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Prevalence and Risk Factors for the Metabolic Syndrome among Patients with Epilepsy Attending a Neuropsychiatric Hospital in Kigali, Rwanda

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ABSTRACT

Background: *Cardiovascular mortality and morbidity are more frequent in people with epilepsy than in the general population. The explanation for this may be the change in biochemical components due to the use of anti-epileptic drugs. We conducted a study to determine the prevalence and risk factors for Metabolic Syndrome (MetS) among Rwandan adults with epilepsy emphasizing the respective anti-epileptic drugs that the patients were receiving.* ***Methods:*** *This was a cross-sectional study conducted from December 2018 to December 2019 at Ndera Neuropsychiatric Hospital in Kigali, Rwanda. Consenting adult Rwandan patients with epilepsy, who had been on anti-epileptic drugs for at least two years, were recruited into the study. Participants had their anthropometric measurements taken and their fasting blood glucose plus lipids assayed. Using a data collection form, patients had their demographic and clinical characteristics recorded.* ***Results:*** *There were 1076 participants (male-to-female ratio, 1.4; age range, 42). Using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) criteria, there were 329 individuals with MetS giving an overall prevalence rate of 30.6%. Significant risk factors for MetS included use of valproic acid (p=0.007), a sedentary lifestyle (p=0.025), waist circumference >102cm (p=0.001), high triglycerides (p=0.001), high blood pressure (p=0.001), and fasting blood glucose >6.1mmol (p=0.001).* ***Conclusion:*** *MetS is highly prevalent among Rwandan patients with epilepsy. Therefore, local physicians are advised to carefully select the type of anti-epileptic medication administered and to regularly request anthropometric as well as laboratory checkups for such patients to predict a diagnosis of MetS and the complications thereof.*

Keywords: Metabolic syndrome, Epilepsy, Prevalence, Anti-epileptic drugs, Rwanda

INTRODUCTION

Metabolic Syndrome (MetS), a group of metabolic risk factors including hyperglycemia, dyslipidemia (elevated triglycerides, reduced high-density lipoproteins), elevated blood pressure, and obesity is increasingly becoming a global public health concern [1]. In the general population, westernization characterized consumption of foods with fat and sugar content combined with less physical exercises are the leading causes of this syndrome, which is a great predictor of cardiovascular disease [2,3].

Compared with the general population, people with epilepsy have elevated rates of cardiovascular mortality and morbidity, which may be driven by metabolic changes [4,5]. Studies have found that this patient group also has an increased risk of developing metabolic syndrome and obesity, both of which are risk factors for vascular disorders [6-9].

The connection between metabolic syndrome and epilepsy has emerged as a public health question of importance to both specialists and primary care practitioners [10]. Studies that investigated the presence of MetS in patients with epilepsy yielded contradicting results. Some of these studies targeted only specific groups of populations, such as

females, young adults, children [6,11,12]. Other researchers investigated different metabolic side effects of Anti-Epileptic Drugs (AEDs) on different organs, tissues, and biochemical components of the human body such as bone and calcium metabolism, glucose metabolism, mental health, blood components, and lipid metabolism [13-17].

In the present study, we estimated the prevalence of MetS in Rwandan Patients with Epilepsy in a cross-sectional survey conducted from December 2018 and December 2019 at Ndera Neuropsychiatric Hospital in Kigali, Rwanda. Data on lifestyle and metabolic risk factors were collected on adult patients with epilepsy. We used the National Cholesterol Education Program (NCEP) Adult Panel III (ATP III) criteria to confirm MetS [18].

METHODS

Subjects

The study was carried out in the Out-patients' Department of Ndera Neuro-Psychiatric Hospital, in Kigali, Rwanda. The study duration was 12 months from December 2018 to December 2019 during which the prevalence of MetS and its components among patients with epilepsy was determined. Study participants, who were adult volunteers having epilepsy and aged between 18 and 60 years, were consecutively enrolled. Participating individuals were on treatment for epilepsy using a single type of anti-epileptic drug.

We excluded patients with malignancies, pregnancy, mental or legal incapacity that prevented them from giving valid consent or hindered them from full participation in the study process or strict adherence to study protocol.

