Prevalence and correlations of hepatorenal functions in diabetes and cardiovascular disease among stratified adults

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Summary. *Background:* The vulnerability of older adults to diabetes and cardiovascular complications is a global concern. Hepatorenal pathophysiology is implicated in these complications, but has yet to be clearly established, especially from rural low-mid income countries. This study investigates differences in prevalence of diabetes in aging groups and correlations of age with hepatorenal variables. *Methods:* 203 participants of both sexes above the age of 18 years underwent anthropometric measurements at Catholic Hospital, Abbi, Nigeria. Questionnaires collected demographic information and medical history. Urinalysis as well as routine liver and renal function tests were performed. Data analysis included determination of levels of hepatorenal abnormalities and prevalence of diseases in age groups. Percentage of disease subpopulations made up by each age-group was also determined as well as Pearson's correlation coefficient between age and hepatorenal variables, and comparison of average age and hepatorenal variables in disease subgroups. *Results:* Percentage hepatorenal abnormalities are not significantly different between age-groups. There is no significant difference in percentage level of disease between groups, but in age-groups constituting disease sub-populations (p<0.00001). The apparently healthy subpopulation comprises of younger adults compared to older adults constituting diabetes and hypertension (p < 0…). Age shows moderate correlation with renal function parameters, especially urea and chloride (r = 0.42), but relatively insignificant with liver function variables. *Conclusion:* This report affirms that diabetes cardiovascular co-morbidity comes with aging. It also indicates that renal pathophysiology may be more associated, than liver, functions in the vulnerability of adults. (www.actabiomedica.it)

Key words: age, cardiovascular complications, diabetes, liver function test, renal function test

Introduction

The liver is important in carbohydrate metabolism since it is responsible for balancing blood glucose levels by homeostasis involving processes such as gluconeogenesis, glycogenesis and glycogenolysis (1). Diabetes can develop as a complication of hepatic disease (cirrhosis) and is known as hepatogenous diabetes (2). It has been observed that fatty liver, obesity and insulin resistance are factors that cause liver damage resulting in hepatic disease. In the presence of hepatic disease, the metabolic homeostasis of glucose is impaired as a result of insulin resistance, glucose intolerance and diabetes (3). The diabetes manifests as liver function deteriorates, thus hepatogenous diabetes can be considered as an indicator of advanced liver disease (4).

It is estimated that prevalence of diabetes and prediabetes in chronic liver diseases are high (5, 6), and that liver transplant is capable of lessening insulin resistance en-route restoring endogenous glucose production and insulin sensitivity in cirrhotic-diabetic patients (7). However, the prevalence of abnormal liver function markers in diabetes relative to non-diabetes

and in young adults compared to older subpopulations are yet to be clearly established, especially in the rural and sub-urban communities of low-mid income countries (LMIC).

Renal complication of diabetes is a significant public health issue and possibly related to the chronic liver disease in hepatorenal syndrome (8, 9). That is, renal disease may also occur in the context of liver cirrhosis, either as glomerular injury or as hepatorenal syndrome (10), beside the fact that patients with diabetes mellitus can also develop renal disease, especially after years of disease progression (11).

Aging is a major risk factor for most chronic diseases such as diabetes and cardiovascular complications. Hence it is a factor in common models of diabetes cardiovascular risk assessment (12, 13). Aging is also a risk factor in vulnerability to acute liver injuries (14). Further, renal diabetes progression and the association of kidney disease with other comorbidities in older people are understudied and therefore poorly understood (15). It is important to study these associations especially in vulnerable groups such as the elderly. What is unknown, especially in rural communities of Nigeria such as Ndokwa local government areas is the level of hepatorenal abnormalities among older adults hence this study evaluates aging-related liver and renal status.

Study objective

This study evaluates the association of hepatorenal function with diabetes and its cardiovascular complication in older adults. Specifically, this study investigates the prevalence of diabetes in stratified age-groups and whether there exists a correlation with hepatorenal variables. Biomarkers of liver and renal functions are also investigated in the study populations with a view to establish associations.

