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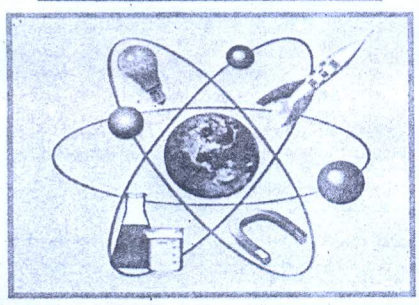
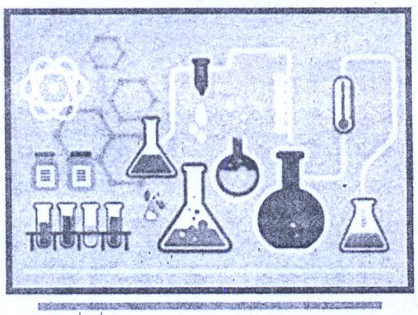
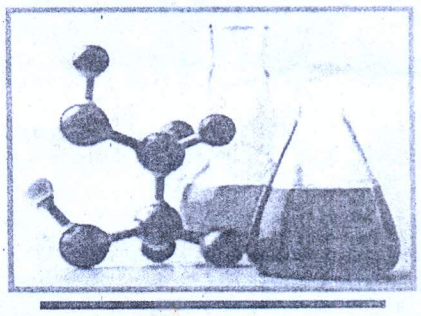

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DIETARY NUTRIENTS AND ADIPONECTIN rs266729 SNP (-11377C>G) ASSOCIATION WITH BLOOD PRESSURE IN NIGERIAN YOUNG ADULTS

By

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Abstract

Studies have shown conflicting associations between adiponectin gene and blood pressure and between intakes of selected nutrients and blood pressure. We investigated the associations of blood pressure with selected nutrients and rs266729, a single nucleotide polymorphism (SNP) in adiponectin gene using a cross-sectional study involving SNP genotyping using MassARRAY and analysis of dietary intake with standardized questionnaire. Linear regression analysis was used to investigate the associations of blood pressure with rs266729 in additive genetic model and the selected nutrients after adjustment for age, sex, body mass index (BMI) and alcohol intake. A reasonably high significant correlation between systolic blood pressure (SBP) and diastolic blood pressure (DBP) was seen (correlation [r], 0.70; 95% confidence interval [CI], 0.58 — 0.79; $P = 2.665e^{-15}$). However, in the adjusted model, dietary intake of calcium was inversely related to SBP (β, -0.0124; SE, 0.0053; P = 0.022) but not DBP (β, -0.0073; SE, 0.0037; P = 0.053). In addition, rs266729 SNP (-11377C>G) was directly related to DBP (β, 5.5095; SE, 2.557; P = 0.035) but not SBP (β, 0.1147; SE, 9.351; P = 0.224). This study has not only further established that strong relationship exists between SBP and DBP but also reinforced the fact that differences between these two traits exist at the genetic and epidemiological levels.

Keywords: Hypertension, blood pressure, rs266729, Nigeria

Introduction

Hypertension (HTN) is a complex disease that is characterized by elevated blood pressure (BP). It increases the risk for cardiovascular diseases (CVDs) such as heart attack, congestive heart failure, stroke, coronary heart disease, and peripheral vascular disease (Chobanian*et al.*, 2003; Lewington *et al.*, 2002; Banegas *et al.*, 1980; William & Kannel, 1996; Hickler, 1988). The prevalence of hypertension in Nigeria according to a review by Ogah *et al.*(2012)is between 8% and 46.8%. Another independent study has also reported the hypertension prevalence in Nigeria within this range (Ekwunife & Aguwa, 2011).

