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Original Article

Low Dose Aspirin Therapy And Renal Function In A Group Of Elderly Patients In The Tropics

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ABSTRACT

Aim; To determine whether low dose aspirin has any deleterious effects on renal functions in elderly Nigerian patients **Methods;** This is a prospective pilot study of 30 adult Nigerians older than 60 years with various chronic ailments necessitating the use of low dose aspirin. Patients gave their consent and institutional ethical clearance was obtained. Each patient's baseline samples at enrolment (before commencing aspirin) served as control and subsequent weekly samples were compared. The weekly mean of each sex group was calculated and difference of means from baseline mean determined. Relative Risk and 95% Confidence Interval was subsequently calculated using the method described by Newcombe Wilson . **Results;** Majority (86.67%) had their basal renal functions in Chronic Kidney Diseases stages 1 and 2. The mean weekly serum and urinary electrolytes, urea, creatinine and uric acid parameters when compared with the corresponding baseline parameters did not change and the confidence interval calculated did not show any statistical significance. Also unlike previous studies, anaemia and hypoalbuminaemia did not affect renal function parameters. However use of low dose aspirin (75mg daily) had a negative effect on the renal function of those on concomitant diuretics and angiotensin converting enzyme inhibitors (ACEI) (Confidence interval showed statistical significance). **Conclusions;** This study only showed deleterious effect of short term, low dose aspirin (75mg daily) on kidney functions in elderly Nigerian patients that were on concomitant diuretics and ACEI. However, caution should also be exercised when dealing with those in renal stages 3-5 and the very elderly age ≥ 80 years.

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1. Introduction

Aspirin is easily available across the counter in most countries including the developing ones such as Nigeria. When indicated, it is a common practice to maintain patients on long term low dose aspirin without assessing their renal status prior to initiation of treatment.

Low dose aspirin is increasingly being used as an antiplatelet to prevent thrombosis and other fatal cardiovascular outcomes in at risk patients [1, 2]. Elderly patients not only form the major bulk of these at risk patients [1, 2], they also do readily succumb to the deleterious effects of aspirin on renal functions. [3-5]. Various studies in the elderly, in Caucasian populations, had shown

that 1-2 weeks of low dose aspirin (75mg – 325mg/day) caused significant decreases in both creatinine and uric acid clearances, as well as elevations of serum creatinine and uric acid.[6–8] These parameters improved on withdrawal of the drug but the decline in glomerular filtration rate however persisted 3 weeks post treatment [6–8]. Thus, long term aspirin administration may have a clinically important deleterious effect on renal function. [8] This study was therefore undertaken as a pilot study to ascertain whether low dose aspirin compromises renal function amongst Nigerians, and if so, alert practicing physicians on the need to show discretion when prescribing this drug.

2. Materials and Methods

This was a cohort of 30 elderly patients (age ≥ 60 years) of Ladoko Akintola University of Technology Teaching Hospital, South – West Nigeria, comprising of 16 male and 14 female patients at the commencement of the study. The United Nations definition of elderly person was used[9]. Institutional ethical

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clearance was obtained and all the patients gave informed consent (verbal and written). The patients were those on long term care and new patients with various medical conditions necessitating the use of low dose aspirin, but in stable clinical conditions throughout the study. Each patient was followed up for a period of 6 weeks with a weekly clinic appointment.

Excluded from the study were subjects with a history of active peptic ulcer, gastro intestinal bleeding, chronic liver diseases, hyperuricaemia, serum creatinine > 1.5mg/dl (132.6 µmol/L), significant history of alcohol consumption, or recent use of anticoagulants, aspirin or non-steroidal anti-inflammatory drugs (NSAIDs). Patients were put on moderate protein intake (0.6-0.8/kg body weight) with the assistance of the dieticians a week prior to the commencement of the study and this was maintained throughout the 6 weeks study. Status quo was maintained for all other drugs (dosages unchanged), including diuretics. Patients who dropped out of the study were included in the calculations till their exit. The study was over a period of 12 months from January to December 2008.

Blood and 24 hour urine were collected before the first dose of aspirin. Aspirin 75mg/day was administered orally after breakfast for 2 weeks and then stopped. Follow-up then continued for a further 4 weeks.