Methods

Ethics and selection criteria

Ethical approval was obtained from various authorities including Charles Sturt University Australia and Novena University Nigeria, as well as a priori approval from Ndokwa West Local Government councils. The study was part of the prediabetes and cardiovascular complications screening (PACCS), an international research collaboration involving the department of Public and Community Health of Novena University and Charles Sturt University (16). This was a descriptive cross sectional study as defined in health research methodology (17) confined to the catchment zone of Catholic Hospital Abbi, and Friends Diagnostic Laboratories Obiaruku, both in Ndokwa communities of Delta State, Nigeria. Participants included males and females above the age of 18 years.

Data collection

Two hundred and three participants comprising 141 females and 62 males of ages ranging from 18-90 years underwent vital signs measurements, which included height, blood pressure, pulse, temperature, and weight. A questionnaire was used to collect other relevant data including anthropometry, family history, lifestyle and social economic status. Provisions were also made on the questionnaire for participants to indicate 'other health conditions' such as arthritis, back pain, stomach ulcer, etc., that may be confounding factors. Blood and urine samples were collected for clinical biochemistry. The haematology tests and urinalysis were performed at the Catholic Hospital Laboratory. The clinical biochemical investigations comprised of routine liver and renal function tests were performed at Friend's Laboratory, Obiaruku.

Statistics

Analyses were performed using MicroSoft Excel Data Analysis ToolPak 2010. The focus of analyses included determination of comparative (1) levels of abnormalities in stratified age groups, (2) percentage distribution of age groups in disease subpopulations, (3) differences in hepatorenal variables between 'healthy vs. diabetes' groups, (4) Pearson's correlation coefficient between age and hepatorenal variables, and (5) comparison of average age and hepatorenal variables in disease subpopulations.

Results

Descriptive statistics of abnormalities in parameters of liver and renal function tests are presented in absolute numbers per stratified age group. When analyzed in terms of percentage (i.e. prevalence) of hepatorenal abnormalities in each age-group and compared, there is no statistical difference between age groups (Table 1). Analysis of variance of the percentage hepatorenal abnormalities does show lowest average prevalence in group 1 (16%), followed by 18% in group 3, and relatively equal level (20%) in other groups.

There is also no significant difference in prevalent levels of disease between groups (Fig. 1). In corrobora-