Data Collection

Data were collected from patients who agreed to participate in the study. They signed a written consent form following a detailed explanation of the study. Participants were then interviewed and examined in a special room for privacy and confidentiality. Demographic details (names, sex, age, and marital status), risk factors (diabetes, hypertension, physical activity, and smoking), and anthropometric measurements (height, weight, and waist circumference) were collected using data collection forms. The interview was carried out by the Principal Investigator (PI) and one Research Assistant (RA) who had been trained before commencing the study.

Anthropometric Measurements

Waist circumference was taken without outer clothing, using a non-stretchable tape measure at the level of the uppermost edge of the hip bone on the abdomen with the tape parallel to the ground and recorded to the nearest 0.5 centimeters. Blood Pressure (BP) was taken from the arm (brachial artery) for all respondents on the first encounter by using a digital sphygmomanometer. BP measurements were performed in the sitting position with the arm supported at heart level and repeated after 5 minutes; the average of the two measurements was taken as the correct BP for the individual. To calculate the Body Mass Index (BMI), subjects were weighed (in kilograms) on a weighing scale while fully dressed but without shoes. Height (in meters) was measured without shoes by using a stadiometer. The BMI was calculated as the weight divided by the height squared (kg/m^2).

Biochemical Tests

Blood samples were collected with BD Vacutainer® venous blood collection tubes. Five milliliters of venous blood were taken from the antecubital fossa and placed in empty sterile vacutainer tubes. The blood samples were separated by centrifugation at 1000 × g for 15 min and the supernatant serum was collected. Serum levels of lipids Triglycerides (TG), Total Cholesterol (TC), High-Density Lipoprotein Cholesterol (HDL-C), blood glucose were measured using commercially available kits (Roche System Reagents) by a Cobas C 311 autoanalyzer using appropriate quality control measures for the reagents and autoanalyzer.

Statistical Analysis

Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 24.0 software (SPSS Inc. Chicago, IL). Means of numeric variables were compared between groups by the student's t-test. Proportions were compared using the Chi-square test. Multivariate logistic regression was used to determine the risk factors associated with MetS in patients with epilepsy. For tests and models, a p-value of less than 0.05 was taken for statistical significance.

Ethical Clearance

Before the commencement of the study, ethical clearance was sought from Mbarara University of Science and Technology-Research Ethics Committee (MUST-REC) in Mbarara, Uganda. Ethical approval was then secured from both Rwanda National Health Research Committee (NHRC) and Rwanda National Ethics Committee (RNEC). We conducted this study following the guidelines of the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects. Information concerning the study was given to all study participants before the interviews and sample collection. A written and duly signed consent was obtained from all participants. Confidentiality was ensured for all individuals who participated in the study by removing all identifiers at the time of data entry. The participation was fully voluntary devoid of any kind of coercion and no participant was paid for their involvement in the study.

RESULTS

During the study period, 1076 adult patients with epilepsy meeting the inclusion criteria were carefully selected to participate in this study. They were 629 males, 58.5%, and 447 females, 41.5%. The mean age of participants was 40.22 ± 10.37 that of males was 40.20.04 ± 10.34 and of females was 40.24.04 ± 10.42. The distribution of age was 33.3% (n=358) between 18-35 years, 34.8% (n=374) between 36-45 years, 32.0% (n=344) between 46-60 years. Valproate treated patients were 328 (30.5%), Carbamazepine; 207 (19.2%), Leveracetam; 145 (13.5%), Phenytoin; 130 (12.1%), Phenobarbital; 135(12.5%), Clonazepam; 95(8.8%) and Topiramate treated patients were 36 (3.3%). Other clinical characteristics of participants are presented in Table 1 and Table 2.

The prevalence of metabolic syndrome in people with epilepsy was 30.6% (329 subjects) and out of these, the number of males was 189 (57.4%) whereas the number of females was 140 (42.6%). The prevalence of metabolic syndrome weighted by age group was 9.0% (97) among the age group of 18-35 years old, 11.2% (120) among the age group of 36-45 years old, and 30.6% (329) among the age group of 46-60 years old. Regarding individual components of MetS, 378 subjects (35.2%) had high abdominal obesity, 316 subjects (29.4%) had high blood pressure, 155 subjects (14.4%) had diabetes mellitus, 283 subjects (26.3%) had low HDLc, and 303 subjects (28.2%) had high level of serum triglycerides.