Blood and 24 hour urine were collected at the end of each treatment week and the 4 consecutive week's follow-up: subjects were taught how to collect their 24 hour urine prior to their clinic day when the blood will be collected. After an overnight fast, 10ml of venous blood was collected at the ante cubital fossa in the sitting position without stasis: 5mls of the blood was put into lithium heparinised bottle and the remaining 5mls into a plain bottle. Serum was obtained after clotting and centrifugation at 3500r.p.m for 10 minutes and immediately stored at -20°C until they were analyzed. Sodium and potassium were analyzed using flame emission photometry (corning 410c machine), bicarbonate by method of back titration and chloride by rapid precision method[10].

Serum creatinine, blood urea nitrogen, uric acid and albumin were analysed by standard methods of Jaffes reaction[11], modified Berthelot[12], enzymatic urease[13], and bromocresol green[14] respectively. Urinary creatinine and uric acid clearances were evaluated by 24hr urine collection for creatinine and uric acid clearances.

2.1. Statistics

Data entry was into standard Pro-forma and statistical analysis was performed. Each patient's baseline samples at enrolment (before commencing aspirin) served as control and subsequent weekly samples were compared. The weekly mean of each sex group was calculated and difference of means from baseline mean determined. Relative Risk (RR) and 95% Confidence Interval (CI) was subsequently calculated using the method described by Newcombe Wilson.[15]

3. Results

A total of 30 subjects participated in this preliminary study. There were 14 (46.7%) females and 16 (53.3%) males with age range between 60 – 88 years and mean ages of 68.44years (+ 8.16) and 70.43 years (+ 9.09) for males and females respectively.

Table I shows the clinical data of the patients. 12 (40%) of the patients had more than one diagnosis. Systemic hypertension was the commonest diagnosis accounting for 18 (60.0%). Hypertension and diabetes mellitus co-existed in 7 (23.3%) of the study participants. All the patients were on multiple drugs with 28 (93.3%) being on diuretics.

Seventeen (56.7%) of the patients were on antihypertensive drugs (excluding thiazides and angiotensin converting enzyme inhibitors). Twelve (40%) were on Angiotensin converting enzyme inhibitors (ACEI).

Table II shows the stages of renal function based on the National Kidney Function/ DOQI guideline: 86.67% had their basal renal function in stages 1 and 2 based on CrCl.

Table Clinical Data

*Diagnosis	No. of patients	%
Systemic Hypertension	18	60.0
Congestive Cardiac Failure	03	10
Diabetes Mellitus	06	20
Peripheral artery disease	02	16.7
Carotid Aneurysm	05	3.3
Ischemic CVD	01	6.7
Parkinson disease	02	6.7
Obesity	01	3.3
Background COPD	03	10
**Drugs		
Diuretics	28	93.3
Anti BPH (& receptor blocker)	01	3.3
Anti-hypertensives	17	56.7
(excluding Thiazides & ACEI)	02	6.7
Digoxin	05	16.7
OHA	02	6.7
Insulin	12	40.0
ACEI		
LEGEND:		

*Some patients had multiple diagnoses

**All the patients were on multiple drugs

CVD - Cerebrovascular disease.

COPD - Chronic Obstructive Pulmonary Disease

BPH - Benign Prostatic Hypertrophy

OHA - Oral Hypoglycaemic Agents

ACEI - Angiotensin Converting Enzyme Inhibitors

TABLE II
NKF/DOQI CLASSIFICATION OF PATIENTS IN THIS STUDY.

GFR (ml/min)	MALE	FEMALE	%
≥90	CrCl%	CrCl%	17(56.7)
60-89	13(43.3)	4(13.3)	9(30.0)
30-59	3(10.0)	6(20.0)	4(13.3)
15-29		4(13.3)	
<15			