Table 1. Absolute number of hepatorenal abnormalities in age groups

	Group 1	Groups 2	Group 3	Group 4	Group 5
Age range (years)	18-39	40-59	60-69	70-79	80+
N	40	53	46	35	29
Urine protein	6	6	8	7	9
Urine glucose	0	2	3	0	0
Blood urea nitrogen	17	30	28	29	23
Serum creatinine (high)	11	31	14	16	7
Plasma sodium	9	9	9	8	8
Plasma potassium	13	24	22	15	16
Plasma bicarbonate	26	32	18	24	11
Plasma chloride	6	16	7	4	11
Serum amino aspartate transferase	4	3	4	3	2
Serum amino alanine transferase	0	0	0	0	0
Serum alkaline phosphatase	1	1	1	0	0
Serum total protein (low)	13	16	20	10	9
Serum total protein (high)	13	12	10	9	9
Serum albumin	1	2	1	0	0
Serum total bilirubin	5	3	2	2	1
Serum direct (conjugated) bilirubin	0	1	0	0	0
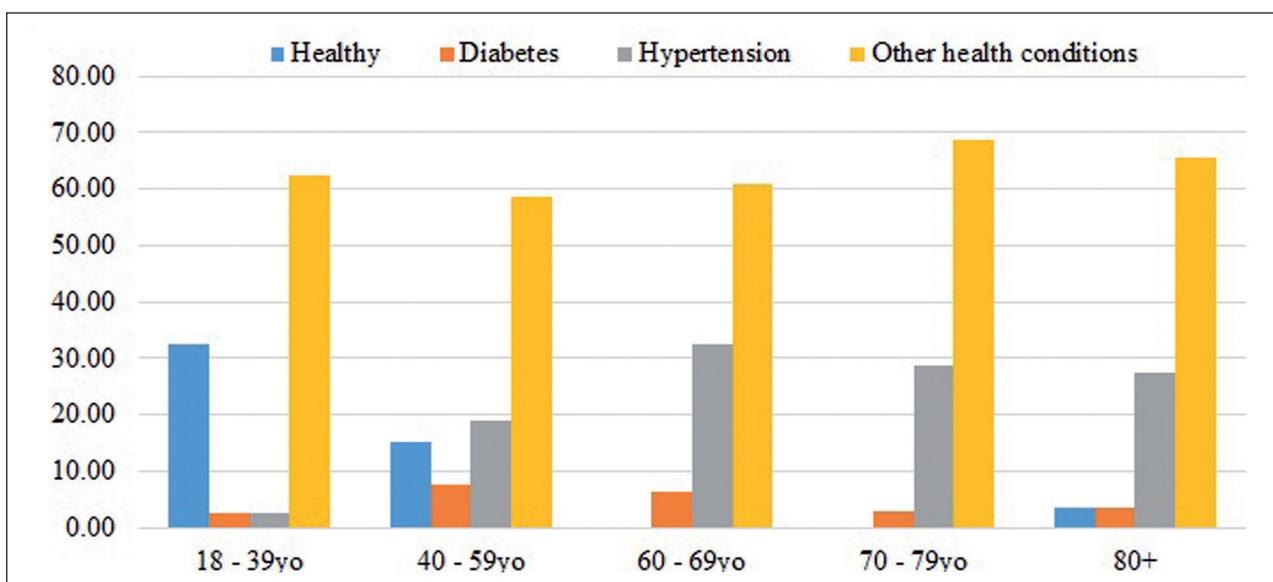
Figure 1. Prevalence of health and diseases in different age groups (p>0.99)
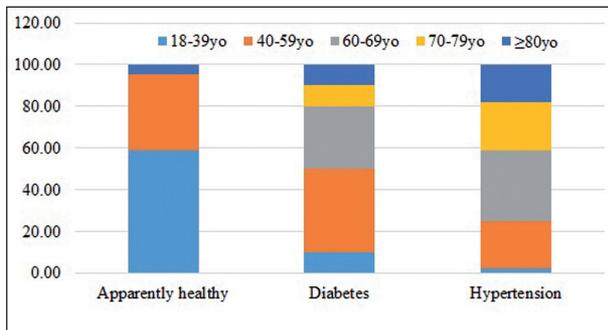
Figure 2. % age-groups that make up disease sub-populations (P<0.00001)

tion with table 1, there highest prevalence apparently healthy individuals in group 1 (33%), followed by 15% in group 2, and 3% in group 4, but none groups 3. Further, the result show that prevalence of other health condition, which includes dyslipidaemia and obesity amongst others, is neither lowest in the youngest group 1, nor highest in oldest group 5. However, a more critical review of the figure show that as from the 60years upward, there is apparent difference in prevalence with good health being little or non-existent, sequentially followed by lower number of diabetes, higher prevalence hypertension and highest proportion being other illnesses (Fig 1).

On the reverse when percentage of the separated apparently healthy, diabetes and hypertension subpopulations made up by each age-group was analyzed,

result show significant different (Fig 2; p<0.00001). A critical review of the figure will show that the apparently health subpopulation is 60% made of the youngest age group 1 and 36% age-group 2. That is, 96% of the research participants who indicated to be apparently healthy are below 60years old. On the corollary, only 2% of the subpopulation with hypertension are below 40 years old (Fig. 2).

A further evaluation of average age among people with diabetes and hypertension relative to apparently health participants indicate significant difference (Fig 3; p<0.00001)). In this study, result show that the apparently healthy subpopulation averaged 38 years old followed by diabetes 58 years compared to those with hypertension averaging 63 years old. This affirms what can only be gleaned by critical review of result presented in Fig 1 – i.e. that as from the 60years upward, there is apparent difference in prevalence with good health being little or non-existent, sequentially followed by lower number of diabetes, higher prevalence hypertension and highest proportion being other illnesses (Fig. 1). Evaluation of average levels of liver and renal function test parameters among people with diabetes and hypertension relative to apparently health participants indicate no significant difference (p>0.50), though blood urea nitrogen show unidirectional change (Fig 3).

