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Risk factors of the brain atrophy detected by computed tomography: A case-control study

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ABSTRACT

Purpose: Brain atrophy is a decline in brain volume caused by the degeneration or death of neurons and their connections. This study aimed to determine the risk factors associated with brain atrophy diagnosed by computed tomography (CT) scan.

Materials and Methods: A prospective case-control design was carried out in this study over six months from October 2022 to March 2023. All participants included in this study were Iraqis aged ≥ 18 years. Cases were selected from those who were subjected to the CT unit and diagnosed with brain atrophy. Controls were selected from the same medical complex who were subjected to a CT unit and diagnosed with normal brain findings. The control group was matched by age (± 3 years) and gender for the cases. A systematic sampling technique was used as a sampling method for cases.

Results: A total of 192 subjects were included and analyzed in this study. Of those, 96 (50.0%) subjects were diagnosed with brain atrophy (cases) and 96 (50.0%) subjects were healthy (controls). The following independent factors were significantly associated with brain atrophy: family history of brain atrophy (p<0.001), smoking habit (p=0.002), alcohol intake (p<0.001), and cardiac disease (p<0.001). However, smoking (p=0.038, OR=2.348, CI= 1.050 – 5.250), alcohol intake (p=0.044, OR=2.503, CI= 0.648 – 9.673), and cardiac disease (p=0.001, OR=5.015, CI= 2.003 – 12.556) were reported to be risk factors for developing brain atrophy.

Conclusion: Smoking, alcohol intake, and cardiac disease were noted to increase the risk of brain atrophy.

KEY WORDS
brain atrophy / risk factors / computed tomography / Iraqi populationIntroduction

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CT provides horizontal-sliced images of the brain.

Brain atrophy, also known as cerebral atrophy, is defined as a decrease in brain volume caused by the degeneration or death of neurons and their connections and is increasingly becoming a common topic in neuroscientific research [1]. It is considered a hallmark of neurodegenerative disease [2]. In adulthood, a gradual loss of cerebral tissues can lead to brain atrophy [3]. The most common cerebral compartments that can be affected by atrophy is the supra-tentorial compartment, cerebral cortex, and hippocampus [4,5]. Computed tomography (CT) is considered the first neuroimaging technique commonly used for brain imaging because it is more cost-effective, shorter imaging time, and is more available in comparison with magnetic resonance imaging [6]. Particularly, it is widely used for revealing brain anatomy and pathologies by providing transverse-sliced images [6]. It has significantly improved the ability to detect, measure, and longitudinal monitor cerebral atrophy over time [7]. With the capability to provide great spatial resolution and determine densities of varying tissue, the CT scan emerges as a critical tool for neurologists [8]. Although age is the most significant risk factor of cerebral atrophy [9], several factors such as systemic, hormonal, vascular, infections, autoimmune, and malnutrition can influence the cerebral tissue volume, degree, and rate of atrophy progression [10,11]. Regarding the aging population, these risk factors are currently the focus of extensive research [12]. However, various intrinsic factors such as age, gender, BMI, cardiovascular disease (e.g. coronary heart disease, peripheral arterial disease, congestive heart failure and/or abdominal and thoracic aneurysm), metabolic syndrome, diabetes mellitus, hypertension, and extrinsic factors such as traumatic brain injury (may cause immediate or delayed cerebral atrophy), substance abuse (e.g. alcoholism and smoking habit) and family history of the brain atrophy were not well studied. Thus, the purpose of the present study was to determine the risk factors (age, gender, BMI, family history of the disease, traumatic brain injury, smoking habit, alcohol intake, metabolic syndrome, diabetes mellitus, hypertension and cardiac disease) associated with brain atrophy diagnosed by CT scan.

Materials and Methods

Study population and design.