Being a complex trait, hypertension could be caused by an interaction of multiple genetic factors and lifestyle exposures including dietary salt intake, alcohol consumption, and body weight (Knight *et al.*, 2009). Observational studies have shown that elevated BP is associated with higher salt intake (Elliott *et al.*, 1996), excessive alcohol consumption (Arkwright *et al.*, 1982), higher BMI (Field *et al.*, 2001) and reduced physical activity (Blair *et al.*, 1984).The heritability of hypertension falls within the range of 30-60% as most studies often report (Hedayati *et al.*, 2011;

Arora & Newton-Cheh, 2010). Its high heritability may be attributable to additive genetic factors (Levy *et al.*, 2000). The intake of some dietary nutrients could influence the process of gene expression and protein synthesis (Doaei *et al.*, 2011). Also, some of the variations in genes could influence the level of nutrients requirements in individuals as people could differ in their requirements and tolerable upper limits of nutrients (Doaei & Gholamalizadeh, 2010; Safavi *et al.*, 2007).

Prevention and management of hypertension pose serious challenges to public health organizations both at an individual and at population level (Schroder *et al.*, 2002). Different approaches to reduce the prevalence and enhance control of hypertension have been focusing on nutrigenomic and non-pharmacological methods that are targeted at lowering blood pressure. Notably, dietary approaches appear to be promising since some macronutrients and micronutrients have been inversely associated with blood pressure (Hermansen, 2000). Also, studies have shown that dietary intervention could reduce significantly blood pressure not only in normotensive, but also in hypertensive persons (Apple *et al.*, 1997).

Although many studies have reported association between dietary salt intake and hypertension, but BP responses to high and low salt intake may be affected by different genetic factors (He & MacGregor, 2003). It has been suggested that sodium intake restriction may not be beneficial to everyone due to their unique genetic profiles (Doaei & Gholamalizadeh, 2014) and so, there is a need to further investigate the genetic and dietary determinants of blood pressure in order to increase our understanding of the mechanisms underlying hypertension. A clearer understanding of the genetic, dietary and lifestyle determinants of BP variation could point to novel ways to prevent HTN and its complications. This present study was therefore aimed at investigating the associations between blood pressure and: i) a single nucleotide polymorphism (SNP) of adiponectin gene and (ii) intakes of sodium, potassium, magnesium, and calcium in a cross-sectional sample of young adults in Nigeria.

Methods

Study population

The present study included 117 healthy 18□30-year old Nigerian young adults recruited from students at Tai Solarin University of Education, Nigeria on a voluntary basis between January 2016 and May 2017. The full design with the detailed inclusion and exclusion criteria for all subjects has been previously published (Ogundele *et al.*, 2017). Briefly, this sample is from a cross-sectional study of one hundred and fifty participants conducted in Ogun state of Nigeria. After excluding participants with incomplete outcome data and who had reported medical problems that may influence their blood pressure, 117 eligible subjects were remaining and thus included in the final analyses. The study was conducted in accordance with the declaration of Helsinki and was approved by the local institutional review committee and the Health Research Ethics Committee (HREC) of Lagos University Teaching Hospital (LUTH) with HREC assigned number ADM/DCST/HREC/APP/800. Each participant signed an informed consent before enrolling in the study.

Anthropometric measurements

Blood pressure was measured following standard clinical procedures using an OMRON M2 basic digital automatic blood pressure monitor which has a measurement range of 0-299mmHg and calibration accuracy of ±3mmHg (O'brien *et al.*, 2002). Briefly, the cuff was placed such that the lower cuff was approximately 2 cm above the elbow of the left arm. Two readings were taken, at least 15 minutes apart and the mean of the two readings recorded. Participants were then classified as normotensive (systolic blood pressure<140mm Hg and diastolic blood pressure<90mm Hg) or hypertensive (systolic blood pressure □ 140mm Hg and/or diastolic blood pressure□ 90mm Hg) according to previous protocol (Schroder *et al.*, 2002). The anthropometric measurements including weight, height and waist circumference were obtained with individuals wearing light cloths and no shoes following standard procedures. A precision scale of easy calibration was used for weight measurement. Height was measured in the standing position and measurements rounded to 0.5 cm. Body mass index (BMI) was determined as weight divided by squared height (kg/m^2). Waist circumference was measured using measurement tape. Waist circumference was measured at the midpoint between the lower border of the rib cage (costal margin) and the iliac crest.