Lastly, comparing average age and hepatorenal variables in disease subpopulations: ANOVA shows no
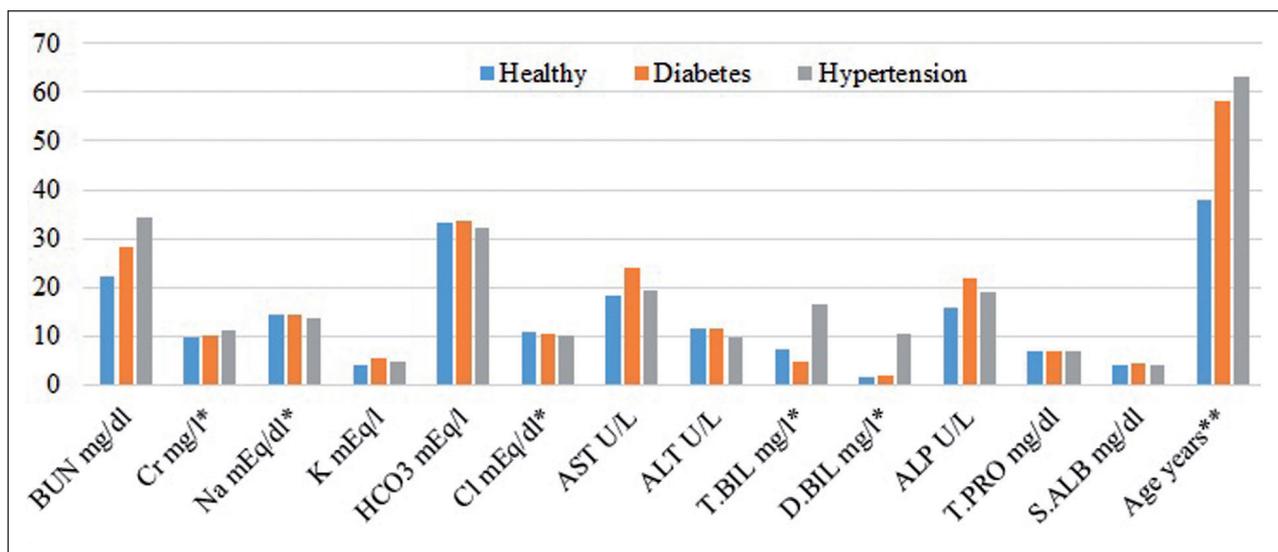
Figure 3. Average age (p<0.0.0001) and hepatorenal levels (p>0.05) in health sub-populations
*Note: Unit of measurement modified for graph purpose only

Table 2. Pearson correlation between age and hepatorenal function in apparently healthy cohort

Measurement	Correlation
Age	1
Blood urea nitrogen/urea	0.42
Creatinine	-0.15
Sodium	0.36
Potassium	0.39
Bicarbonate	0.02
Chloride	0.42
Amino aspartate transaminase	-0.10
Amino alanine transaminase	0.11
Total bilirubin	-0.15
Direct (conjugated) bilirubin	0.21
Alkaline phosphatase	0.09
Total protein	0.08
Albumin	0.16

unidirectional change or significant difference in the liver function tests, but there is indication that the 'apparently' healthy subpopulation are of lowest age compared to the cohort with hypertension, being of oldest adults. There is also unidirectional change in urea levels that seems to tally with age (Fig. 2; $p<0.001$), and corroborates with the correlation result (Table 2).