A matched case-control study was conducted over six months from October 2022 to March 2023. This study was carried out at the Medical City Complex, Baghdad. The subjects who admit to this complex are symptomatic and usually come from all provinces of Iraq. Thus, the study population was almost homogenous and represented the Iraqi population. The inclusion criteria of this study include individuals aged ≥ 18 years, both genders and participants who were diagnosed on medical imaging with/without brain atrophy were subjected as cases/controls, respectively. On the contrary, the subjects who had brain tumors, previous brain surgery, underwent chemotherapy/radiotherapy, encephalitis, cerebral palsy, multiple sclerosis, human immunodeficiency virus, Huntington's disease, and leukodystrophies were excluded from the study. Each respondent was verbally informed about the study and informed consent forms were signed by all participants before the start of the study. The personal information and data of the participants were confidentially preserved. Ethical approval from the Educational Medical City Department, Training and Human Development Center, Ministry of Health, Baghdad, was obtained.

Selection of cases and controls

All individuals who were subjected to the CT unit and diagnosed with brain atrophy were selected as "cases". A systematic sampling technique was used as a sampling method for cases. "Controls" were selected from the same medical complex who were subjected to a CT unit and diagnosed with normal brain findings (Figure 1a,1b). The control group was matched by age (± 3 years) and gender for the cases. The age is restricted to over 18 years old due to age being as main confounder which can be controlled in this design phase by matching age and gender. Both cases and controls were selected based on the selection criteria of the study.

A stadiometer (PRESTIGE 210 cm, height measuring scale, India) was used to measure body height whereas a weighting scale (MCP BR2020, Deluxe analog personal weighting scale, India) was used to measure body weight. BMI was calculated by dividing weight in kilogram (kg) over height in meter square (m^2). Based on World Health Organization guidelines for the Asia-Pacific region [13], BMI categories were as follows: normal ≤ 22.9 kg/ m^2, overweight =23.0 – 24.9 kg/ m^2, obese =25.0 – 29.9 kg/ m^2, and severe obese ≥ 30.0 kg/ m^2.

According to the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III (National Institute of Health, 2002) [14], the blood pressure was