Blood collection, DNA isolation and SNPs genotyping

Details of blood collection, DNA isolation and SNPs genotyping methods have been previously described (Ogundele *et al.*, 2017). In brief, blood samples were obtained from participants after a 9-hour fast as dried blood spots (DBS) samples through finger picking. DBS samples were spotted on Whatman FTA® cards (Whatman Inc., Brentford, UK) and were dried for 24 hours at room temperature according to the method of (Choi *et al.*, 2014). They were then kept in separate clean zipper bags and stored at room temperature prior to molecular analysis. Genomic DNA was then isolated from the DBS samples using Zymo Research (ZR) DNA Card Extraction Kits following manufacturer's protocol. *ADIPOQ* rs266729 was genotyped by using Sequenom MassARRAY Genotyping System (Sequenom, San Diego, CA, USA). The genotyping efficiency was >92%.

Questionnaire

Food Frequency Questionnaire (FFQ), adapted from the validated FFQ (Mulligan *et al.*, 2014; Awofala *et al.*, 2016) was used to collect data on dietary nutrients of participants. Data on time spent walking, in moderate- and vigorous-intensity physical activity (PA) were collected using the short form of International Physical Activity Questionnaire (IPAQ) adapted from Craig *et al.*(2003). Physical activity was expressed as metabolic equivalent task (MET)-minutes based on self-reported types and durations of activities per week. One MET-minute is equivalent to energy expenditure while sitting quietly for 1 minute.

Statistical analysis

Continuous data were summarized as mean ± standard deviation (SD) unless otherwise stated and whether they significantly differed by sex or blood pressure categories was tested by t-test. Differences between groups of categorical variables were assessed by the use of □ test. Multiple linear regression analysis was carried out after adjusting for potential confounders such as sex, age, BMI and alcohol intake to test the association of sodium, calcium, potassium, magnesium

intakes and *ADIPOQ* rs266729 (additive model) with systolic and diastolic blood pressures. Analysis of the data was conducted using R package for Windows (version 3.1.3) statistical software package. Deviation from Hardy-Weinberg equilibrium was assessed using an exact test (HWExact) implemented in the R package. In all statistical tests performed P values of<0.05 were considered significant. The sample size and power of the study was calculated by using Quanto version 1.2.4 software.

Results and Discussion

Main characteristics of the subjects are shown in Table1. Generally, more males than females had significantly higher systolic blood pressure but non-significantly higher diastolic blood pressure. Male subjects consumed significantly more alcohol but less carbohydrate than their female counterparts. No significant differences of either macronutrient or micronutrient intake among groups were observed with respect to sex and largely hypertension (Table 1). However, intake of calcium was significantly higher in the hypertensive group than in the normotensive group. The ratio of sodium to potassium intake in the normotensive group was lower than in the hypertensive group; however, this difference did not reach statistical significance. Neither alcohol consumption nor the level of physical activity (depicted as total, low, moderate and vigorous) was significantly different between the hypertensive and the normotensive group.

In the multiple linear regression analysis adjusting for sex, age, BMI and alcohol intake ADIPOQ rs266729 (-11377C>G) polymorphism was associated with DBP but not SBP (Table 2). The potential association between ADIPOQ gene and hypertension has been evaluated in both animal and human studies (Ohashi *et al.*, 2006; Kim *et al.*, 2013; Chu *et al.*, 2016). For instance, Ohashi and colleagues showed that adiponectin knockout mice developed hypertension compared with the wild type after a 3-weeks high salt-diet (Ohashi *et al.*, 2006). In addition, Kim and colleagues in a meta-analysis of 17598 adults from 43 non-cohort studies and 5 cohort studies found that adiponectin level in hypertensive adults was 1.64 μgml^{-1} lower than that in normotensive adults, and the risk of hypertension was reduced by 6% per 1 μgml^{-1} increase in plasma adiponectin levels (Kim *et al.*, 2013). In our study, the SNP rs266729 promoter region of the gene was significantly associated with DBP. This further confirmed that the adiponectin gene might be involved in the mechanisms governing BP regulation. Interestingly, we have recently shown that SNP rs266729 was associated with some measures of obesity involving body mass index, waist circumference and hip circumference (Ogundele *et al.*, 2017).

