	0	10	5	1	88	4	140	4	93	5
	M	47	72	45	15	35	0	10	5	2	88	4	140	4	93	5
	F	72	71.1	44.4	8.4	30.6	0	17.7	1.1	1.4	75	2.11	139.7	4.28	108.1	5
SD	M&F	119	8.055	4.507	10.626	13.138	45.692	42.049	12.546	1.181	46.726	6.666	5.01	0.676	7.971	1.96
	M	47	5.987	5.365	12.261	17.128	43.49	51.936	3.964	1.285	27.406	4.959	4.949	0.61	7.463	1.45
	F	72	9.166	3.864	8.647	9.542	47.471	32.96	15.839	1.003	56.043	7.582	5.009	0.613	8.14	2.2
Variance	M&F	119	64.886	20.31	112.92	172.61	2087.8	1768.1	157.39	1.395	2183.3	44.43	25.1	0.457	63.535	3.85
	M	47	35.847	28.779	150.33	293.38	1891.4	2697.4	15.717	1.652	751.09	24.594	24.488	0.372	55.69	2.11
	F	72	84.02	14.935	74.77	91.051	2253.5	1086.4	250.86	1.01	3140.9	57.488	25.089	0.375	66.256	4.81
Skewness	M&F	119	-1.734	-1.279	1.251	3.67	0.953	2.825	9.766	1.782	6.403	8.014	-0.492	0.204	0.349	4.85
	M	47	-384	-0.83	0.902	3.885	0.892	2.285	1.667	2.566	2.338	6.321	-0.696	0.171	-0.241	1.24
	F	72	-1.884	-1.987	1.35	0.767	0.982	3.27	8.112	1.318	6.085	7.921	-0.393	-0.026	0.626	5.15
SES	M&F	119	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.21
	M	47	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.347	0.36
	F	72	0.283	0.283	0.283	0.283	0.285	0.283	0.283	0.283	0.283	0.283	0.283	0.283	0.283	0.26
Kurtosis	M&F	119	9.434	2.497	1.138	25.189	-0.321	8.74	102.14	6.526	56.019	69.876	0.171	-0.046	0.137	36.2
	M	47	0.204	0.925	0.022	21.27	-0.312	5.59	2.581	9.461	10.657	41.959	-0.69	-0.104	-0.541	2.61
	F	72	9.053	4.977	1.734	0.404	-0.329	11.471	67.694	2.29	45.698	64.436	0.674	-0.214	0.105	35.8
SEK	M&F	119	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.44	0.42
	M	47	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.681	0.7
	F	72	0.559	0.559	0.559	0.559	0.563	0.559	0.559	0.559	0.559	0.559	0.559	0.559	0.559	0.51
Range	M&F	119	67	25	47	117	164	251	136	8	501	67	26	3	43	18.2
	M	47	28	24	47	117	144	248	16	7	175	35	17	3	28	7
	F	72	66.64	21.61	40.5	44.7	164	173.1	136	5.2	500.8	66.559	25.9	2.78	40.7	18
Minimum	M&F	119	24	28	5	6	0	5	1	0	4	0	124	3	81	3.8
	M	47	58	29	5	6	0	8	2	1	42	2	128	3	81	4
	F	72	27.36	28.22	5.3	8.3	0	4.9	1	0.1	4.2	0.241	124	3.1	83.1	4
Maximum	M&F	119	94	53	52	123	164	256	137	8	505	67	150	6	124	22
	M	47	86	53	52	123	144	256	18	8	217	37	145	6	109	11
	F	72	94	49.83	45.8	53	164	178	137	5.3	505	66.8	149.9	5.88	123.8	22
Percentiles																
2.5	M&F	119	57	30	5	9	0	8	1	0	39	2	128	3	82	3.86
	M	47	58.6	29.2	5	6.6	0	8.2	2	1	43.2	2	128	3	81.2	4
	F	72	50.99	29.8	5.63	8.55	0	7.62	1.08	0.1	32.1	1.57	126.31	3.14	85	4
97.5	M&F	119	90	52	46	52	144	178	18	4	147	12	149	6	112	10.9
	M	47	85.6	52.8	52	108.8	144	241.6	18	7.2	199.2	31	145	5.8	108.8	10.8
	F	72	92.2	49.2	41.1	50.4	155.4	178	33.55	4.31	209.65	21.34	149.1	5.57	114.9	11

These results indicate that based on the differences on the values of mean, median, and mode, and the skewness and kurtosis values for the age category 70-95 years for combined males and females, and separate males and females, the dataset was generally non-parametric. Significant skewness and kurtosis values were demonstrated by 31/42 (73.81%) and 28/42 (66.76%), respectively, of the measured biochemistry analytes. However, based on the mean, median, mode, skewness and kurtosis, potassium (K) and chloride (CL) dataset were normally distributed.

These results indicate that based on the differences on the values of mean, median, and mode, and the skewness and kurtosis values for the age category 60-70 years for combined males and females, and separate males and females, the dataset is non-parametric. Significant skewness and kurtosis values were demonstrated by 29/42 (69.05%) and 32/42 (76.19%), respectively, of the measured biochemistry analytes. However, based on the mean, median, mode, skewness and kurtosis, alkaline phosphatase (ALP) dataset was normally distributed.

These results indicate that based on the differences on the values of mean, median, and mode, and the skewness and kurtosis values for combined males and females, and separate males and females, the dataset was mostly non-parametric. Significant skewness and kurtosis values for the age category 50-60 years were demonstrated by 26/42 (61.90%) and 24/42 (57.14%), respectively, of the measured biochemistry analytes. However, based on the mean, median, mode, skewness and kurtosis, alkaline phosphatase (ALP), sodium (NA), potassium (K) and chloride (CL) dataset were normally distributed. Results were therefore expressed as median and 95% range. Statistical significance was assessed using Kruskal-Wallis H test followed by Mann-Whitney U test with an adjusted significant ρ-value of less than 0.0167.