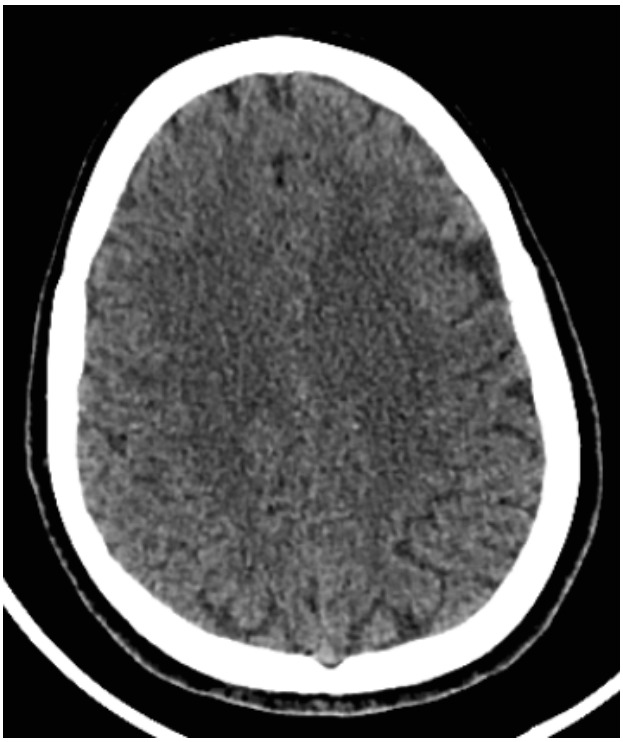

Figure 1a: *Non-contrast axial CT image shows normal cerebral sulci and gyrus.*

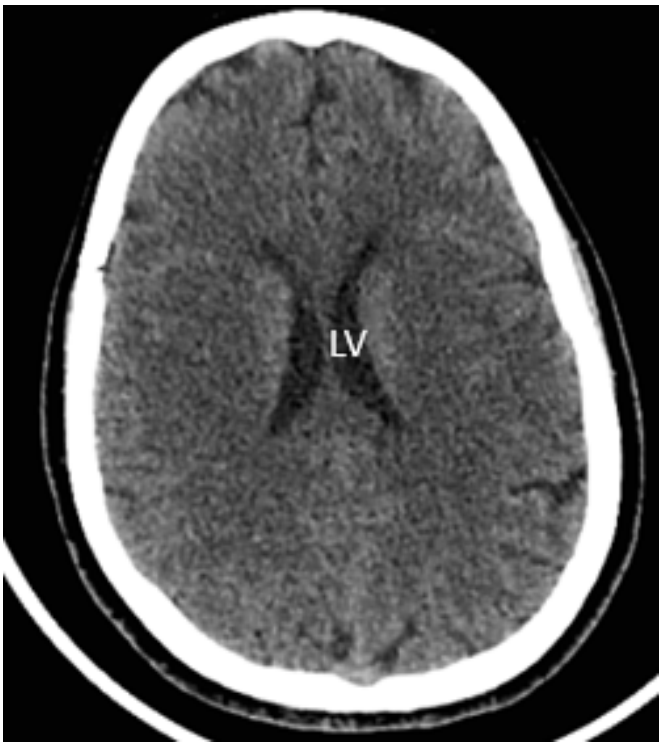

Figure 1b: *Non-contrast axial CT image shows normal lateral ventricular (LV).*

measured while the subject was in a sitting position, utilizing a standardized sphygmomanometer. A patient was diagnosed to have hypertension when he/she had been taking blood pressure lowering medication(s), he/she had a self-reported history of hypertension, or he/she had systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg at the time of examination. In light of this, a diabetic patient was considered when he/she had been taking antidiabetic medication(s), he/she had a self-reported history of diabetes mellitus, and he/she had FBG of >5.6 mmol/L or HbA1c of ≥ 6.5%. In the same context, the patient was reported to have metabolic syndrome when he/she met at least two of the aforementioned components (obesity "BMI ≥ 30.0 kg/m^2", diabetes mellitus, and hypertension).

A smoker was defined as having any tobacco cigarette smoking in the past month [15]. Males who had been consuming alcohol > 140 g/week and females> 70g/week were classified as alcoholic drinkers [16]. A family history of brain atrophy was considered if the patient's parents, siblings, grandparents, aunts, and uncles were previously reported with brain atrophy on medical imaging. For traumatic brain injury, it was considered if the previous medical imaging diagnosed that subject with a violent blow to the head, an object within brain tissues such as a bullet, skull fragments, and shrapnel, causing parenchymal torn, hemorrhage and other physical damage to the brain. Moreover, the patient was considered to have a cardiovascular disease if he/she had previously reported coronary heart disease such as angina, myocardial infarction, and/or congestive heart failure, had cerebrovascular disease such as stroke and/or transient ischemic attach, had peripheral artery disease and/or aortic atherosclerosis including abdominal and thoracic aneurysm [17].

CT imaging

Each individual in both groups underwent non-enhanced brain CT imaging using a Siemens multi-detector, 64-slice CT scanner, 2010. Each scan was performed using 16×1.0 mm primary slices (120 kV, 355 mAs, CTDI 57 mGy=2.2 mSv) reconstructed to axial and coronal MPR with 5- and 3-mm slice thickness, respectively. The subject was lying in a supine position in which no preparation was required. The scan was performed by two radiology technicians who have 10 year's experience of in spiral CT imaging. The diagnosis was reported by three