Table 1 Clinical characteristic of subjects with epilepsy with and without metabolic syndrome

	Total number of subjects (n=1076)	**Participants without metabolic syndrome [n=747 (69.4%)]**	**Participants with metabolic syndrome [n=329 (30.6%)]**	**p-value**
Gender				
Males	629 (58.5%)	440 (40.9%)	189 (17.6%)	0.655
Females	447 (41.5%)	307 (28.5%)	140 (13.0%)	
Age groups N (%)				
18-35	358 (33.3%)	261 (24.3%)	97 (9.0%)	0.214
36-45	374 (34.8%)	254 (23.6%)	120 (11.2%)	
46-60	344 (32.0%)	252 (21.6%)	329 (30.6%)	
Antiepileptic drugs N (%)				
Valproic acid	428 (30.5 %)	209 (19.4%)	119 (11.1%)	**0.007**
Carbamazepine	207 (19.2%)	140 (13.4%)	67 (6.2%)	0.534
Leveracetam	145 (13.5%)	104 (9.7%)	41 (3.8%)	0.518
Phenytoin	130 (12.1%)	97 (9.0%)	33 (3.1%)	0.799
Phenobarbital	135 (12.5%)	95 (8.8%)	40(3.7%)	0.171
Clonazepam	95 (8.8%)	74(6.9%)	21 (2.0%)	0.061
Topiramate	36 (3.3%)	28 (2.6%)	8 (0.7%)	0.268
Metabolic parameters (mean ± SD)				

FBG (mmol/L)	5.75 ± 0.70	5.63 ± 0.65	6.01 ± 0.74	**0.001**
Total cholesterol (mmol/L)	3.78 ± 0.88	3.75 ± 0.82	3.84 ± 0.98	0.141
LDLc (mmol/L)	3.20 ± 1.18	3.09 ± 1.11	3.44 ± 1.28	**0.001**
HDLc (mmol/L)	1.15 ± 0.20	1.18 ± 0.19	1.09 ± 0.20	**0.001**
Triglycerides (mmol/L)	1.34 ± 0.58	1.25 ± 0.53	1.54 ± 0.62	**0.001**
Component of metabolic syndrome				
High abdominal obesity	378 (35.2%)	182 (16.9%)	196 (18.3%)	**0.001**
High blood pressure	316 (29.4%)	90 (8.4%)	101 (9.5%)	**0.001**
Diabetes mellitus	155 (14.4%)	84 (7.8%)	71 (6.6%)	0.001
Low HDLc	283 (26.3%)	144 (13.4)	139 (12.9%)	0.001
High triglycerides	303 (28.2%)	141 (13.1%)	162 (15.1%)	0.001

HDLc: High-Density Lipoprotein cholesterol; FBG: Fasting Blood Glucose; LDLc: Low-Density Lipoprotein cholesterol; N: Number; SD: Standard Deviation; %: percentage; bold values indicate the ones which have attained statistical significance

Table 2 Comparison of clinical and metabolic parameters between males and females

	Males [N=629 (58.5%)	**Females [N=447 (41.5%)]**	**p value**
Age groups N (%)			
18-35	214 (19.9%)	144 (13.4%)	0.214
36-45	215 (20.0%)	159 (14.8%)	
46-60	200 (18.6%)	144 (13.4%)	
Ages in years, (mean ± SD)	40.20 ± 10.34	40.24 ± 10.42	
Antiepileptic drugs N (%)			
Valproic acid	199 (18.5%)	129 (12.0%)	
Carbazepine	126 (11.7%)	81 (7.5%)	
Leveracetam	81 (7.5%)	64 (5.9%)	
Phenytoin	77 (7.2%)	53 (4.9)	
Phenobarbital	72 (6.7%)	63 (5.9%)	
Clonazepam	58 (5.4%)	37 (3.4%)	
Topiramate	16 (1.5%)	20 (1.9%)	
Metabolic parameters (mean ± SD)			
FBG (mmol/L)	5.74 ± 0.69	5.75 ± 0.72	0.805
Total cholesterol (mmol/L)	3.72 ± 0.85	3.85 + 0.90	**0.017**
LDLc (mmol/L)	3.19 ± 1.15	3.20 + 1.21	0.89
HDLc (mmol/L)	1.15 ± 0.20	1.16 ± 0.20	0.666
Triglycerides (mmol/L)	1.34 ± 0.56	1.33 ± 0.60	0.767
Component of metabolic syndrome			
High abdominal obesity	215 (20%)	163 (15.1%)	0.885
High blood pressure	112 (10.4%)	79 (7.3%)	0.763
Diabetes mellitus	97 (0.9%)	58 (5.4%)	0.26
Low HDLc	166 (15.4%)	117 (10.9%	0.937
High triglycerides	183 (17.0%)	120 (11.2%)	0.419