Reference interval limits for liver and kidney function tests, and electrolytes for adults and geriatrics of Taita-Taveta County, Kenya

The established median reference interval limits for liver and kidney function tests, and electrolytes for adult and geriatric male population of Taita-Taveta County, Kenya for random blood glucose (RBS), total protein (TP), albumin (ALB), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (T-BIL), blood urea nitrogen (BUN), sodium (NA), potassium (K), and chloride (CL) was statistically similar to that of the female population of the same age range ($\rho > 0.05$). Therefore, a combined male and female reference interval limits for these liver and kidney function tests, and electrolytes for this population were established. The established combined reference interval limits for liver and kidney function tests, and electrolytes for the adult and geriatric population of Taita-Taveta County, Kenya for RBS is 5.5 (4.2-10.8) mmol/L, TP is 74.15 (57.4-88.5) g/L, ALB is 44.1 (33.1-49.7) g/L, AST is 20.9 (8.3-66.5) U/L, ALP is 21 (0-147.6) U/L, T-BIL is 4.55 (1-19.7) µmol/L, BUN is 3.68 (1.8-8.6) mmol/L, NA is 138 (122.2-148.9) mmol/L, K is 4.28 (3.2-5.7) mmol/L, and CL is 97 (81.8-112.3) mmol/L.

Table 3: Median reference interval limits for liver and kidney function tests and electrolytes for adult and geriatric population of Taita-Taveta County, Kenya.

Analyte (unit)	Sex	N	Mean±SD	Percentile		Reference Interval	IV	Difference between M & F	
			(Median)	2.5th	97.5th			Z value	Sig
RBS (mmol/L)	M&F	310	6.05±1.94					-1.191	ρ = 0.234
			5.5	4.2	10.82	4.2-10.8	6.6		
	F	178	6.05±2.11						
			6.05	4.2	10.9	4.2-10.9	6.7		
	M	132	6.05±1.70						
			5.7	3.93	10.31	3.9-10.3	6.4		
TP (g/L)	M&F	304	73.87±7.01					-1.863	ρ = 0.062
			74.15	57.41	88.5	57.4-88.5	31.1		
	F	154	74.31±7.61						
			75	56.88	88.25	56.9-88.3	31.4		
	M	150	73.46±6.41						
			73	61.33	89	61.3-89	27.7		
ALB (U/L)	M&F	304	43.23±4.33					-0.555	ρ = 0.576
			44.1	30.07	49.65	33.1-49.7	16.6		
	F	154	43.23±3.93						
			44	30.88	49	30.9-49.0	18.1		
	M	150	43.23±4.79						
			44	29.78	51.23	29.9-51.2	21.3		

ALT (U/L)	M&F	304	17.73±19.91					-2.522	ρ = 0.012
			14.2	5.13	44.4	5.1-44.4	39.3		
	F	154	15.39±8.21						
			13.5	5.88	37	5.9-37	31.1		
	M	150	20.14±26.91						
			15	4.78	52	4.8-52	47.2		
AST (U/L)	M&F	304	24.32±15.35					-1.728	ρ = 0.084
			20.9	8.3	66.54	8.3-66.5	58.2		
	F	154	22.68±12.35						
			20	8	50	Aug-50	42		
	M	150	26.00±17.81						
			22	9	93.8	9-93.8	84.8		
ALP (U/L)	M&F	304	42.12±50.97					-0.277	ρ = 0.781
			21	0	147.56	0-147.6	147.6		
	F	154	43.66±52.88						
			19	0	160.5	0.0-160.5	160.5		
	M	150	40.21±49.01						
			19.5	0	138.58	0.0-138.6	138.6		
GGT (U/L)	M&F	304	36.36±38.16					-2.811	ρ = 0.005
			23.85	8.8	174.25	8.8-174.3	165.5		
	F	154	31.97±32.84						
			21.5	7.63	160.5	7.6-160.5	152.9		
	M	150	40.98±42.57						
			27	9	186.25	9-186.3	177.3		
T-BIL (μmol/L)	M&F	304	6.50±10.91					-1.491	ρ = 0.136
			4.55	1	19.7	1-19.7	18.7		
	F	154	6.77±14.63						
			4	1	20	20-Jan	19		
	M	150	6.25±4.77						
			5	1	20	20-Jan	19.3		
D-BIL (μmol/L)	M&F	304	1.91±1.62					-2.196	ρ = 0.028
			1.6	0.26	5.81	0.3-5.8	5.5		
	F	154	1.76±1.54						
			4	0	6	0-6	6		
	M	150	2.05±1.74						
			2	0	6	0-6	6		
BUN (mmol/L)	M&F	304	4.30±4.68					-0.317	ρ = 0.751
			3.68	1.84	8.59	1.8-8.6	6.8		
	F	154	4.33±5.35						
			4	2	8.38	2-8.4	6.4		
	M	150	4.25±3.90						
			4	2	11.02	11-Feb	9		
CREAT (μmol/L)	M&F	304	80.68±37.34					-2.546	ρ = 0.011
			75	41	144.5	41-144.5	103.5		
	F	154	77.51±41.55						
			72	34.13	134.75	34.1-134.8	100.7		
	M	150	83.93±32.28						
			77.5	44.33	163.45	44.3-163.5	119.2		

NA (mmol/L)	M&F	304	137.63±6.61					-0.16	ρ = 0.873
			138	122.19	148.9	122.2-148.9	26.7		
	F	154	137.69±5.83						
			138	123.4	148.9	123.4-148.9	25.2		
	M	150	137.66±7.35						
			138	119.3	155	119.3-155	35.7		
K (mmol/L)	M&F	304	4.40±1.64					-0.927	ρ = 0.354
			4.28	3.2	5.68	3.2-5.7	2.5		
	F	154	4.52±2.26						
			4	3	6	06-Mar	3		
	M	150	4.25±0.63						
			4	3	5.22	3-5.2	2.2		
CL (mmol/L)	M&F	304	97.33±8.54					-0.014	ρ = 0.989
			97	81.8	112.31	81.8-112.3	30.5		
	F	154	97.55±8.24						
			97	82.88	114.34	82.9-114.3	31.4		
	M	150	97.11±8.91						
			97	79.88	113.15	79.9-113.2	33.3		

The established median reference interval limit for liver and kidney function tests for adult and geriatric male population of Taita-Taveta County, Kenya for alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), direct bilirubin (D-BIL), and creatinine (CREAT) significantly differed from that of adult and geriatric female population of the same age range ($\rho < 0.05$). The established reference interval limits for liver and kidney function tests for this adult and geriatric population of Taita Taveta County, Kenya for ALT is 15 (4.8-52) U/L for males and 13.5 (5.9-37) U/L for females ($U = 9617.5$, $z = -2.522$, $\rho = 0.012$, $r = 0.1446$), GGT is 27 (9-186.3) U/L for males and 21.5 (7.6-160.5) U/L for females ($U = 9396$, $z = -2.811$, $\rho = 0.005$, $r = 0.1612$), D-BIL is 2 (0-6) µmol/L for males and 4 (0-6) µmol/L for females ($U = 9869$, $z = -2.196$, $\rho = 0.028$, $r = 0.1259$), and CREAT is 77.5 (44.3-163.5) µmol/L for males and 72 (34.1-134.8) µmol/L for females ($U = 9599.5$, $z = -2.546$, $\rho = 0.011$, $r = 0.1460$) (Table 3).