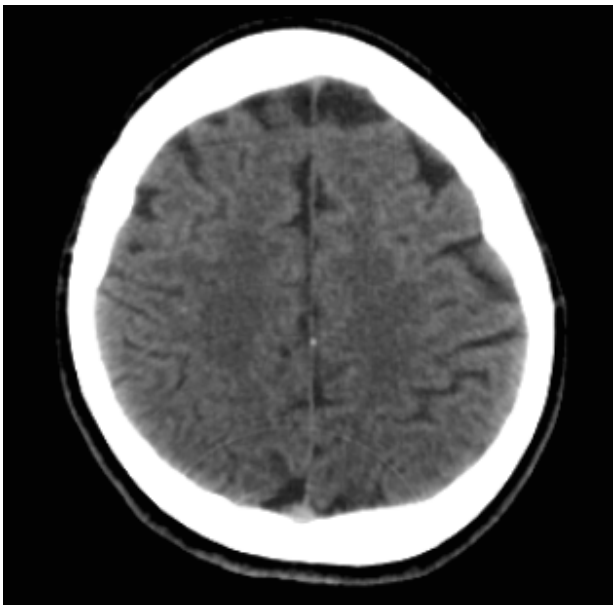

Figure 2a: *Non-contrast axial CT image shows cortical atrophy.*

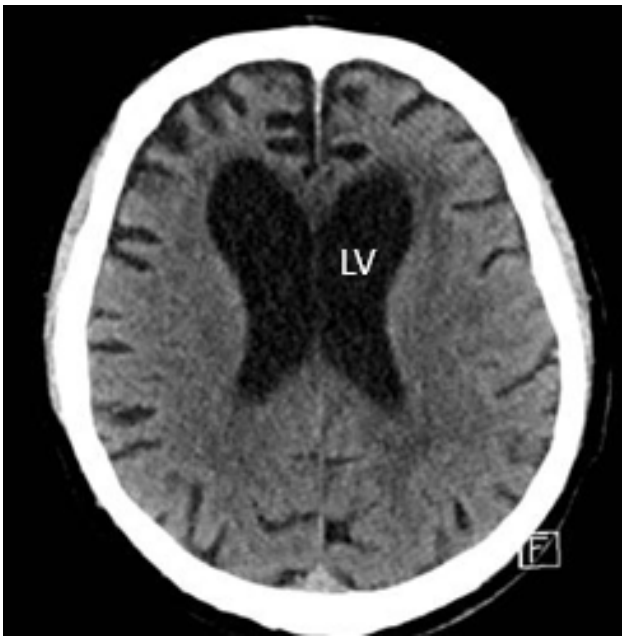

Figure 2b: *Non-contrast axial CT image shows dilated lateral ventricular (LV).*

radiologists who have an experience of more than 10 years in diagnostic neuroradiology. If the diagnosis was different between two radiologists, it was judged by the third radiologist. Thus, an interreader agreement was evaluated for this purpose. Cerebral atrophy was qualitatively diagnosed based on morphological evidence of cerebral parenchymal loss which is usually observed on axial images. The qualitative assessment of brain atrophy on CT scans is simple and suitable [18]. The diagnostic features of the brain atrophy are widened cerebral sulci and thinned gyrus (cortical atrophy) (Figure 2a), dilated Sylvian fissures, and ventricular system (central atrophy) (Figure 2b) with no bulging of the 3rd ventricular cavities [19].

Statistical analysis

Data were analyzed with SPSS 22.0. The statistical tests were performed based on the specific objectives of the study. To describe the characteristics of the study population, categorical variables were represented by frequencies and proportions (%), whereas continuous variables were represented by mean ±standard deviation. Association between categorical variables was conducted using the Chi-square test. Univariate analysis was used to determine the strength of association in the presence of particular factors was expressed as an odds ratio with 95% confidence intervals. Multivariate analysis was performed to determine the risk factors. *P* value <.20 on univariate analysis was subjected to multiple logistic regression analysis. P value <.05 was considered significant.

Results

Study population.

The distribution of the study population is shown in Table 1. A total of 192 subjects were included and analyzed in this study. Of those, 96 (50.0%) subjects were diagnosed with brain atrophy (cases) and 96 (50.0%) subjects were healthy (controls). The mean age of the participants was 56.4 ±16.2 years. Our study population was predominantly males (66.7%). In the meanwhile, the highest prevalence of BMI was for normal (37.5%), followed by obese (29.7%) and overweight (16.7%) whereas the lowest prevalence was reported for severe obesity (16.1%). In light of this, non-smokers and non-alcoholics were overwhelmingly (64.1% and 87.0%, respectively) in the study population. Furthermore, 161 (83.9%) subjects were reported without a family history of brain atrophy. In the same context, the patients with the following diseases were found to have the lowest proportions among the study population: metabolic syndrome (26.6%), diabetes mellitus (20.8%), hypertension (22.9%), cardiac disease (24.5%) and traumatic brain injury (24.0%).