Table 1: Characteristics of participants

	Female n=91	Male n=26	Normotensive n=100	Hypertensive n=17
Age	22.24 ± 2.72	22.24 ± 2.33	22.30 ± 2.67	21.94 ± 2.41
Body mass index (kgm^{-2})	18.17 ± 9.16	18.19 ± 5.65	18.91 ± 8.66	19.60 ± 8.46
SBP (mmHg)	121.99 ± 14.18[a]	132.09 ±12.54[a]	119.95±10.86[b]	144.12±8.70[b]
DBP (mmHg)	75.13 ± 9.98	76.64 ± 8.66	72.63±7.18[b]	87.71±9.80[b]
WC (cm)	75.91 ± 8.97	75.34 ± 5.43	75.04 ± 8.51	77.07 ± 7.81
Alcohol (g)	3.10 ± 7.52[a]	11.61 ± 25.92[a]	4.38 ± 14.15	8.60 ± 14.31
Energy (kJ)	12345.53	12139.18	11660.92	16057.02
Carbohydrates (%)*	49.29[a]	47.34[a]	48.97	47.19
Fats (%)*	31.24	32.35	30.42	33.44
Protein (%)*	19.47	20.31	20.61	19.37
Saturated fatty acids (g)	39.74	39.01	36.92	55.23
Monounsaturated fatty acids (g)	47.26	48.52	44.16	56.54
Polyunsaturated fatty acids (g)	19.70	20.11	18.51	27.33
Cholesterol (mg)	514.04	480.86	490.13	603.95
Dietary fibre (g)	19.55	18.52	18.31	25.20
Vitamin C (mg)	122.51	122.72	112.15	183.75
β Carotene (mcg)	2809.26	2677.22	2679.09	3373.03
αTocopherol (mg)	21.49	20.35	19.80	29.69
Potassium (mg)	4437.56	4478.50	4227.47	5735.98
Calcium (mg)	1016.21	972.88	980.92[b]	1157.54[b]
Sodium (mg)	3408.37	2957.28	3154.05	4214.46
Magnesium (mg)	407.67	406.13	392.72	493.26
Na/K	0.76	0.68	0.68	0.74
Vigorous PA (MET-minutes/week)	1234.56	1880.92	1404.82	708.24
Moderate PA (MET-minutes/week)	1323.29	1420.00	1288.78	1249.41
Walk PA (MET-minutes/week)	1341.27	1542.37	1392.18	904.59
Total PA (MET-minutes/week)	3900.11	4843.29	4085.77	2862.24

[a] $p < 0.05$ between females and males; [b] $p < 0.05$ between normotensive and hypertensive groups; * in percentage of energy intake; PA, physical activities; MET, metabolic equivalent of task.