Results are expressed as mean ± standard deviation (SD), and median and 95% range for the number of referents in the column labeled N. Statistical comparisons of the median reference interval limits between male and female referents were carried out using Mann-Whitney U test. Differences were considered statistically significant at $\rho < 0.05$.

Effect of age and gender on the developed reference interval limits for liver and kidney function tests, and electrolytes for adult and geriatric population of Taita-Taveta County, Kenya

The effects of age on the established reference interval limits for liver and kidney function tests, and electrolytes for adult and geriatric population of Taita-Taveta County, Kenya was assessed by categorizing the results into three age categories as follows: (a) age ≥ 50-60 years, (b) age ≥ 60-70 years, and (c) age ≥ 70-95 years. Significant reference interval limits differences between males and females for the measured analytes were estimated by Mann-Whitney U test within each age category. Significant reference interval limits differences for the measured analytes within and between the three age categories was estimated using Kruskal-Wallis H test followed by Mann-Whitney U test with Bonferroni correction where ρ-values less than 0.0167 was considered statistically significant. The Mean ± SD, Median and 95 % range, sex and age categories are presented in Table 4.

Table 4: Effect of age and gender on the developed median reference interval limits for liver and kidney function tests and electrolytes for adults and geriatrics of Taita-Taveta County, Kenya.

Analyte (units)	Gender	N	≥ 50-60 years	N	≥ 60-70 years	N	≥ 70-95 years
RBS (mmol/L)	M&F	131	5.75±1.96	128	6.33±2.15	51	6.13±1.31
			5.2 (3.9-10.9)		5.6 (4.4-15.7)[a]		6 (4.4-10.4)b
	M	44	5.82±1.45	68	6.22±2.39	20	6.05±1.10
			6 (4-10.8)		6 (4-16)		6 (5-7)
	F	87	5.71±2.19	60	6.50±2.39	31	6.19±1.54
			5 (4-11)		6 (4-16)[a]		6 (4-7)
TP (g/L)	M&F	119	74.12±8.05	104	74.02±5.91	81	73.31±6.73
			74.3 (56.6-89.9)		74.9 (60.4-87.1)		73.2 (51.5-91.3)
	M	47	74.02±5.99	58	73.41±6.35	45	72.93±6.98
			74 (58.6-85.6)		73 (54.2-89)		73 (52.7-76)
	F	72	74.20±9.17	46	74.83±5.34	36	73.81±6.66
			74.9 (51.0-92.2)		76 (60.4-85.48)		74.5 (51-77.5)
ALB (U/L)	M&F	119	43.33±4.48	104	43.30±4.53	81	42.98±3.86
			44.3 (29.9-51.68)		44.1 (28.75-49.91)		44 (30.8-48.2)
	M	47	43.30±5.37	58	42.97±5.05	45	43.49±3.78
			44 (29.2-52.8)		44 (28-50.5)		44 (30.3-49)
	F	72	43.41±3.86	46	43.78±3.92	36	42.25±3.95
			44.3 (29.8-49.2)		44 (30.1-50.7)		44 (31-45)
ALT (U/L)	M&F	119	18.61±10.60	104	19.00±31.17	81	14.84±8.56
			15.6 (5.3-45.8)		14.2 (5.6-45.6)		12.9 (4.2-36.9)↓b
	M	47	22.38±12.26	58	21.95±41.08	45	15.47±8.73
			18 (5-52)*		14 (5.5-194.7)↓a		13 (4-18.5)↓b
	F	72	16.16±8.65	46	15.17±7.41	36	14.11±8.34
			14.1 (5.6-41.1)		14 (4.35-35.83)		12.5 (4-17.3)
AST (U/L)	M&F	119	25.14±13.10	104	23.44±17.24	81	24.25±15.97
			23.6 (8.6-51.5)		19.3 (8.3-101.9)a		20.9 (8.3-89.1)
	M	47	27.28±17.13	58	24.74±17.38	45	26.29±19.29
			24 (6.6-108.8)		21.5 (12-106.2)		22 (9.2-33)
	F	72	23.73±9.34	46	21.74±17.10	36	21.69±9.97
			22.8 (8.6-50.4)		18 (8-106.9)		20 (8-25.4)
ALP (U/L)	M&F	119	36.30±45.64	104	42.37±49.82	81	49.85±58.74
			3.9 (0-143.8)		16.9 (0-160.5)		43.9 (0-265.6)
	M	47	36.66±43.49	58	38.43±44.64	45	46.22±59.33
			16 (0-144)		15 (0-129.9)		44 (0-69)
	F	72	36.52±47.47	46	47.24±55.79	36	54.44±58.43
			1.4 (0-155.4)		34 (0-202.9)		54 (0-74.8)
GGT (U/L)	M&F	119	38.13±42.06	104	33.60±28.34	81	37.30±43.08
			23.8 (8.2-178)		26.25 (8.3-135.3)		21.5 (8.9-214.4)
	M	47	47.96±51.94	58	35.12±27.93	45	41.24±47
			27 (8.2-241.6)		27.5 (9.43-147.73)		23 (10.3-57.5)
	F	72	31.73±32.96	46	31.80±29.01	36	32.58±37.8
			22.4 (7.62-178)		23 (5.7-150)		21 (5-49.3)