HDLc: High-Density Lipoprotein cholesterol; FBG: Fasting Blood Glucose; LDLc: Low-Density Lipoprotein cholesterol; N: Number; SD: Standard Deviation; %: Percentage; bold values indicate the ones which have attained statistical significance

Regarding the occurrence of MetS in patients under different anti-epileptic drugs, we found that valproic acid was significantly associated with MetS (p=0.007). Indeed, among 328 valproic acid-treated patients, 119 (36.3%) of them had MetS. We did not find any statistically significant differences between the other AEDs and MetS. The distribution of MetS in other AEDs treated patients is found in Table 3.

Table 3 Frequency of metabolic syndrome in patients under different anti-epileptic drugs

	Metabolic syndrome present		
	No	**Yes**	**Total**
Valproic acid	209 (63.7%)	119 (36.3%)	328
Carbamazepine	140 (67.6%)	67 (32.4)	207
Levetiracetam	104 (71.1%)	41 (28.3%)	145
Phenytoin	95 (70.4%)	40 (29.6%)	135
Phenobarbital	97 (74.6%)	33 (25.4%)	130
Clonozepam	74 (77.9%)	21 (22.1%)	95
Topiramate	28 (77.8%)	8 (22.2%)	36

In this study, multivariate logistic regression analysis did not reveal any significant correlation between the occurrence of MetS in patients with epilepsy and some clinical characteristic such as sex, age gender, family history of diabetes, and family history of hypertension (Table 4).

On the other hand, a significant correlation was found between the occurrence of MetS and quite number of components such as waist circumference (OR=1.067; p=0.001; 95% CI=1.052-1.016), fasting blood glucose (OR=1.810; p=0.001; 95% CI=0.866-1.809), serum triglyceride (OR=2.797; p=0.001; 95% CI=2.122-3.685), systolic blood pressure (OR=1.32; p=0.001; 95% CI=1.018-1.046) and diastolic blood pressure (OR=1.102; p=0.001; 95% CI=1.071-1.232).

Table 4 Multivariate analysis of risk factors associated with metabolic syndrome

Component	**Odd Ratio (OR)**	**95% confidence interval**		
		Lower	**Upper**	**p-value**
Gender	1.272	0.933	1.734	0.128
Age	1.001	0.986	1.016	0.903
Waist circumference >102 cm	1.067	1.052	1.016	**0.001**
Fasting blood glucose >6.1 mmol	1.81	0.866	1.809	**0.001**
HDLc <1.03 mol	0.066	0.029	0.148	**0.001**
Triglyceride >130 mol	2.797	2.122	3.685	**0.001**
Systolic blood pressure >130 mmHg	1.032	1.018	1.046	**0.001**
Diastolic blood pressure >85 mmHg	1.102	1.071	1.232	**0.001**
Family history of diabetes	0.978	0.029	0.148	0.906
Family history of hypertension	1.252	0.866	1.809	0.232

DISCUSSION

To the best of our knowledge, this was the first published study that sought to determine the prevalence of MetS and

cardiovascular risk factors among Rwandan patients with epilepsy. In this study, MetS were defined as a constellation of interconnected physiological, biochemical, clinical, and metabolic factors that directly increase the risk of atherosclerotic cardiovascular disease, type 2 diabetes mellitus, and all-cause mortality [19]. In Rwanda, a country with approximately 0.7% patients with epilepsy, the prevalence of MetS among these individuals was found to be 30.6% [20]. This was significantly higher than for other prevalence rates reported from surveys conducted among the general population in Africa. For instance, using the ATP III criteria, the prevalence of MetS in Ethiopia has been reported as 10.0% in men and 16.2% in women [21]. Regarding other countries in the African region, the prevalence of MetS was found to be as follows: South Africa, 18.5%; Ghana, 15.0%; Nigeria, 25.2% and Cameroon, 1.8%-1.9% [22-25]. However, some research findings from overseas among the general population indicated higher prevalence rates of MetS than that of Rwanda. For instance, a community study from Eastern India reported an overall prevalence of 33.5% [26]. A study conducted in Croatia among obese children and adolescents presenting with some components of MetS reported a prevalence rate of 30.3% which is comparable to our present study. Other studies which reported higher prevalence rates of MetS than ours include a study from Brazil which reported a prevalence ranging from 55.6%-74% [27]. Some studies that were looking at the prevalence of metabolic syndrome in certain categories of patients with epilepsy found closely related prevalence. In young adults Indian with epilepsy the MetS prevalence has been reported as 29.5%, while the MetS prevalence of 25.8% has been reported from Estonian in adults patients with epilepsy who were under VA treatment [6,28]. Other studies reported a higher prevalence of MetS: 47% among Chinese obese patients with epilepsy on VA and 43.5% in Italian overweight epileptic patients treated with VA [12,29].