Discussion

Studies report that diabetes cases will increase from 2.8% in 2000 to 4.4% in 2030 or from 171 million in 2000 to 366 million in 2030, and especially among adults aged 65 years and older (18). This depicts a global public health problem, which is acknowledged as 'vulnerability of older adults to diabetes and its cardiovascular complications'. Diabetes causes serious complications and World Health Organization's estimates showed that in 2012, diabetes caused about 1.5 million deaths (19). It is further estimated that by 2025 there may be up to 380 million people who will suffer type 2 diabetes and another 418 million with impaired glucose tolerance (20). Further, liver and renal abnormalities (hepatorenal patho-physiology) are implicated in diabetes and its cardiovascular complications (21-24). Our observations show that in study population, approximately 23% and 5% indicated to have diagnosis of cardiovascular disease and diabetes,

respectively. Obesity was approximately 9%, while existing diagnosis of dyslipidemia among the study population appeared to be <0.5% (Table 1), and these comprised clients who attended a previous screening exercise in the ongoing research activities. Since lipid profile testing is relatively inaccessible and unaffordable in the rural low-mid income communities, therefore this observation may not be a true representation of dyslipidaemia prevalence. Hence in the analysis, obesity and dyslipidaemia have been discretionally included among the 'other health condition'.

With emphasis on prevalence of diabetes and cardiovascular disease (indicated by hypertension) and in the context of vulnerability of older adults; the young adults age-group 18-39 years has the highest percentage of healthy people (about 33%), lowest percentage of diabetes and hypertension (less than 5%), but 62% have other health conditions such as arthritis and back pain, amongst others (Fig. 1). Indeed, studies report of increasing prevalence of adults with back pain in LMICs (25). Age-group 40-59 years had the lowest percentage of healthy people (about 15%), higher percentage of diabetes (7%), hypertension (19%) and 58% have other health conditions. The two age-groups 60-69 and 70-79 years have the least percentage of healthy people (<1%), 60-69 years has highest percentage of hypertension (32%) and 61% have other health conditions; while 70-79 years has highest 68 prevalence of other health condition (Fig. 1).

Thus, the non-significant difference in health status between age-groups can be attributed to existence of 'other health conditions' being present in >58% in every age-group. That is, 'other health conditions' being present in most individuals regardless of age-group may be a confounding factor. This conclusion is further supported by the observation of statistical non-significance in percentage of hepatorenal abnormalities being 16% in 18-39 years, 18% in age-group 60-69 years and 20% in other three age-groups (Table 1). Further, the observation corroborates with findings that neither outcome of diabetes treatment, nor consequent improvement in health status varies with stratified age groups (26).

The non-significant difference in health status between age-groups needs to be differentiated from how the age groups constitute disease sub-populations, or

average age of members constituting disease-groups. Results show that age-group 18-39 years constitutes the highest percentage of healthy population (60%), 10% of diabetes subgroup and only 2% of those with hypertension. This is followed by age-group 40-59 years constituting 37% of healthy sub-population but also the highest percentage of diabetes sup-population (40%) and 23% of those with high blood pressure. In contrast, age-group 80+ years constitutes only about 5% of healthy sub-population, 10% of diabetes and approximately 20% of the hypertension sub-population. Age-groups 60-69 and 70-79 years constitute the lowest percentage of healthy subpopulation (<1%) and highest percentage (>35%) of sub-population suffering hypertension (Fig 2; P<0.00001). Such observations are consistent with reports from other studies that show the risk factors for non-communicable diseases to be higher in older persons than the young (27). The result also affirm the concern on vulnerability of older adults to diabetes and cardiovascular diseases, which to our knowledge is the first from a rural low-mid income country setting.

Further, statistical non-significance in percentage of hepatorenal abnormalities between age-groups must be differentiated from correlation of individual biomarkers with age. Although, ANOVA showed no unidirectional change or significant difference in the liver function tests with aging, there is moderate correlation between age and renal function test parameters, especially BUN and some electrolytes (Table 2), which is corroborate with unidirectional change in BUN with age (Fig. 3).

Conclusion

The implication of hepatorenal functions in vulnerability of adults to diabetes and its cardiovascular complications has been investigated. It has been observed that 'other health conditions' existing in most individuals regardless of age-group may confound observation of significant difference between young versus older adults. However, there is observation that while prevalence of diabetes with cardiovascular co-morbidity increases with age, there is also renal abnormality indicated by BUN being unidirectional with increasing age. This study looked at age distribution

and future studies need to consider sex distribution as well as studying the subtypes of diabetes and liver disease separately in regards to liver function association with diabetes.

Acknowledgement

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