T-BIL (µmol/L)	M&F	119	6.25±12.53	104	5.97±4.97	81	7.57±13.64
			4.6 (2.9-17.9)		4.25 (1-20.4)		4.9 (1-19.6)
	M	47	6.02±3.96	59	6.43±5.63	45	6.24±4.42
			5 (2-18)		4 (1-22.6)		5 (1-8.5)
	F	72	6.41±15.84	46	5.39±4.03	36	9.25±19.89
			4.1 (1.1-33.6)		4 (1-19.3)		5 (1-18.7)
D-BIL (µmol/L)	M&F	119	1.69±1.13	104	2.07±1.89	81	2.02±1.83
			1.5 (0.3-4.4)		1.6 (0.3-5.8)		1.8 (0.2-6.3)
	M	47	2.00±1.29	59	2.28±2.15	45	1.80±1.55
			2 (1-7.2)*		2 (0-10.7)		2 (0-2.5)
	F	72	1.49±1.00	46	1.91±1.47	36	2.19±2.20
			1.4 (0.1-4.3)		2 (0-6)		2 (0-3.1)
BUN (mmol/L)	M&F	119	4.74±6.66	104	4.03±2.98	81	3.97±2.38
			3.9 (1.9-11.7)		3.6 (1.9-7.9)		3.4 (1.7-10.8)
	M	47	4.60±4.96	58	4.10±3.75	45	4.07±2.72
			4 (2-31)		3 (1.5-19.6)		4 (1.2-5)
	F	72	4.79±7.58	46	3.98±1.54	36	3.89±1.92
			3.9 (1.6-21.3)		4 (2-8)		3 (2-4.8)
CREAT (µmol/L)	M&F	119	84.84±46.72	104	76.89±22.39	81	79.42±37.02
			80 (39-147)		74 (28.1-134.8)		70 (45.2-193.9)
	M	47	85.68±27.41	58	79.59±21.02	45	87.69±46.14
			88 (43.2-199.2)		76 (43.4-145.5)		76 (30.6-103.7)*
	F	72	84.30±56.04	46	73.50±23.79	36	69.08±16.08
			76 (32.1-209.7)		70 (4.5-131.6)		65.5 (49-78.8)b
NA (mmol/L)	M&F	119	138.67±5.05	104	138.09±7.18	81	135.52±7.43
			139.7 (127.7-148.9)		138.1 (117.7-151)		136.8 (114.2-154.3)bc
	M	47	137.89±4.95	58	138.24±8.48	45	136.7±7.92
			139 (128-145)		139 (110-164)		138 (111.8-141)
	F	72	139.23±5.01	46	138.00±5.29	36	134.14±6.58
			139.8 (126.3-149.1)		138 (123.1-149)		135 (114-138.8)bc
K (mmol/L)	M&F	119	4.34±0.57	104	4.50±2.69	81	4.38±0.56
			4.3 (3.2-5.5)		4.21 (3.2-6)		4.3 (3.2-5.7)
	M	47	4.38±0.61	104	4.19±0.66	81	4.21±0.60
			4 (3-5.8)		4 (3-5.5)		4 (3-5.9)
	F	72	4.34±0.61	58	4.83±4.00	45	4.20±0.59
			4.4 (3.1-5.6)		4 (3-26.6)		4 (3-5.9)
CL (mmol/L)	M&F	119	96.89±7.93	104	97.53±8.05	81	97.70±9.96
			96.4 (82.5-111.7)		97.8 (81-110.8)		97.5 (78.5-124.2)
	M	47	95.49±7.46	58	97.74±9.06	45	98±10
			96 (81.2-108.8)		97.5 (76-125.2)		100 (76.7-104)
	F	72	97.82±8.14	46	97.26±6.79	36	97.31±10.02
			96.6 (85-114.9)		98 (84.2-111.7)		96.5 (78-102.8)

Among the measured analytes, total protein (TP), serum albumin (ALB), γ-glutamyltransferase (GGT), alkaline phosphatase (ALP), total bilirubin (T-BIL), direct bilirubin (D-BIL), blood urea nitrogen (BUN), potassium (K), and chloride (CL) are not significantly affected by advancement in age for the studied adults and geriatrics of Taita-Taveta County, Kenya (ρ > 0.05). However, the other measured analytes including random blood glucose (RBS), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (CREAT), and sodium (NA) are significantly affected by advancement in age for adults and geriatrics of Taita-Taveta County, Kenya (ρ > 0.05).

A Kruskal-Wallis H test for random blood glucose (RBS) for the study male and female referent participants was significantly affected by advancement in age ($\chi2$ (2) = 12.113, ρ = 0.002). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant increase in median random blood glucose (RBS) levels between the fifth decade (5.2 (3.82-10.94) mmol/L) with mean rank of 116.41 and the sixth decade (5.6 (4.4-15.73) mmol/L) with mean rank of 143.91 (U = 6604, z = -2.955, ρ = 0.003, r = 0.1836), and between the fifth decade (5.2 (3.82-10.94) mmol/L) with mean rank of 84.62 and the seventh decade onwards (6 (4.4-10.35) mmol/L) with mean rank of 109.91 (U = 2439.5, z = -2.825, ρ = 0.005, r = 0.2094). However, there was no significant difference in the median random blood glucose (RBS) levels between the sixth decade and the seventh decade onwards.

A Kruskal-Wallis H test for random blood glucose (RBS) for all the study female referent participants was significantly affected by advancement in age ($\chi2$ (2) = 9.057, ρ = 0.011). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant increase in median random blood glucose (RBS) levels between the fifth decade (5 (4-11) mmol/L) with mean rank 66.66 and the sixth decade (6 (4-16) mmol/L) with mean rank of 84.65 (U = 1971, z = -2.613, ρ = 0.009, r = 0.2155). However, there was no statistically significant difference in the female median random blood glucose (RBS) levels between the fifth decade with mean rank of 55.36 and the seventh decade onwards (z = -2.281, ρ = 0.023), and between the sixth decade and the seventh decade onwards (z = -0.065, ρ = 0.948). A Kruskal-Wallis H test for random blood glucose (RBS) for the study male referent participants was not statistically significantly affected by advancement in age ($\chi2$ (2) = 1.167, ρ = 0.558). There was therefore no need for a follow-up pairwise comparison using Mann-Whitney U test with adjusted ρ-value.

A Kruskal-Wallis H test for alanine aminotransferase (ALT) activity for the study combined male and female referent participants was significantly affected by advancement in age ($\chi2$ (2) = 9.949, ρ = 0.007). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant decrease in median alanine aminotransferase (ALT) activity between the fifth decade (15.6 (5.3-45.8) U/L) with mean rank of 110.83 and the seventh decade onwards (12.9 (4.21-36.88) U/L) with mean rank of 85.33 (U = 3590.5, z = -3.059, ρ = 0.002, r = 0.2163). However, there was no significant difference in the median alanine aminotransferase (ALT) activity between the fifth decade with mean rank of 118.03 and the sixth decade with mean rank of 105.10 (z = -1.494, ρ = 0.135), and between the sixth decade with mean rank of 99.54 and the seventh decade onwards with mean rank of 84.60 (z = -1.882, ρ = 0.060).