In our study, all age groups had different frequencies of MetS. However, this difference did not reach statistical significance (9.0% in the 18-35 years old group, 11.2% in the 36-45 years old group, and 30.6% in the 46-60 years old group, p=0.214). In this regard, if we compare our results with results from other studies conducted among patients with epilepsy elsewhere, we agree with Jiaji Fang who also did not find the significant difference of MetS across age groups [29]. However, our results disagree with the results of Nair who found a significantly higher prevalence of MetS in the oldest age group [6].

Men and women were all affected though with different proportions [189 subjects (17.6%) versus 140 subjects (13.0%), p=0.655)]. The interpretation is that AEDs and other risk factors can trigger MetS in people with epilepsy regardless of their gender and age group. Our results are therefore concordant with those published by Verroti, et al. Nair, et al. and Jiaji Fang, et al who also found no difference in the occurrence of MetS between males and females [6,12,29]. However, Prasad reported significant gender differences with a higher prevalence of MetS in females compared to males (p=0.00) [26].

We observed that across all age groups, Valproic Acid (VA) treated patients are more prone to develop MetS than other EADs treated patients (11.1%, p=0.007). The least prevalence of MetS was found in topiramate-treated patients (0.7%, p=0.268).

This confirms earlier reports from several studies which emphasize that the use of VA for treating epilepsy is linked with a high probability of experiencing metabolic and hormonal disturbances [22,23,30-36].

Regarding individual components of MetS, we found that the most prevalent one was high abdominal obesity with diabetes mellitus being the least prevalent. However, in some general population studies, the most frequent MetS component was low serum HDL cholesterol in women and elevated High Blood Pressure (HBP) in men [22,25]. Similar results have been found by other investigators and abdominal obesity was significantly correlated with MetS (p=0.001) [37].

Increased abdominal obesity has constantly been reported by several researchers working on studies of patients with epilepsy who are under AEDs medication especially VA and current evidence supports that abdominal obesity is predictive of metabolic risk factors [10-12,38]. In our study, HBP was the second most MetS individual component we found. According to Jiaji Fang, et al. HBP was also found to be very common in Chinese obese patients with epilepsy on VA. VA causes MetS in some patients but not all. Genetic factors and several molecular pathways of energy homeostasis might influence the occurrence of MetS [12]. Our study showed that the prevalence of hyperglycemia was 14.4% which suggests that hyperglycemia is higher among patients with epilepsy than in the general population. The Rwanda Non-communicable Diseases Risk Factors Report released in 2015 pointed out that in the general population of Rwanda, impaired fasting glucose levels and raised blood glucose affect 3.1% of the population in Rwanda [40].

Hyperglycemia may be due to drugs that are known to cause hyperglycemia like VA or due to a combination of MetS risk factors commonly found among patients with epilepsy like obesity and lower exercise capacity that make body cells less sensitive or resistant to insulin.

CONCLUSION

Results of our study form an informative tool for clinicians and other policymakers in the management of epilepsy in Rwanda. Understanding the prevalence of metabolic syndrome and other metabolic abnormalities among patients with epilepsy is immensely useful to practitioners to help affected patients undergo risk-reducing interventions. This also lays a good foundation for further research in related areas such as the interactions of AEDs and other medications, markers of genetic susceptibility of MetS in patients with epilepsy.

DECLARATIONS

Contributors

All authors played a role in the study design. FXN and JBG conducted the study and collected data. FXN, BN, and SPR analyzed and interpreted the data. FXN, BN, and SPR wrote the manuscript and approved its final version before submission for publication.