Table 2: Association between adiponectin rs266729, systolic (SBP), diastolic (DBP) blood pressures and selected mineral intake

	SBP			DBP		
*Model	B	SE	*P*	B	SE	*P*
rs266729	0.1147	9.3507	0.224	5.5095	2.5571	**0.035**
Calcium (mg)	-0.0119	0.0057	**0.039**	-0.0065	0.0038	0.090
Potassium (mg)	0.0015	0.0016	0.346	0.0016	0.0011	0.143
Sodium (mg)	0.0003	0.0015	0.859	0.0005	0.0010	0.847
Magnesium (mg)	0.0082	0.0221	0.711	-0.0026	0.0146	0.862

* Adjusted for sex, age, BMI and alcohol intake

This study also revealed an inverse relationship between the dietary intake of calcium and SBP but no significant relationship between DBP and calcium (Table 2) intake albeit there was a significant correlation between SBP and DBP ($r = 0.70$; p-value = $2.665e^{-15}$ and data not shown) in the population investigated. Interestingly, the importance of diet as a non-pharmacological approach in the prevention and treatment of hypertension has been stressed by several studies (Houston *et al.*, 2008; Binia *et al.* 2015; Vamvakis *et al.*, 2017). Notably, dietary intake of sodium, calcium, magnesium and potassium are known to affect blood pressure (Houston *et al.*, 2008; Binia *et al.* 2015). In addition, evidence demonstrating a linear relationship between sodium intake and blood pressure exists (Vamvakis *et al.*, 2017). Moreover, epidemiological analyses indicated that association between calcium intake and blood pressure was indirect (Houston *et al.*, 2008; Vamvakis *et al.*, 2017). Importantly, that lower blood pressure in response to a reduced sodium intake is strongly related to sodium sensitivity has long been stressed (Masia *et al.*, 1998). Thus the negative significant relationship between dietary calcium and SBP in our study further confirmed the role of calcium on blood pressure. Notably, while the association of calcium with SBP was moderate in the present study, it is not surprising that we did not see any significant relationship between dietary sodium and blood pressure. This is because dietary assessments generally underestimate sodium intake, yet urinary samples which would have been the most accurate way to estimate dietary sodium intake were not collected in the present study.

As this study employs a single SNP, we were unable to carryout haplotype analysis that has a great advantage over an individual SNP analysis for genetic study of complex diseases such as hypertension. In addition, an assessment of self-reported diet was imperfect due to errors of selection and recall. However, we used a validated FFQ (Awofala *et al.* 2017) that assessed weekly consumption and any dietary errors are likely to be random and bias associations toward the null.

Conclusion

In conclusion, the present study found that the common variant rs266729 of ADIPOQ gene was significantly associated with DBP while dietary calcium intake was significantly negatively associated with SBP in young Nigerian population. Studies with larger sample size are needed to confirm these results.

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References

Appel, L.J., Moore, T.J., Obarzanek, E., Vollmer, W.M., Svetkey, L.P., Sacks, F.M., Bray, G.A., Vogt, T.M., Cutler, J.A., Windhauser, M.M. & Lin, P.H.(1997). A clinical trial of the effects of dietary patterns on blood pressure. *New England Journal of Medicine*, *336*(16), 1117-1124.

Arkwright, P. D., Beilin, L. J., Rouse, I., Armstrong, B. K., &Vandongen, R. (1982).Effects of alcohol use and other aspects of lifestyle on blood pressure levels and prevalence of hypertension in a working population. *Circulation*, *66*(1), 60-66.

Arora, P., & Newton-Cheh, C. (2010). Blood pressure and human genetic variation in the general population. *Current Opinion in Cardiology*, *25*(3), 229.

Awofala, A. A., & Ogundele, O. E. (2017). Association between alcohol intake and subjective cognitive complaints in southwest Nigeria: a cross-sectional observational study. *Alexandria Journal of Medicine*.http://dx.doi.org/10.1016/j.ajme.2017.08.001

Banegas, J. R., Rodríguez-Artalejo, F., de la Cruz Troca, J. J., Guallar-Castillón, P., & del Rey Calero, J. (1998). Blood pressure in Spain. *Hypertension*, *32*(6), 998-1002.

Binia, A., Jaeger, J., Hu, Y., Singh, A., & Zimmermann, D. (2015). Daily potassium intake and sodium-to-potassium ratio in the reduction of blood pressure: a meta-analysis of randomized controlled trials. *Journal of Hypertension*, *33*(8), 1509-1520.