A Kruskal-Wallis H test for alanine aminotransferase (ALT) activity for the study male referent participants was significantly affected by advancement in age ($\chi2$ (2) = 13.379, ρ = 0.001). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant decrease in median alanine aminotransferase (ALT) levels between the fifth decade (18 (5-52 U/L) with mean rank of 61.65 and the sixth decade (14 (5.48-194.7) U/L) with mean rank of 45.99 (U = 956.5, z = -2.625, ρ = 0.009, r = 0.2562) and between the fifth decade (18 (5-52 U/L) with mean rank of 55.84 and the seventh decade onwards (13 (4-18.49) U/L) with mean rank of 36.74 (U = 618.5, z = -3.437, ρ = 0.001, r = 0.3583). However, there was no significant difference in the median alanine aminotransferase (ALT) levels between the sixth decade with mean rank of 55.55 and the seventh decade onwards with mean rank of 47.42 (z = -1.374, ρ = 0.384). A Kruskal-Wallis H test for alanine aminotransferase (ALT) for the study female referent participants was not significantly affected by advancement in age ($\chi2$ (2) = 2.436, ρ = 0.296). There was therefore no need for a follow-up pairwise comparison using Mann-Whitney U test with adjusted ρ-value.

A Kruskal-Wallis H test for aspartate aminotransferase (AST) activity for the study combined male and female referent participants was significantly affected by advancement in age ($\chi2$ (2) = 7.047, ρ = 0.029). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant decrease in median aspartate aminotransferase (AST) activity between the fifth decade (23.6 (8.6-51.5) U/L) with mean rank of 122.51 and the seventh decade onwards (19.3 (8.3-101.9) U/L) with mean rank of 99.97 (U = 4937, z = -2.603, ρ = 0.009, r = 0.1743). However, there was no significant difference in the median aspartate aminotransferase (ALT) levels between the fifth decade with mean rank of 105.93 and the sixth decade with mean rank of 92.52 (z = -1.608, ρ = 0.108), and between the sixth decade with mean rank of 90.30 and the seventh decade onwards with mean rank of 96.460 (z = -0.776, ρ = 0.438).

A Kruskal-Wallis H test for aspartate aminotransferase (AST) activity for the study female referent participants was not significantly affected by advancement in age ($\chi 2$ (2) = 4.968, ρ = 0.083). Further, a Kruskal-Wallis H test for aspartate aminotransferase (AST activity for the study male referent participants was not significantly affected by advancement in age ($\chi 2$ (2) = 3.799, ρ = 0.150). There was therefore no need for a follow-up of separate male and female aspartate aminotransferase (AST) activity pairwise comparison using Mann-Whitney U test with adjusted ρ-value.

A Kruskal-Wallis H test for creatinine (CREAT) level for the study female referent participants was significantly affected by advancement in age ($\chi 2$ (2) = 6.417, ρ = 0.040). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant decrease in median creatinine (CREAT) levels between the fifth decade (76 (32.09-209.65) μmol/L) with mean rank of 59.72 and the seventh decade onwards (65.5 (49-78.75) μmol/L) with mean rank of 44.07 (U = 920.5, z = -2.488, ρ = 0.014, r = 0.2394). However, there was no significant difference in the median creatinine (CREAT) levels between the fifth decade with mean rank of 62.48 and sixth decade with mean rank of 54.84 (z = -1.184, ρ = 0.236) and between the sixth decade with mean rank of 44.89 and the seventh decade onwards with mean rank of 37.17 (z = -1.458, ρ = 0.145).

A Kruskal-Wallis H test for creatinine (CREAT) level for the study combined male and female referent participants was not significantly affected by advancement in age ($\chi 2$ (2) = 5.600, ρ = 0.061). Further, a Kruskal-Wallis H test for creatinine (CREAT) for the study male referent participants was not significantly affected by advancement in age ($\chi 2$ (2) = 2.406, ρ = 0.300). There was therefore no need for a follow-up pairwise comparison for combined male and female referents, and male only referents using Mann-Whitney U test with adjusted ρ-value.

A Kruskal-Wallis H test for sodium (NA) level for the study combined male and female referent participants was significantly affected by advancement in age ($\chi 2$ (2) = 13.386, ρ = 0.001). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant decrease in median sodium (NA) levels between the fifth decade (139.7 (127.7-148.9) mmol/L) with mean rank of 112.40 and the seventh decade onwards (136.8 (114.2-154.26) mmol/L) with mean rank of 83.01 (U = 3403, z = -3.526, ρ = 0.000, r = 0.2493), and between the sixth decade (138.1 (117.69-151.04) mmol/L) with mean rank of 102.32 and the seventh decade onwards (136.8 (114.2-154.26) mmol/L) with mean rank of 81.03 (U = 3242.5, z = -2.683, ρ = 0.007, r = 0.1973. However, there was no significant difference in the median sodium (NA) levels between the fifth decade with mean rank of 116.25 and the sixth decade with mean rank of 107.13 (z = -1.053, ρ = 0.292).

A Kruskal-Wallis H test for sodium (NA) level for the study female referent participants was significantly affected by advancement in age ($\chi 2$ (2) = 16.865, ρ = 0.000). Pairwise comparisons using Mann-Whitney U test with adjusted significant ρ-value of less than 0.0167 indicates that there was a significant decrease in median sodium (NA) levels for female referents between the fifth decade (139.75 (126.31-149.08) mmol/L) with mean rank of 63.14 and the seventh decade onwards (135 (114-138.75) mmol/L) with mean rank of 37.22 (U = 674, z = -4.064, ρ = 0.000, r = 0.3911), and between the sixth decade (138 (123.05-149) mmol/L) with mean rank of 55.26 and the seventh decade onwards (135 (114-138.75) mmol/L) with mean rank of 47.80 (U = 533.5, z = -2.759, ρ = 0.006, r = 0.3947). However, there was no significant difference in the median sodium (NA) levels for female referents between the fifth decade with mean rank of 62.61 and the sixth decade with mean rank of 54.63 (z = -1.240, ρ = 0.215).