Table 1: Characteristics of the study population (n=192 subjects)

Variables	n (%)	Mean ±SD
Age		56.4 ±16.2
Gender		
Female	64 (33.3)	
Male	128 (66.7)	
BMI categories		
Normal	72 (37.5)	
Overweight	32 (16.7)	
Obese	57 (29.7)	
Severe obese	31 (16.1)	
Family history of the disease		
No	161 (83.9)	
Yes	31 (16.1)	
Traumatic brain injury		
No	146 (76.0)	
Yes	46 (24.0)	
Smoking habit		
No	123 (64.1)	
Yes	69 (35.9)	
Alcohol intake		
No	167 (87.0)	
Yes	25 (13.0)	
Metabolic syndrome		
No	141 (73.4)	
Yes	51 (26.6)	
Diabetes mellitus		
No	152 (79.2)	
Yes	40 (20.8)	
Hypertension		
No	148 (77.1)	
Yes	44 (22.9)	
Cardiac disease		
No	145 (75.5)	

Yes	47 (24.5)	
Brain atrophy		
No	96 (50.0)	
Yes	96 (50.0)	

BMI: Body Mass Index

Conventional factors associated with brain atrophy.

An association between factors and brain atrophy is illustrated in Table 2. As this study matched with age and gender, there was no significant association was reported between age (p=0.899) and gender (p=0.561) with brain atrophy. For BMI, lower proportions of patients with overweight (15.6%), obese (27.1%), and severely obese (14.6%) were noted in the brain atrophy group than those in the control group (17.7%, 32.3%, and 17.7%), respectively. However, the patients with normal BMI were noted to be higher in the brain atrophy group (42.7%) than in the control group (32.3%). This indicates no significant association between BMI categories (normal, overweight, obese, and severely obese) and brain atrophy (p=0.524). Nevertheless, a proportion of patients with a family history of brain atrophy was observed to be significantly higher in the brain atrophy group (29.2 %) than in the control group (3.1%) (p< 0.001). Patients with traumatic brain injury had a higher prevalence in the brain atrophy group (29.2%) than in the control group (18.8%), showing no significant differences (p=0.091). On the contrary, smokers and alcohol drinkers had greater proportions of brain atrophy (46.9% and 21.9%) as compared with the counterparts in the control group (25.0% and 4.2%), showing significant association (p=0.002 and p< 0.001), respectively. Likewise, a significantly higher proportion (p< 0.001) of patients with cardiac disease was found in the brain atrophy group (39.6%) than in the control group (9.4%). However, no significant differences were found in the proportions of patients with metabolic syndrome (p=0.141), diabetes mellitus (p=0.076), and hypertension (p=0.086) between both groups.

Risk factors for brain atrophy.

The OR with 95% CI was adjusted on univariate and multivariate analysis. Univariate analysis shows that patients who have following factors: family history of the disease (p< 0.001, OR=12.765, 95% CI= 3.727 – 43.717), smoking (p=0.002, OR=2.647, 95% CI= 1.436 – 4.880), alcohol intake (p=0.001, OR=6.440, 95% CI=2.118 – 19.578), cardiac disease (p < 0.001, OR=6.333, 95% CI= 2.849 – 14.080) were significantly associated with brain atrophy (Table 3).

Multivariate analysis shows that alcohol intake could increase the risk of brain atrophy by 2.5 times concerning those who were not drinking (p=0.044, OR=2.503, CI= 0.648 – 9.673). Similarly, smokers were more likely by around 2 times to have brain atrophy than non-smokers (p=0.038, OR=2.348, CI= 1.050 – 5.250). In the same context, patients with cardiac disease were observed to have a significant risk by approximately 5 times in the progression of brain atrophy (p=0.001, OR=5.015, CI= 2.003 – 12.556). However, family history (p=0.072, OR=3.902, CI= 0.885 – 17.211) was not reported to be a significant risk factor for developing brain atrophy.