KEY:
GFR- GLOMERULAR FILTRATION RATE
CrCl- CREATININE CLEARANCE

TABLE III. COMPARISON OF WEEKLY PARAMETERS WITH THE BASELINE PARAMETERS MALES

Parameters	Weeks (n)	Mean	SD	DOM	C.I	SIGNIFICANCE
*Serum Potassium (mmol/L)	Wk 0 (16)	3.506	0.377			
	Wk 1 (16)	3.413	0.453	0.0938	-0.21 - 0.39	NS
	Wk 2 (15)	3.567	0.387	-0.0604	-0.34 - 0.22	NS
	Wk 3 (13)	3.615	0.456	-0.109	-0.43 - 0.21	NS
	Wk 4 (12)	3.725	0.277	-0.219	-0.48 - 0.05	NS
	Wk 5 (12)	3.575	0.311	-0.0687	-0.34 - 0.21	NS
Serum Urea	Wk 0 (16)	6.475	3.912			
	Wk 1 (16)	6.038	3.318	0.438	-2.18 - 3.06	NS
	Wk 2 (15)	5.093	1.487	1.382	-0.82 - 3.58	NS
	Wk 3 (13)	5.108	1.278	1.367	-0.96 - 3.69	NS
	Wk 4 (12)	4.792	1.391	1.683	-0.75 - 4.12	NS
	Wk 5 (12)	5.000	1.109	1.475	-0.93 - 3.88	NS
Plasma Albumin	Wk 0 (16)	34.313	6.935			
	Wk 1 (16)	34.250	8.218	0.0625	-5.43 - 5.55	NS
	Wk 2 (15)	33.733	6.798	0.579	-4.47 - 5.63	NS
	Wk 3 (13)	34.692	8.351	-0.380	-6.20 - 5.44	NS
	Wk 4 (12)	34.917	7.280	-0.604	-6.16 - 4.96	NS
	Wk 5 (12)	36.0833	7.787	-1.771	-7.51 - 3.97	NS
Urinary uric acid	Wk 0 (16)	36.167	7.918	-1.854	-7.64 - 3.93	NS
	Wk 0 (16)	1.184	0.318			
	Wk 1 (16)	1.233	0.236	-0.049	-0.25 - 0.15	NS
	Wk 2 (15)	1.234	0.273	-0.050	-0.27 - 0.17	NS
	Wk 3 (13)	1.220	0.224	-0.036	-0.25 - 0.18	NS
	Wk 4 (12)	1.270	0.195	-0.086	-0.30 - 0.13	NS
Urinary Creatinine	Wk 5 (12)	1.332	0.260	-0.148	-0.38 - 0.08	NS
	Wk 6 (12)	1.350	0.236	-0.167	-0.39 - 0.06	NS
	Wk 0 (16)	1341.56	297.02			
	Wk 1 (16)	1401.88	316.24	-60.32	-281.83 - 161.19	NS
	Wk 2 (15)	1368.40	209.36	-26.84	-216.81 - 163.13	NS
	Wk 3 (13)	1307.62	208.88	33.94	-166.44 - 234.32	NS
Volume of Urine (ml)	Wk 4 (12)	1468.50	363.93	-126.94	-383.63 - 129.75	NS
	Wk 5 (12)	1455.75	271.90	-114.19	-339.21 - 110.83	NS
	Wk 6 (12)	1513.75	376.40	-172.19	-433.52 - 89.14	NS
	Wk 0 (16)	1048.38	275.20			
	Wk 1 (16)	917.19	317.46	131.19	-83.32 - 345.70	NS
	Wk 2 (15)	1112.33	286.74	-63.95	-270.37 - 142.47	NS
Plasma Creatinine	Wk 3 (13)	1075.39	273.03	-27.01	-237.11 - 183.09	NS
	Wk 4 (12)	955.00	363.41	93.38	-154.31 - 341.07	NS
	Wk 5 (12)	991.25	314.77	57.13	-172.55 - 286.81	NS
	Wk 6 (12)	948.33	244.93	100.05	-106.25 - 306.35	NS
	Wk 0 (16)	91.06	18.67			
	Wk 1 (16)	89.56	17.95	1.50	-11.72 - 14.72	NS
Plasma Creatinine	Wk 2 (15)	81.60	22.62	9.46	-5.73 - 24.65	NS
	Wk 3 (13)	84.77	13.40	6.29	-6.38 - 18.96	NS
	Wk 4 (12)	80.83	10.94	10.23	-2.22 - 22.68	NS
	Wk 5 (12)	85.25	10.02	5.81	-6.44 - 18.06	NS
	Wk 6 (12)	84.17	14.56	6.89	-6.50 - 20.28	NS