A Kruskal-Wallis H test for sodium (NA) level for the study male referent participants was not significantly affected by advancement in age ($\chi 2$ (2) = 1.888, ρ = 0.389). There was therefore no need for a follow-up for sodium (NA) pairwise comparison using Mann-Whitney U test with adjusted ρ-value of less than 0.0167 (Table 4).

Results on the effect of gender on the developed reference interval limits indicate that in the fifth decade, the median reference interval limits for alanine aminotransferase (ALT) activity for males (18 (5-52) U/L) with mean rank of 71.71 is significantly higher than that of females (14.1 (5.63-41.1) U/L) with mean rank of 52.35 of Taita-Taveta County, Kenya (U = 1141.5, z = -2.996, ρ = 0.003, r = 0.2747). Further, in the fifth decade, the median reference interval limits for direct bilirubin (D-BIL) levels for males (2 (1-7.2) mmol/L) with mean rank of 69.34 is significantly higher than that of females (1.4 (0.1-4.31) mmol/L) with mean rank of 53.90 of Taita-Taveta County, Kenya (U = 1253, z = -2.535, ρ = 0.011, r = 0.2324). In the seventh decade onwards, the median reference interval limits for creatinine (CREAT) levels for males (76 (30.55-103.65) μmol/L) with mean rank of 45.96 is significantly higher than that of females (65.5 (49-78.75) μmol/L) with mean rank of 34.81 of Taita-Taveta County, Kenya (U = 587, z = -2.120, ρ = 0.034, r = 0.2356) (Table 4).

Results are expressed as mean ± standard deviation (SD), and median and 95% range of the number of subjects indicated in the column labeled N. *ρ < 0.05 when male reference interval limits are significantly different when compared to female reference

interval limits per each age category by Mann-Whitney U test; aρ < 0.0167 when reference interval limits in age range ≥ 55-60 years is significantly different when compared to reference interval limits in age range ≥ 60-70 years, bρ < 0.0167 when reference interval limits in age range ≥ 55-60 years is significantly different when compared to reference interval limits in age range ≥70-95 years, and cρ < 0.0167 when reference interval limits in age range ≥ 60-70 years is significantly different when compared to reference values in age range ≥ 70-95 years by Kruskal-Wallis H test followed by Mann-Whitney U test with Bonferroni correction.

Comparison of developed reference interval limits for liver and kidney function tests and electrolytes for adult and geriatric population of Taita-Taveta County, Kenya with those reported in medical literature

A comparison of the developed reference interval limits for liver and kidney function tests and electrolytes for adult and geriatric population of Taita-Taveta County, Kenya with those reported in medical literature is presented in Table 5. For the liver function tests, results indicate that: the combined male and female lower reference interval limit for random blood glucose (RBS) of the Taita-Taveta population is similar to that of the Canadian separate male and female population while the upper reference interval limit is higher than that of the Canadian population. The combined male and female lower reference interval limit for total protein (TP) of the Taita-Taveta population is lower than that of combined males and females of the Chinese and Canadian population while the upper reference interval limit is similar to that of the Chinese and higher than that of the Canadian population. The combined male and female lower reference interval limit for serum albumin (ALB) of the Taita-Taveta population is lower than that of combined males and females of the Chinese and Canadian population while the upper reference interval limit is similar to that of the Chinese and Canadian population. However, the separate male and female lower reference interval limits for albumin (ALB) reported for Asmara Eritreans while the upper reference interval limit is similar for males and higher for females than that of the combined male and female reference interval limit for Taita-Taveta county population.

Table 5: Comparison of developed reference interval limits for liver and kidney function tests and electrolytes for adult and geriatric population of Taita-Taveta County, Kenya with those reported in medical literature.

Analyte (unit)	Gender	This study RI	Chinese population	Canadian population	Han population	Eritrea population
RBS (mmol/L)	M&F	4.2-10 8				
	F			4.4-5.9↓		
	M			4.2-6.4↓		
TP (g/L)	M&F	57.4-88.5	↑61.9-85.1	↑65-78↓		
	F					
	M					
ALB (U/L)	M&F	33.1-49.7	↑43.4-54.6	↑42-50		
	F					↑41-55↑
	M					↑39-52
ALT (U/L)	M&F					↑9-35
	F	5.9-37	↑9-60↑	↑16-44↑		
	M	4.8-52	↑9-50	↑20-62↑		
AST (U/L)	M&F	8.3-66.5		↑18-39↓		↑13.8-33.2↓
	F					
	M					
ALP (U/L)	M&F	0-147.6	↑49-134↓			↑55-156
	F			↑40-122↓		
	M			↑50-116↓		
GGT (U/L)	M&F					
	F	7.6-160.5	↓7-42↓	↑10-54↓		
	M	9-186.3	↑10-58↓	↑13-109↓		
T-BIL (μmol/L)	M&F	1-19.7				
	F		↑5-23.8↑	↑1.7-17↓		↑6.84-20.52
	M		↑5.9-30.4↑	↑1.7-20.5		↑6.84-28.91↑

D-BIL (µmol/L)	M&F	0-6				
	F	0-6				0-4.28↓
	M	0-6				0-5.13↓
BUN (mmol/L)	M&F	1.8-8.6		1.7-4.3↓		↑2.54-7.86
	F					
	M					
CREAT (µmol/L)	M&F					
	F	34.1-134.8		↑53-88↓		↑61.9-167.9↑
	M	44.3-163.5		↑62-106↓		↑53.0-132.6↓
NA (mmol/L)	M&F	122.2-148.9		↑136-143	↑136-146	
	F					↑134-148
	M					↑135-145
K (mmol/L)	M&F	3.2-5.7		↑3.8-4.9↓	↑3.6-5.2↓	↑3.6-5.3
	F					
	M					
CL (mmol/L)	M&F	81.8-112.3		↓28.8-30.5↓	↑99-110	↑101-113
	F					
	M					

The separate male and female lower reference interval limit for alanine aminotransferase (ALT) of the Taita-Taveta population is lower than that of separate male and female of the Chinese and Canadian population while the upper reference interval limit is similar to that of the Chinese male population but lower than that of the Chinese female population and lower than that of the Canadian separate male and female population. The combined male and female lower reference interval limit for aspartate aminotransferase (AST) of the Taita-Taveta population is lower than that of Canadian and Asmara Eritrean combined male and female population while the upper reference interval limit is higher than that of the Canadian and Asmara Eritrean population.