Discussion

The present study is unique in determining the risk factors associated with brain atrophy diagnosed by a CT scan. Determination of the factors associated with developing cerebral atrophy changes is important since they can contribute to mental decline. Furthermore, the control or treatment of these injurious factors may reversibly alter the neurodegenerative mechanism [10]. Although the previous study by Scahill et al. suggested that cerebral atrophy did not accelerate until 70 years old [20], the data from Enzinger et al. (particularly consistent with a younger group from a previous study) [21] proposed that rates of cerebral atrophy could increase progressively in the youngers. This finding could help to provide monitoring of the therapy responsiveness [22]. Moreover, it has implications for future efforts to predict the early stages of neurodegenerative changes using serial brain volume measurements [23]. Thus, age is considered as the most risk determinant of brain atrophy changes [9], therefore; the controls were matched by age (± 3 years) with cases.

To our knowledge, the association between BMI and

Table 2: Association between risk factors and brain atrophy (n=192 subjects)

Variables	Brain atrophy group (n=96)	Control group (n=96)	P-value
Age group (years), n (%)			0.899
18 – 33	6 (6.3)	9 (9.4)	
34 – 49	25 (26.0)	25(26.0)	
50 – 65	26 (27.1)	25 (26.0)	
≥ 66	39 (40.6)	37 (38.6)	
Gender, n (%)			0.561
Female	32 (33.3)	32 (33.3)	
Male	64 (66.7)	64 (66.7)	
BMI categories, n (%)			0.524
Normal	41 (42.7)	31 (32.3)	
Overweight	15 (15.6)	17 (17.7)	
Obese	26 (27.1)	31 (32.3)	
Severe obese	14 (14.6)	17 (17.7)	
Family history of the disease, n (%)			< 0.001
No	68 (70.8)	93 (96.9)	
Yes	28 (29.2)	3 (3.1)	
Traumatic brain injury, n (%)			0.091
No	68 (70.8)	78 (81.3)	
Yes	28 (29.2)	18 (18.8)	
Smoking habit, n (%)			0.002
No	51 (53.1)	72 (75.0)	
Yes	45 (46.9)	24 (25.0)	
Alcohol intake, n (%)			< 0.001
No	75 (78.1)	92 (95.8)	
Yes	21 (21.9)	4 (4.2)	
Metabolic syndrome, n (%)			0.141
No	66 (68.8)	75 (78.1)	
Yes	30 (31.3)	21 (21.9)	
Diabetes mellitus, n (%)			0.076
No	71 (74.0)	81 (84.4)	
Yes	25 (26.0)	15 (15.6)	
Hypertension, n (%)			0.086
No	69 (71.9)	79 (82.3)	
Yes	27 (28.1)	17 (17.7)	

Cardiac disease, n (%)			< 0.001
No	58 (60.4)	87 (90.6)	
Yes	38 (39.6)	9 (9.4)	

BMI: Body Mass Index

brain volume is still controversial and is an active area of the studies, and understanding of this link is continually improving. Some studies showed that obesity is linked with brain parenchymal changes whereas others did not confirm this association. For instance, the present study revealed that no association was found between BMI and brain atrophy. In contrast, a cohort study from Austria by Enzinger et al. assessed the brain volume changes over six years for two hundred and one health subjects using 1.5-T MRI. The authors found that a greater rate of brain atrophy was observed in subjects with high BMI [24]. This conflict may be due to that obesity is a complex disorder with numerous contributing factors such as genetics, nutrition, and physical activity. Therefore, not all patients with obesity may suffer the same physiological alterations in the brain parenchyma [25]. Furthermore, the studies may use different techniques and methodologies, including imaging modalities, study location, sample sizes, and characteristics of the study population. Hence, these variations might result in inconsistent outcomes across research. The effectiveness of obesity on the brain may differ based on when it starts and how long it continues. Obesity that persists for a long term or childhood obesity could have different efficacy on the brain tissues than that in adults-onset [25]. In this study, it was expected that a family history of brain atrophy was significantly associated with brain atrophy itself. However, it was not reported to be a risk predictor for the condition.