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Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Gaillard, Trudy R. "The metabolic syndrome and its components in African-American women: Emerging trends and implications." *Frontiers in Endocrinology,* Vol. 8, 2018, p. 383.

[2] Wang, Guang-Rong, et al. "Prevalence of metabolic syndrome among urban community residents in China." *BMC Public Health,* Vol. 13, No. 1, 2013, pp. 1-9.

[3] Galassi, Andrea, Kristi Reynolds, and Jiang He. "Metabolic syndrome and risk of cardiovascular disease: A meta-analysis." *The American Journal of Medicine,* Vol. 119, No. 10, 2006, pp. 812-19.

[4] Yuen, Alan WC, et al. "Mortality and morbidity rates are increased in people with epilepsy: Is stress part of the equation?" *Epilepsy and Behavior,* Vol. 10, No. 1, 2007, pp. 1-7.

[5] Annegers, John F., W. Allen Hauser, and Sally B. Shirts. "Heart disease mortality and morbidity in patients with epilepsy." *Epilepsia,* Vol. 25, No. 6, 1984, pp. 699-704.

[6] Nair, Sruthi S., et al. "Metabolic syndrome in young adults with epilepsy." *Seizure,* Vol. 37, 2016, pp. 61-64.

[7] Hwang, Lee-Ching, Chyi-Huey Bai, and Chien-Jen Chen. "Prevalence of obesity and metabolic syndrome in Taiwan." *Journal of the Formosan Medical Association,* Vol. 105, No. 8, 2006, pp. 626-35.

[8] Ritchie, S. A., and J. M. C. Connell. "The link between abdominal obesity, metabolic syndrome and cardiovascular disease." *Nutrition, Metabolism and Cardiovascular Diseases,* Vol. 17, No. 4, 2007, pp. 319-26.

[9] Bonora, Enzo. "The metabolic syndrome and cardiovascular disease." *Annals of Medicine,* Vol. 38, No. 1, 2006, pp. 64-80.

[10] Kim, Jee Young, and Hyang Woon Lee. "Metabolic and hormonal disturbances in women with epilepsy on antiepileptic drug monotherapy." *Epilepsia,* Vol. 48, No. 7, 2007, pp. 1366-70.

[11] Dhir, Aditi, et al. "Parameters of metabolic syndrome in Indian children with epilepsy on valproate or phenytoin monotherapy." *Journal of Pediatric Neurosciences,* Vol. 10, No. 3, 2015, p. 222.

[12] Verrotti, Alberto, et al. "The metabolic syndrome in overweight epileptic patients treated with valproic acid." *Epilepsia,* Vol. 51, No. 2, 2010, pp. 268-73.

[13] Verrotti, Alberto, et al. "Bone and calcium metabolism and antiepileptic drugs." *Clinical Neurology and Neurosurgery,* Vol. 112, No. 1, 2010, pp. 1-10.

[14] Theodore, William H. "Antiepileptic drugs and cerebral glucose metabolism." *Epilepsia,* Vol. 29, 1988, pp. S48-S55.

[15] Reynolds, E. H. "Mental effects of antiepileptic medication: A review." *Epilepsia,* Vol. 24, 1983, pp. S85-S95.

[16] Naithani, Manisha, et al. "Studies on adverse metabolic effects of antiepileptics and their correlation with blood components." *Current Neurobiology,* Vol. 1, No. 2, 2010, pp. 117-20.

[17] Mintzer, Scott, et al. "Effects of antiepileptic drugs on lipids, homocysteine, and Creactive protein." *Annals of Neurology,* Vol. 65, No. 4, 2009, pp. 448-56.

[18] Lab CE. "NCEP: ATP III Diagnostic Criteria for Metabolic Syndrome." https://www.labce.com/spg362891_ncep_atp_iii_diagnostic_criteria_for_metabolic_syn.aspx

[19] Grundy, Scott M., ed. "Atlas of atherosclerosis and metabolic syndrome." *Springer Science and Business Media*, 2011, pp. 1-26.

[20] Simms, Victoria, et al. "Prevalence of epilepsy in Rwanda: A national cross sectional survey." *Tropical Medicine and International Health,* Vol. 13, No. 8, 2008, pp. 1047-53.

[21] Tran, A., et al. "Prevalence of metabolic syndrome among working adults in Ethiopia." *International Journal of Hypertension,* Vol. 2011, 2011.