Plasma Uric acid	Wk 0 (16)	0.328	0.0852			
	Wk 1 (16)	0.324	0.0497	0.0032	-0.05 - 0.05	NS
	Wk 2 (15)	0.320	0.0470	0.0076	-0.04 - 0.06	NS
	Wk 3 (13)	0.313	0.0488	0.0151	-0.04 - 0.07	NS
	Wk 4 (12)	0.333	0.0462	-0.0055	-0.06 - 0.05	NS
	Wk 5 (12)	0.333	0.0454	-0.0057	-0.06 - 0.05	NS
	Wk 6 (12)	0.322	0.0429	0.0053	-0.05 - 0.06	NS
Creatinine clearance	Wk 0 (16)	106.913	24.266			
	Wk 1 (16)	97.869	22.533	9.044	-7.86 - 25.95	NS
	Wk 2 (15)	117.707	20.807	-10.794	-27.45 - 5.86	NS
	Wk 3 (13)	118.254	20.654	-11.341	-28.76 - 6.07	NS
	Wk 4 (12)	113.325	21.503	-6.412	-24.57 - 11.75	NS
	Wk 5 (12)	114.217	23.317	-7.304	-26.04 - 11.43	NS
	Wk 6 (12)	115.092	22.500	-8.179	-26.65 - 10.30	NS
Uric acid clearance	Wk 0 (16)	3.010	1.353			
	Wk 1 (16)	2.475	1.135	0.5438	-0.36 - 1.45	NS
	Wk 2 (15)	3.067	1.095	-0.0479	-0.96 - 0.86	NS
	Wk 3 (13)	2.931	0.893	0.0878	-0.81 - 0.99	NS
	Wk 4 (12)	2.567	1.056	0.4518	-0.52 - 1.42	NS
	Wk 5 (12)	2.833	1.102	0.1858	-0.80 - 1.17	NS
	Wk 6 (12)	2.775	0.778	0.2438	-0.66 - 1.14	NS

*Potassium - Initial marginal rise in serum potassium by 1st week, however, by 2nd week, the mean level dropped below the baseline, maximal by week 4.

Parameters	Weeks (n)	Mean	SD	DOM	C.I	SIGNIFICANCE
Potassium (mmol/L)	Wk 0 (14)	3.536	0.680			
	Wk 1 (14)	3.743	0.595	-0.207	-0.70 - 0.29	NS
	Wk 2 (14)	3.557	0.643	-0.021	-0.54 - 0.49	NS
	Wk 3 (13)	3.331	0.715	0.205	-0.35 - 0.76	NS
	Wk 4 (13)	3.562	0.519	-0.026	-0.51 - 0.46	NS
	Wk 5 (13)	3.600	0.607	-0.064	-0.58 - 0.45	NS
	Wk 6 (13)	3.777	0.537	-0.241	-0.73 - 0.25	NS
	Wk 0 (14)	5.014	2.392			
	Wk 1 (14)	5.357	2.314	-0.343	-2.17 - 1.49	NS
	Wk 2 (14)	5.186	1.942	-0.171	-1.86 - 1.52	NS
	Wk 3 (13)	5.031	2.073	-0.017	-1.80 - 1.76	NS
	Wk 4 (13)	5.562	4.351	-0.547	-3.30 - 2.21	NS
	Wk 5 (13)	4.677	2.034	0.337	-1.43 - 2.10	NS
Wk 6 (13)	4.931	1.977	0.084	-1.66 - 1.83	NS	
Albumin	Wk 0 (14)	35.214	8.859			
	Wk 1 (14)	34.000	8.067	1.214	-5.37 - 7.80	NS
	Wk 2 (14)	34.500	8.564	0.714	-6.06 - 7.48	NS
	Wk 3 (13)	35.385	9.377	-0.170	-7.40 - 7.06	NS
	Wk 4 (13)	34.539	8.540	0.676	-6.23 - 9.58	NS
	Wk 5 (13)	35.692	7.825	-0.478	-7.12 - 6.17	NS
	Wk 6 (13)	34.923	6.238	0.291	-5.83 - 6.41	NS
	Wk 0 (14)	1.551	0.714			
	Wk 1 (14)	1.567	0.766	-0.015	-0.59 - 0.56	NS
	Wk 2 (14)	1.586	0.735	-0.034	-0.60 - 0.53	NS