Our findings showed that the association between traumatic brain injury and brain atrophy was not found to be significant. This finding was inconsistent with the finding from McKee et al. in which head traumas could cause cerebral atrophy over time [26]. This inconsistency may be attributed to the severity of repeated traumatic brain injuries in which the brain tissues could be more affected [1]. Some literature indicated that brain volume loss can develop gradually within months or even years following a traumatic brain injury rather than immediately [26,27].

In the same context, the current study documented that smoking and alcohol intake could induce brain atrophy. In more detail, smokers and alcohol drinkers were more likely to have brain atrophy than those who were non-smokers and non-alcohol drinkers. A longitudinal cohort study showed that alcohol drinkers, even those who consumed moderate levels (14-21 units/week) were more likely by 3 times to have hippocampal atrophy whereas no evidence of brain atrophy in those who were drinking lightly (1-<7 units/week). For those drinking heavily, the corpus callosum was also affected by a rapid decline in lexical fluency [28]. Smoking was also implicated in the acceleration of this condition [29].

For metabolic syndrome, our results stated unexpectedly no link between metabolic syndrome and brain atrophy. In a recent study, Porte Jr et al. indicated that components of metabolic syndrome such as obesity and diabetes contributed to dysfunction of the central nervous system [30]. Metabolic syndrome is considered a heterogeneous disorder in which the patients may have different terms of severity as well as a combination of its components [31]. This diversity may result in the challenge of confirming a consistent link with cerebral atrophy. In addition, individuals may be influenced differently by metabolic syndrome, depending on genetic factors, lifestyle, medical history of brain diseases, and demographic factors. Therefore, not everyone suffering from metabolic syndrome may have the same level of cerebral atrophy [32]. Metabolic syndrome in patients with high levels of HbA1c was significantly related to late-life brain volume loss [24]. Although possible interaction between HbA1c and age is considered [33], the present finding found that diabetic patients had no risk of developing brain atrophy. This may explain why the brain is considered as "an insulin-insensitive organ" [34]. However, this finding was inconsistent with findings from the cohort of healthy elderly individuals in which higher HbA1c was highly associated with brain atrophy [24]. In light of this, previous literature documented an association between a higher rate of atrophy and diabetes [35]. Interestingly, the rate of cerebral atrophy was significantly higher even in patients with normal HbA1c levels in clinical practice

Table 3: Risk factors of brain atrophy using univariate analysis (n=192 subjects)

Variables	B	S.E.	Wald	df	Sig.	OR	95% CI for EXP (B)	
							Lower	Upper
Age (Years)								
< 45	-	-	-	-	-	1.00	-	-
≥ 45	2.376	0. 443	28.787	1	0.099	1.758	4.517	25.623
Gender								
Female	-	-	-	-	-	1.00	-	-
Male	0.000	0.306	0.000	1	1.000	1.000	0.549	1.822
BMI								
Normal	-	-	-	-	-	1.00	-	-
High	0.104	0. 453	0.000	1	1.000	1.000	0. 411	2.431
Family history of the disease								
No	-	-	-	-	-	1.00	-	-
Yes	2.547	0.628	16.440	1	< 0.001	12.765	3.727	43.717
Traumatic brain injury								
No	-	-	-	-	-	1.00	-	-
Yes	0.579	0.345	2.822	1	0.093	1.784	0.908	3.506
Smoking habit								
No	-	-	-	-	-	1.00	-	-
Yes	0.973	0.312	9.730	1	0.002	2.647	1.436	4.880
Alcohol intake								
No	-	-	-	-	-	1.00	-	-
Yes	1.863	0.567	10.779	1	0.001	6.440	2.118	19.578
Metabolic syndrome								
No	-	-	-	-	-	1.00	-	-
Yes	-0.485	0.331	2.145	1	0.143	0.616	0.322	1.178
Diabetes mellitus								
No	-	-	-	-	-	1.00	-	-
Yes	0.643	0.365	3.102	1	0.078	1.901	0.930	3.887
Hypertension								
No	-	-	-	-	-	1.00	-	-
Yes	0.598	0.351	2.907	1	0.088	1.818	.914	3.616
Cardiac disease								
No	-	-	-	-	-	1.00	-	-
Yes	1.846	0.408	20.504	1	< 0.001	6.333	2.849	14.080