Blair, S. N., Goodyear, N. N., Gibbons, L. W., & Cooper, K. H. (1984). Physical fitness and incidence of hypertension in healthy normotensive men and women.*Journal of American Medical Association*, *252*(4), 487-490.

Chobanian, A.V., Bakris, G.L., Black, H.R., Cushman, W.C., Green, L.A., Izzo Jr, J.L., Jones, D.W., Materson, B.J., Oparil, S., Wright Jr, J.T. & Roccella, E.J. (2003). The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. *Journal of American Medical Association*, 289(19), 2560-2571.

Choi, E. H., Lee, S. K., Ihm, C., & Sohn, Y. H. (2014). Rapid DNA extraction from dried blood spots on filter paper: potential applications in biobanking. *Osong Public Health and Research Perspectives*, *5*(6), 351-357.

Chu, C., Wang, Y., Ren, K.Y., Yan, D.Y., Guo, T.S., Zheng, W.L., Yuan, Z.Y. & Mu, J.J.(2016). Genetic variants in adiponectin and blood pressure responses to dietary sodium or potassium interventions: a family-based association study. *Journal of Human Hypertension*, *30*(9), 563-570.

Craig, C.L., Marshall, A.L., Sjöström, M., Bauman, A.E., Booth, M.L., Ainsworth, B.E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J.F. & Oja, P.(2003). The IPAQ Consensus Group and the IPAQ Reliability and Validity Study Group. International Physical Activity Questionnaire (IPAQ): 12-country reliability and validity. *Medicine & Science in Sports & Exercise*, 35(13), 81-95.

Doaei, S., & Gholamalizadeh, M. (2010). The association between dietary fat with gene polymorphisms. *Proceedings of the 11th Iranian Nutrition Congress*, Shiraz, Iran.

Doaei, S., & Gholamalizadeh, M. (2014). The association of genetic variations with sensitivity of blood pressure to dietary salt: A narrative literature review. *ARYA Atherosclerosis*, *10*(3), 169-74.

Doaei, S., Gholamalizadeh, M., Akbari, M., & Safavi, S. M. (2011). Nutritional genomics: a window to the future.1st Ed. Andishe Mandegar Publication, Qom, Iran.

Ekwunife, O. I., & Aguwa, C. N. (2011). A meta analysis of prevalence rate of hypertension in Nigerian populations. *Journal of Public Health and Epidemiology*, *3*(13), 604-607.

Elliott, P., Stamler, J., Nichols, R., Dyer, A. R., Stamler, R., Kesteloot, H., & Marmot, M. (1996). Intersalt revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations. *British Medical Journal*, 312(7041), 1249-1253.

Field, A.E., Coakley, E.H., Must, A., Spadano, J.L., Laird, N., Dietz, W.H., Rimm, E. & Colditz, G.A. (2001). Impact of overweight on the risk of developing common chronic diseases during a 10-year period. *Archives of Internal Medicine*, *161*(13), 1581-1586.

He, F. J., & MacGregor, G. A. (2003). How far should salt intake be reduced?. *Hypertension*, *42*(6), 1093-1099.

Hedayati, S. S., Elsayed, E. F., & Reilly, R. F. (2011). Non-pharmacological aspects of blood pressure management: what are the data?. *Kidney International*, *79*(10), 1061-1070.

Hermansen, K. (2000). Diet, blood pressure and hypertension. *British Journal of Nutrition*, *83*(S1), S113-S119.

Hickler, R. B. (1988). " Hypertensive emergency": a useful diagnostic category. *American Journal of Public Health*, 78(6), 623-624.

Houston, M. C., & Harper, K. J. (2008). Potassium, magnesium, and calcium: their role in both the cause and treatment of hypertension. *The Journal of Clinical Hypertension*, *10*(7), 3-11.