Weekly Parameters	Baseline Serum Albumin P-Value (95% C.I)	Baseline PCV P-Value (95% C.I)	Use of ACEI P-Value (95% C.I)
Baseline Plasma Urea	0.676 (-3.047 - 2.004)	0.307 (-7.497 - 2.447)	0.041 (0.103 - 4.801)
Week 1 Plasma Urea	0.539 (-2.830 - 1.513)	0.429 (-6.016 - 2.631)	0.026 (0.288 - 4.287)
Week 2 Plasma Urea	0.425 (-0.789 - 1.818)	0.760 (-2.974 - 2.196)	0.085 (-0.160 - 2.323)
Week 3 Plasma Urea	0.370 (-0.766 - 1.983)	0.254 (-3.986 - 1.103)	0.011 (0.418 - 2.844)
Week 4 Plasma Urea	0.300 (-1.313 - 4.076)	0.739 (-5.835 - 8.110)	0.027 (0.418 - 2.844)
Week 5 Plasma Urea	0.605 (-1.031 - 1.729)	0.641 (-4.299 - 2.699)	0.143 (-0.351 - 2.279)
Week 6 Plasma Urea	0.220 (0.522 - 2.152)	0.678 (-4.197 - 2.780)	0.039 (0.075 - 2.573)
Baseline Plasma Creatinine	0.828 (-12.436 - 15.419)	0.076 (-50.038 - 2.610)	0.031 (1.407 - 27.022)
Week 1 Plasma Creatinine	0.715 (-10.908 - 15.694)	0.097 (-46.647 - 4.075)	0.013 (3.455 - 27.313)
Week 2 Plasma Creatinine	0.083 (-1.850 - 28.033)	0.241 (-47.885 - 12.588)	0.021 (2.747 - 31.215)
Week 3 Plasma Creatinine	0.226 (-5.217 - 21.026)	0.657 (-30.720 - 19.720)	0.228 (-5.240 - 20.933)
Week 4 Plasma Creatinine	0.065 (-0.878 - 26.553)	0.922 (-39.251 - 35.667)	0.397 (-8.432 - 20.496)
Week 5 Plasma Creatinine	0.406 (-6.441 - 15.363)	0.611 (-20.923 - 34.840)	0.322 (-5.499 - 16.025)
Week 6 Plasma Creatinine	0.215 (-4.933 - 20.790)	0.293 (-15.768 - 50.018)	0.915 (-13.906 - 12.534)
Baseline Plasma Uric Acid	0.184 (-0.102 - 0.021)	0.618 (-0.0947 - 0.157)	0.137 (-0.106 - 0.015)
Week 1 Plasma Uric Acid	0.845 (-0.052 - 0.043)	0.353 (-0.504 - 0.137)	0.056 (-0.877 - 0.011)
Week 2 Plasma Uric Acid	0.857 (-0.055 - 0.046)	0.309 (-0.480 - 0.146)	0.207 (-0.793 - 0.179)
Week 3 Plasma Uric Acid	0.395 (-0.035 - 0.085)	0.431 (-0.0684 - 0.155)	0.396 (-0.084 - 0.345)
Week 4 Plasma Uric Acid	0.556 (-0.050 - 0.090)	0.794 (-0.201 - 0.155)	0.542 (-0.900 - 0.486)
Week 5 Plasma Uric Acid	0.375 (-0.014 - 0.029)	0.807 (-0.148 - 0.117)	0.552 (-0.067 - 0.037)
Week 6 Plasma Uric Acid	0.211 (-0.0079 - 0.018)	0.827 (-0.141 - 0.113)	0.456 (-0.067 - 0.031)
Baseline Creatinine Clearance	0.672 (-23.937 - 15.660)	0.693 (-31.899 - 47.328)	0.001 (-45.423 - 12.676)
Week 1 Creatinine Clearance	0.738 (-23.929 - 17.159)	0.728 (-34.038 - 48.124)	0.027 (-40.244 - 2.553)
Week 2 Creatinine Clearance	0.801 (-16.366 - 12.761)	0.403 (-39.927 - 16.557)	0.792 (-12.616 - 16.369)
Week 3 Creatinine Clearance	0.132 (-3.400 - 24.338)	0.080 (-2.918 - 48.102)	0.225 (-22.555 - 5.570)
Week 3 Uric Acid Clearance	0.520 (-0.899 - 1.730)	0.582 (-1.798 - 3.131)	0.608 (-0.984 - 1.645)
Week 4 Uric Acid Clearance	0.674 (-1.540 - 2.340)	0.626 (-3.736 - 6.078)	0.539 (-1.339 - 2.497)
Week 5 Uric Acid Clearance	0.442 (-2.148 - 0.969)	0.995 (-4.013 - 3.988)	0.811 (-1.384 - 1.751)
Week 6 Uric Acid Clearance	0.905 (-1.200 - 1.348)	0.743 (-2.704 - 3.738)	0.542 (-0.879 - 1.632)