The combined male and female lower reference interval limit for alkaline phosphatase (ALP) of the Taita-Taveta population is lower than that of Chinese and Asmara Eritrean combined male and female population and Canadian separate male and female population while the upper reference interval limit is lower than that of the Chinese combined and Canadian separate male and female population, respectively, but similar to that of Asmara Eritreans. The combined male and female lower reference interval limit for gamma-glutamyltransferase (GGT) of the Taita-Taveta population is lower than that of the Canadian separate male and female population, lower than that of the male and lower than that of the female Chinese population, respectively, while the upper reference interval limit is higher than that of the Chinese and Canadian separate male and female populations.

The combined male and female lower reference interval limit for total bilirubin (T-BIL) of the Taita-Taveta population is lower than that of the Chinese, Canadian and Asmara Eritrean separate male and female populations while the upper reference interval limit is lower than that of the Chinese separate male and female population, similar to the male and higher than the female Canadian populations, respectively, and lower than the male and similar to the female Asmara Eritreans, respectively. The combined male and female lower reference interval limit for direct bilirubin (D-BIL) of the Taita-Taveta population is similar to that of Asmara Eritreans separate males and females while the upper reference interval limits are lower.

For the kidney function tests, results indicate that: the combined male and female lower reference interval limit for blood urea nitrogen (BUN) of the Taita-Taveta population is similar to that of the Canadian combined male and female population but lower than that of Asmara Eritreans while the upper reference interval limit is higher than that of the Canadian population but similar to that of Asmara Eritreans. The separate male and female lower reference interval limit for creatinine (CREAT) for the Taita-Taveta population is lower than that of the Canadian and Asmara Eritrea male and female population while the upper reference interval limit is higher than that for Canadian male and female population and higher than that of the male and lower than that of the female Asmara Eritreans. The combined male and female lower reference interval limit for sodium (NA) for the Taita-Taveta population is lower than that of

the Canadian, Chinese Han, and Asmara Eritrea separate male and female population, respectively, while the upper reference interval limit are similar to those of Canadian, Chinese Han and Asmara Eritrea separate male and female population.

The combined male and female lower reference interval limit for potassium (K) for the Taita-Taveta population is lower than that of the Canadian, Chinese Han and Asmara Eritrea population, while the upper reference interval limit is higher than that of the Canadian and Chinese Han population but similar to that of Asmara Eritrea population. The combined male and female lower reference interval limit for chloride (CL) for the Taita-Taveta population is higher than that of the Canadian population, but lower than that of Chinese Han and Asmara Eritrea populations while the upper reference interval limit is higher than that of the Canadian population but similar to those of Chines Han and Asmara Eritrea populations.

Chinese population by Mu et al., 2013; Canadian population by Adeli et al., 2015; Chinese Han population by Jia et al., 2015; Asmara, Eritrea population by Achila et al. (2017).

Discussion

Results indicating statistically similar serum biochemistry analytes reference interval limits for the adult and geriatric male and female population of Taita-Taveta County for random blood glucose (RBS mmol/L), total protein (TP g/L), albumin (ALB g/L), aspartate aminotransferase (AST U/L), alkaline phosphatase (ALP U/L), total bilirubin (T-BIL µmol/L), direct bilirubin (D-BIL µmol/L), blood urea nitrogen (BUN mmol/L), sodium (NA mmol/L), chloride (CL mmol/L), and potassium (K mmol/L) imply that these parameters are gender independent. The developed gender independent serum biochemistry reference interval limits for the adult and geriatric male and female population of Taita-Taveta County, Kenya is 4.2-10.8 mmol/L for random blood glucose (RBS), 57.4-88.5 g/L for total protein (TP), 33.0-49.5 g/L for serum albumin (ALB), 8.3-66.5 U/L for aspartate aminotransferase (AST), 0-147.6 U/L for alkaline phosphatase (ALP), 1-19.7 µmol/L for total bilirubin (T-BIL), 1.8-8.6 mmol/L for blood urea nitrogen (BUN), 122.2-148.9 mmol/L for sodium (NA), 3.2-5.7 mmol/L for potassium (K), and 81.8-112.3 mmol/L for chloride (CL).

These results are in agreement with those reported by Mu et al. (2013) and Adeli et al. (2015) who reported gender independent reference interval limits for albumin (ALB) (for 20-79 and 55-79 years old, respectively) and total protein (TP) (for 20-79 years old). Mu et al. (2013) and Achila et al. (2017) reported gender independent reference interval limits for alkaline phosphatase (ALP) (for 20-79 and 60-80 years old, respectively). Adeli et al. (2015) and Achila et al. (2017) reported gender independent reference interval limits for aspartate aminotransferase (AST) (for 55-79 and 60-80 years, respectively) and blood urea nitrogen (BUN) (for 60-79 and 60-80 years old, respectively). Adeli et al. (2015), Jia et al. (2015) and Achila et al. (2017) reported gender independent reference interval limits for potassium (K) (for 6-79, 20-80 and 60-80 years old, respectively) and chloride (CL) (for 6-79, 20-80 and 60-80 years old, respectively). Adeli et al. (2015) and Jia et al. (2015) reported gender independent reference interval limits for sodium (NA) (for 50-79 and 20-80 years old, respectively).

In contrast, these results disagree with those reported by Adeli et al. (2015), Jia et al. (2015) and Achila et al. (2017) who reported gender dependent reference interval limits for sodium (NA) (for 50-79, 20-80 and 60-80 years old, respectively), alkaline phosphatase (ALP) (for 22-79 and 60-80 years old, respectively), and albumin (ALB) (55-79 and 60-80 years old, respectively). Mu et al. (2013), Adeli et al. (2015) and Achila et al. (2017) reported gender dependent reference interval limits for total bilirubin (T-BIL) (for 49-79 and 60-80 years old, respectively). Achila el al. (2017) reported gender dependent reference interval limits for direct bilirubin (D-BIL) (for 60-80 years old).

Results indicating statistically different serum biochemistry analytes reference interval limits for the adult and geriatric male and female population for ALT (U/L), GGT (U/L), D-BIL (µmol/L), and CREAT (µmol/L) of Taita-Taveta County, Kenya imply that these parameters are gender dependent. The developed gender dependent serum biochemistry reference intervals for adults and geriatric male and female population of Taita-Taveta County, Kenya for ALT is 15 (4.8-52) U/L for males and 13.5 (5.9-37) U/L for females, GGT is 27 (9-186.3) U/L for males and 21.5 (8.8-160.5) U/L for females, D-BIL is 2 (0-6) µmol/L for males and 4 (0-6) µmol/L for females, and CREAT is 77.5 (44.3-163.5) µmol/L for males and 72 (34.1-134.8) µmol/L for females; three of them except D-BIL are higher in males than females.