Kannel, W. B. (1996). Blood pressure as a cardiovascular risk factor: prevention and treatment. *Journal of American Medical Association*, *275*(20), 1571-1576.

Kim, D. H., Kim, C., Ding, E. L., Townsend, M. K., & Lipsitz, L. A. (2013). Adiponectin Levels and the Risk of Hypertension. *Hypertension*, 62(1),27-32.

Knight, B. S., Sunn, N., Pennell, C. E., Adamson, S. L., & Lye, S. J. (2009). Developmental regulation of cardiovascular function is dependent on both genotype and environment. *American Journal of Physiology-Heart and Circulatory Physiology*, *297*(6), H2234-H2241.

Levy, D., DeStefano, A.L., Larson, M.G., O'donnell, C.J., Lifton, R.P., Gavras, H., Cupples, L.A. & Myers, R.H. (2000). Evidence for a gene influencing blood pressure on chromosome 17. *Hypertension*, *36*(4), 477-483.

Lewington, S., Clarke, R., Qizilbash, N., Peto, R.& Collins, R. (2002). Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *The Lancet*, *360*(9349), 1903-1913.

Masiá, R., Pena, A., Marrugat, J., Sala, J., Vila, J., Pavesi, M., Covas, M., Aubó, C. & Elosua, R.(1998). High prevalence of cardiovascular risk factors in Gerona, Spain, a province with low myocardial infarction incidence. REGICOR Investigators. *Journal of Epidemiology & Community Health*, *52*(11), 707-715.

Mulligan, A.A., Luben, R.N., Bhaniani, A., Parry-Smith, D.J., O'Connor, L., Khawaja, A.P., Forouhi, N.G. & Khaw, K.T.(2014). A new tool for converting food frequency questionnaire data into nutrient and food group values: FETA research methods and availability. *BMJ open*, *4*(3), e004503.

O'brien, E., Pickering, T., Asmar, R., Myers, M., Parati, G., Staessen, J., Mengden, T., Imai, Y., Waeber, B., Palatini, P. & Gerin, W. (2002). Working Group on Blood Pressure Monitoring of the European Society of Hypertension International Protocol for validation of blood pressure measuring devices in adults. *Blood Pressure Monitoring*, *7*(1), 3-17.

Ogah, O. S., Okpechi, I., Chukwu, I. I., Akinyemi, J. O., Onwubere, B. J. C., Falase, A. O., Stewart, S. &Sliwa, K. (2012). Blood pressure, prevalence of hypertention and hypertension related complications in Nigerian Africans: A review. *World Journal of Cardiology*,4(12), 327-40.

Ogundele, O. E., Adekoya, K. O., Osinubi, A. A., Awofala, A. A., & Oboh, B. O. (2017). Association of adiponectin gene (ADIPOQ) polymorphisms with measures of obesity in Nigerian young adults. *Egyptian Journal of Medical Human Genetics*.http://dx.doi.org/10.1016/j.ejmhg.2017.08.005

Ohashi, K., Kihara, S., Ouchi, N., Kumada, M., Fujita, K., Hiuge, A., Hibuse, T., Ryo, M., Nishizawa, H., Maeda, N. & Maeda, K.(2006). Adiponectin replenishment ameliorates obesity-related hypertension. *Hypertension*, *47*(6), 1108-1116.

Safavi, S. M., Doaei, S., & Gholamalizadeh, M. (2007). Unsaid of nutrition and genetics. *The World of Nutrition Journal*, *6*(60), 22-3.

Schröder, H., Schmelz, E., & Marrugat, J. (2002). Relationship between diet and blood pressure in a representative Mediterranean population. *European Journal of Nutrition*, *41*(4), 161-167.

Vamvakis, A., Gkaliagkousi, E., Triantafyllou, A., Gavriilaki, E., & Douma, S. (2017). Beneficial effects of nonpharmacological interventions in the management of essential hypertension. *JRSM Cardiovascular Disease*, *6*, 2048004016683891.