[22] Motala, Ayesha A., et al. "The prevalence of metabolic syndrome and determination of the optimal waist circumference cutoff points in a rural South African community." *Diabetes Care,* Vol. 34, No. 4, 2011, pp. 1032-37.

[23] Gyakobo, Mawuli, et al. "Prevalence of the metabolic syndrome in a rural population in Ghana." *BMC Endocrine Disorders,* Vol. 12, No. 1, 2012, pp. 1-9.

[24] Isezuo, S. A., and E. Ezunu. "Demographic and clinical correlates of metabolic syndrome in Native African type-2 diabetic patients." *Journal of the National Medical Association,* Vol. 97, No. 4, 2005, pp. 557-63.

[25] Fezeu, Leopold, et al. "Metabolic syndrome in a sub-Saharan African setting: Central obesity may be the key determinant." *Atherosclerosis,* Vol. 193, No. 1, 2007, pp. 70-76.

[26] Prasad, D. S., et al. "Prevalence and risk factors for metabolic syndrome in Asian Indians: A community study from urban Eastern India." *Journal of Cardiovascular Disease Research,* Vol. 3, No. 3, 2012, pp. 204-11.

[27] Rodrigues, Lúcia Gomes, Ana Paula Mattos, and Sérgio Koifman. "Prevalence of metabolic syndrome in overweight and obese outpatient children and adolescents: Comparative analysis using different clinical definitions." *Revista Paulista de Pediatria,* Vol. 29, No. 2, 2011, pp. 178-85.

[28] Rakitin, Aleksei, et al. "Comparison of the metabolic syndrome risk in valproate-treated patients with epilepsy and the general population in Estonia." *PLoS One,* Vol. 9, No. 7, 2014, p. e103856.

[29] Fang, Jiajia, et al. "Metabolic syndrome among Chinese obese patients with epilepsy on sodium valproate." *Seizure,* Vol. 21, No. 8, 2012, pp. 578-82.

[30] Novak, Gerald P., et al. "Risk of excessive weight gain in epileptic children treated with valproate." *Journal of Child Neurology,* Vol. 14, No. 8, 1999, pp. 490-95.

[31] Tan, Hüseyin, et al. "Valproate-induced insulin resistance in prepubertal girls with epilepsy." *Journal of Pediatric Endocrinology and Metabolism,* Vol. 18, No. 10, 2005, pp. 985-90.

[32] Masuccio, Fabio, et al. "Weight gain and insulin resistance in children treated with valproate: The influence of time." *Journal of Child Neurology,* Vol. 25, No. 8, 2010, pp. 941-47.

[33] Verrotti, Alberto, et al. "Insulin resistance in epileptic girls who gain weight after therapy with valproic acid." *Journal of Child Neurology,* Vol. 17, No. 4, 2002, pp. 265-68.

[34] Luef, Gerhard, et al. "Increase in postprandial serum insulin levels in epileptic patients with valproic acid therapy." *Metabolism-Clinical and Experimental,* Vol. 51, No. 10, 2002, pp. 1274-78.

[35] Isojärvi, Jouko IT, et al. "Valproate, lamotrigine, and insulin-mediated risks in women with epilepsy." *Annals of Neurology,* Vol. 43, No. 4, 1998, pp. 446-51.

[36] Luef, Gerhard, et al. "Polycystic ovaries, obesity and insulin resistance in women with epilepsy." *Journal of Neurology,* Vol. 249, No. 7, 2002, pp. 835-41.

[37] Duncan, Glen E., Sierra M. Li, and Xiao-Hua Zhou. "Prevalence and trends of a metabolic syndrome phenotype among US adolescents, 1999-2000." *Diabetes Care,* Vol. 27, No. 10, 2004, pp. 2438-43.

[38] Azevedo Fernandez, Rochelly, et al. "Anthropometric profile and nutritional intake in patients with epilepsy." *Hospital Nutrition,* Vol. 32, No. 2, 2015, pp. 817-22.

[39] Després, Jean-Pierre, and Isabelle Lemieux. "Abdominal obesity and metabolic syndrome." *Nature,* Vol. 444, No. 7121, 2006, pp. 881-87.

[40] Muhimpundu, M. A., and A. Binagwaho. "Republic of Rwanda-Rwanda non-communicable diseases risk factors report." 2015, p. 112.