These results agree with those reported by Adeli et al. (2015) and Mu et al. (2013) who reported gender dependent reference interval limits for alanine transaminase (ALT) (20-79 and 50-79 years, respectively) and gamma-glutamyltransferase (GGT) (36-79 years). Adeli et al. (2015) reported gender dependent reference interval limits for creatinine (CREAT) (16-79 years). In contrast, Achila et al. (2017) reported gender independent reference interval limits for alanine transaminase (ALT).

The observed increase of random blood glucose (RBS) and decreased creatinine (CREAT) level with advancement age from the fifth decade to the sixth decade and plateauing thereafter and in the seventh decade onwards, respectively, especially in females indicates that these parameters are age dependent. This observation could be due to age related decrease in liver and kidney

function resulting in elevated random blood glucose leading to increased insulin levels which leads to insulin resistance. Insulin resistance results in a decrease in glucose tolerance due to higher total percent adipose mass and visceral fat accumulation which contributes to insulin-signaling imbalances between liver and adipose cells (Adeli et al. 2015). An elevated hemoglobin level is a biomarker for high levels of iron in humans which is associated with increased activity of alanine transaminase (ALT) (Chen et al. 2010). The capacity of insulin receptors is reduced in geriatrics (Palmer, 2017). The observed decrease in creatinine (CREAT) levels with advancement in age in the seventh decade onwards is due to reduced muscle mass due to increased muscle mass necrosis and decreased creatine synthesis due to either disease or non-disease processes (Palmer, 2017). The decrease in sodium (NA) concentration with advancement in age in the sixth decade onwards in females and combined males and females could be due to consumption of low quantities of diets poor in sodium (NA) levels (Charlton and Donald, 2001). Creatinine clearance decreases with age and more so in geriatrics (Palmer, 2017).

The decrease in the activity of alanine transaminase (ALT) in the sixth decade and plateauing upto the seventh decade onwards relative to the fifth decade could be due to the decreased liver function due to muscle necrosis and decreased protein synthesis including alanine transaminase (ALT) with age especially in geriatrics (Palmer, 2017). Palmer (2017) reported increased alanine transaminase (ALT) activity in the fifth decade which decreases in the sixth decade to the levels of young adults. The decreased aspartate transaminase (AST) activity in the sixth decade relative to the fifth decade and its reversion to the level of the fifth decade in the seventh decade onwards is supported by Palmer (2017) report indicating increases in aspartate transaminase (AST) activity between 60 to 90 years. This may be due to uptake of diets low in or lacking vitamin B6 in their sixth decade as reported by Yanagita et al. (2020) reverting to the uptake of normal diets in the seventh decade onwards. These results contrast age independent reference interval limits for alanine transaminase (ALT) and aspartate transaminase (AST) reported by Mu et al. (2013) and Achila et al. (2017) for Chinese and Eritrea population. Further, Adeli et al. (2015) reported age independent reference interval limits for glucose (GLU) (males [55-79 years]; females [40-79 years]), alanine transaminase (ALT) (males [50-79 years]; females [50-79 years]), aspartate transaminase (AST) (males and females [55-79 years]), creatinine (CREAT) (males [16-79 years]; females [17-79 years]), and sodium (NA) (male and females [50-79 years]) levels for Canadian population.

Significant sex differences were seen in the median and 95% range for creatinine (CREAT), direct bilirubin (D-BIL) and alanine transaminase (ALT) in male and female adults of Taita-Taveta population in the fifth decade with males having higher values than females. This observation could be due to the greater muscle mass and hemoglobin in males compared to females in the fifth decade; creatinine is a catabolic product of muscles and direct bilirubin is a catabolic product of hemoglobin. The higher alanine transaminase (ALT) activity in males compared to females is related to the higher hemoglobin (HB) and body mass index (BMI) of adult males relative to adult females in this decade. The high hemoglobin in males compared to females is due to a direct stimulatory effect of androgen (testosterone) on erythropoietin production in the kidneys in adult men and an inhibitory effect of estrogen on the bone marrow in adult females and increase in skeletal muscle cells and hence muscle tissue in males (Bimerew et al., 2018). In addition to hormonal influences, iron deficiency due to blood loss during menstruation could also be a factor (Bimerew et al., 2018).

The differences in the lower and upper limits between the developed serum biochemistry reference interval limits for adults and geriatrics of Taita-Taveta population relative to those previously reported in literature could be due to several factors. These factors include inadequate dietary intake, genetics, race, ethnicity, lifestyles such as smoking, taking of herbal medicines contaminated with toxic compounds and heavy metals, living in environments infested with parasitic infections such as malaria, helminthes and environments polluted with heavy metals, altitude above sea level, geographical location, methods and instrumentation used in measuring analytes, and the robustness of the inclusion and exclusion criteria.

This study had several limitations. One of the limitations of this study is that the age stratification of reference interval limits was developed using a sample size of less than 120 referent individuals for each age category and sex as recommended by EP28 A3c guidelines. Secondly, the healthy status of the referent individuals was based on self-reported information through a questionnaire which was not validated clinically by laboratory reports; therefore, some referent individuals may have been recruited with subclinical conditions or infections which may have affected the measured biochemistry analytes. Further, the medical conditions associated with the elderly population which may affect the measured analytes may not have been thoroughly screened through laboratory medicine requests and reports. In addition, some factors such as dietary habits, history of smoking or alcoholism, altitude, among others, which affect some of measured analytes were not collected and analysed. Finally, ultrasonography was not used to confirm the presence or absence of fatty liver disease (FLD) or non-alcoholic fatty liver disease (NAFLD).

In conclusion, this study has established age and sex specific reference interval limits for serum biochemistry analytes for adult

and geriatric population of Taita-Taveta County, Kenya, which are different from those previously reported in medical literature; it is therefore inappropriate to adopt and use reference interval limits for serum biochemistry analytes provided by the manufacturers without verification. These developed reference interval limits for adult and geriatric population of Taita-Taveta County, Kenya, should be adopted and used for accurate diagnosis, treatment and monitoring the performance of the treatment regimen of serum biochemistry analytes related diseases.

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