BMI: Body Mass Index

Table 4: Risk factors of brain atrophy using multivariate analysis (n=192 subjects)

Variables	B	S.E.	Wald	df	Sig.	OR	95% CI for EXP (B)	
							Lower	Upper
Family history of the disease								
No	-	-	-	-	-	1.00	-	-
Yes	1.361	0.757	3.233	1	.072	3.902	0.885	17.211
Smoking habit								
No	-	-	-	-	-	1.00	-	-
Yes	0.854	0.410	4.324	1	0.038	2.348	1.050	5.250
Alcohol intake								
No	-	-	-	-	-	1.00	-	-
Yes	0.918	0.690	1.770	1	0.044	2.503	0.648	9.673
Cardiac disease								
No	-	-	-	-	-	1.00	-	-
Yes	1.613	0.468	11.860	1	0.001	5.015	2.003	12.556

BMI: Body Mass Index

(third quartile: 5.6 to 5.8%) [36]. In the same context, Hirabayashi et al. indicated that diabetes for a longer period as well as high levels of post-load glucose could increase the risk of developing hippocampal atrophy [37]. Furthermore, the present study showed that hypertensive patients were not observed to stimulate brain atrophy. Nevertheless, Raz et al. noted that hypertension could lead to parenchymal changes in the brain, such as dilatation of the lateral ventricles as well as decline in the brain volume [38]. This inconsistency of association between hypertension and brain atrophy across studies may be attributed to variability in methods and techniques used, sample sizes, and homogeneity of study population which in turn lead to inconsistent outcomes.

Regarding cardiovascular disease, this study revealed (in conjunction with previous studies [29,39] that patients with cardiac disease were more likely to have brain atrophy than those without cardiac disease. Unexpectedly, Enzinger et al. demonstrated no significant association between vascular diseases and brain atrophy [24]. Moreover, Kappus et al. showed that patients with one or more cardiovascular diseases could increase their risk of developing brain atrophy, particularly in those with multiple sclerosis [40].

There are some limitations in this study. Firstly, our results may not be generalized to the adult population as the number of subjects aged between 18 – 33 years was too small in both groups. Secondly, metabolic syndrome components included in this study were 3 out of 6 which are obesity, diabetes, and hypertension as most patients who attended for brain CT scan did not have lipid profile test for triglycerides and high-density lipoproteins-cholesterol (HDL-C) levels. Thirdly, brain atrophy was diagnosed qualitatively which is a subjective method, leading to inaccurate outcomes, therefore, Fourthly, some patients had no knowledge or memory about the family history of the condition, so the authors depended on previous imaging/clinical reports to confirm this issue. Fifthly, traumatic brain injury documentation was reliable based on medical imaging and a history of accidents. In the case of the latter, however; it was limited how is the brain being affected. Moreover, future works are needed to include further factors associated with grades (mild, moderate, and severe) of brain atrophy. It is also needed to determine the association of brain atrophy with the severity of traumatic brain injury. To enhance the validity of qualitative assessment of brain atrophy, quantitative volumetric analysis of global and local brain volume is recommended.

In conclusion, the family history of brain atrophy,

alcohol intake, smoking, and cardiac disease were independent factors associated with brain atrophy. Furthermore, multivariate analysis showed that these factors (except a family history of brain atrophy) were risky for the development of brain atrophy. **R**

Acknowledgment
None

Conflict of interest

The authors declare that they have no conflicts of interest, financial or otherwise.

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