KEY:**PCV - PACKED CELL VOLUME****ACEI - ANGIOTENSIN CONVERTING ENZYME INHIBITORS**

acid	Wk 3 (13)	1.759	1.084	-0.208	-0.93 – 0.51	NS
	Wk 4 (13)	1.796	1.059	-0.245	-0.96 – 0.47	NS
	Wk 5 (13)	1.795	1.056	-0.244	-0.95 – 0.47	NS
	Wk 6 (13)	1.793	0.966	-0.242	-0.91 – 0.43	NS
	Wk 0 (14)	1344.29	268.99			
	Wk 1 (14)	1233.29	130.25	111.00	-53.19 – 275.19	NS
Creatininu	Wk 2 (14)	1308.50	189.60	35.79	-145.00 – 216.58	NS
	Wk 3 (13)	1313.39	152.39	30.90	-144.29 – 206.09	NS
	Wk 4 (13)	1344.62	248.89	-0.33	-206.21 – 205.55	NS
	Wk 5 (13)	1273.92	213.51	70.37	-123.14 – 263.88	NS
	Wk 6 (13)	1170.00	139.96	174.29	2.26 – 346.32	NS
	Wk 0 (14)	1004.29	189.82			
Urine (n	Wk 1 (14)	1033.71	334.65	-29.42	-240.78 – 181.94	NS
	Wk 2 (14)	1098.57	295.56	-94.28	-287.25 - 98.69	NS
	Wk 3 (13)	1139.23	280.09	-134.94	-323.32 – 53.44	NS
	Wk 4 (13)	1030.77	341.77	-26.48	-243.44 – 190.48	NS
	Wk 5 (13)	1036.92	367.64	-32.63	-262.01 - 196.75	NS
	Wk 6 (13)	1063.08	268.04	-58.79	-241.79 – 124.21	NS
Creatininu	Wk 0 (14)	86.36	18.16			
	Wk 1 (14)	86.50	17.44	-0.14	-13.97 – 13.69	NS
	Wk 2 (14)	82.57	18.24	3.79	-10.35 – 17.93	NS
	Wk 3 (13)	85.08	19.40	1.28	-13.61 – 16.17	NS
	Wk 4 (13)	85.54	21.96	0.82	-15.10 – 16.74	NS
	Wk 5 (13)	88.00	15.56	-1.64	-15.10 – 11.82	NS
as m a I	Wk 6 (13)	88.54	16.87	-2.18	-16.10 – 11.74	NS
	Wk 0 (14)	0.335	0.083			
	Wk 1 (14)	0.349	0.074	-0.014	-0.07 – 0.05	NS

KEY:

SD = Standard deviation

DOM = Difference of means

C.I = Confidence Interval

4. Discussion

Data entry was into standard Pro-forma and statistical analysis was performed. Each patient's baseline samples at enrolment (before commencing aspirin) served as control and subsequent weekly samples were compared. The weekly mean of each sex group was calculated and difference of means from baseline mean determined. Relative Risk (RR) and 95% Confidence Interval (CI) was subsequently calculated using the method described by Newcombe Wilson.[15]

5. Conclusion

This study has shown deleterious effect of short term, low dose aspirin (75mg) on the renal function of only the subset of elderly patients on concomitant diuretics and ACEI therapy. The 6 weeks study was cumbersome for most of the patients and this precluded participation of a lot of eligible geriatric patients. Not all the 30 patients completed the study but their data for the period of participation were included in the analysis.

The small size occasioned by the tasking nature of the study in a peculiar setting might have affected the result. We suggest more studies in our own environment with larger sample size and possibly in a predominantly geriatric centre.

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