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ASSOCIATION OF GENERAL OBESITY WITH AN INCREASED RISK OF STROKE: HOSPITAL-BASED CASE CONTROL STUDY

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ABSTRACT

Obesity is one of the most prevalent conditions making a significant impact on public health worldwide. This study aims to evaluate the contribution of general and abdominal obesity to the risk of stroke based on a hospital-based case-control study conducted in a tertiary hospital in Riyadh, Saudi Arabia. The present study evaluates a total of 94 stroke patients and 188 stroke-free patients with age (±5years) and sex-matched controls and investigates associations between different markers of obesity (BMI, waist-to-hip ratio, waist circumference, and waist-to-height ratio) and evaluates the risk of stroke using logistic regression analysis adjusted for other risk factors. The results reveal that there is no significant difference in the BMI between the control and case group ($p > 0.05$). However, stroke patients from the case group have a significantly higher waist circumference, waist-to-hip ratio, and waist-to-height ratio as compared to non-stroke patients in the control group ($p < 0.05$). Central indices show the strongest correlation and better prediction of any obesity-related metric with the occurrence of stroke. Regardless of other vascular risk variables, WHR is the most accurate predictor of the obesity markers under investigation.

Keywords: *BMI, case control, hospital-based, risk marker, stroke, obesity, waist circumference, waist-to-hip ratio.*

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Acknowledgments: The research process was initiated after receiving approval from the Open University Malaysia Ethical Approval Committees. Data collection was started after obtaining approval from the study hospital's review board committees. The aims and benefits of the study were explained to all the cases and controls. Informed written consent was obtained before collecting the data. Anonymity and confidentiality of data were maintained throughout the study.

1. INTRODUCTION

Obesity is a common and consequential medical problem all over the world, and Saudi Arabia is one of the countries that has been greatly affected by the current obesity epidemic. At present, health officials of KSA stated that more than 40 percent of Saudi citizens are suffering from obesity (Al Kinani, 2019). In a recent national study that included more than 10,000 adult participants, findings show that 28.7% were obese (BMI ≥30 kg/m 2) and women have a higher prevalence of obesity (33.5%) than men (24.1%) (Memish et al., 2014). Another recent study done among the Saudi population indicates that the majority of the patients with stroke were obese due to bad eating habits as well as lack of physical activity with the prevalence of obesity higher in females compared to male patients (Alharbi et al., 2019).

A stroke is a medical emergency that is one of the major causes of morbidity and mortality throughout the world. The executive summary report from the American Heart Association, states the high incidence and prevalence of strokes as one of the main causes of disability worldwide (Mozaffarian et al., 2016). Obesity has been recognized as a contributing risk factor to the development of vascular diseases including stroke (Oesch et al., 2017). Excess body weight predisposes to factors that elevate the risk of stroke which include heart disease, high blood pressure, and diabetes (Esenwa & Gutierrez, 2015).

Globally, strokes inflict a substantial economic burden on the healthcare system. A systematic analysis for the Global Burden of Disease (GBD) Study 2015 by the neurological disorders collaborator group found that strokes were the leading cause of age-standardized disability-adjusted life years (DALY) rates in 18 of 21 GBD regions. In 2015, stroke was listed among the neurological disorders accounting for more than 10 percent of global DALYs and more than 15 percent of all mortalities (Feigin et al., 2017). A systematic review revealed that the costs spent for overall post-stroke care were highest in the USA and lowest in Australia, with rehabilitation and nursing care were the main cost driver (Rajsic et al., 2019). An authoritative research study exposed that the economic burden of CVD in KSA will increase three times to nearly 10 billion USD by the year 2035 from 3.5 billion USD in 2016 (Saudi Gazette, 2018). These high costs associated with strokes strongly signify an urgent need for effective prevention methods to lessen the national disbursement for healthcare services associated with strokes.

Unfortunately, a study on stroke patients in KSA found that the majority of them were obese and overweight (Jameel Ahmed et al., 2018). Despite having knowledge of the seriousness of obesity and its influence on health, its prevalence is still growing in Saudi Arabia, which also puts a considerable financial burden on government and individual resources (Almohsen. et al., 2017). Apart from hypertension, dyslipidemia, and diabetes mellitus, obesity is identified as the major risk factor for stroke among the Saudi population and might be considered critical factors for primary and secondary prevention of stroke (Alharbi et al., 2019).

Evidence from many epidemiological studies have shown that different anthropometric indices for abdominal obesity such as BMI, Waist circumference (WC), and Waist to hip ratio (WHR) are strong and consistent indicators for non-communicable diseases (Ahmad et al., 2016). Since there is a high prevalence of obesity among the Saudi population and both obesity and strokes are major public health problems, a study to assess the relationship of obesity as a risk factor for stroke becomes a major concern. The purpose of this research is to ascertain, using a case-control methodology, if general obesity is associated with an elevated risk of stroke.

2. REVIEW OF LITERATURE

Stroke and obesity both show a growing number of incidences worldwide (Oesch et al., 2017). In the Kingdom of Saudi Arabia (KSA), obesity is a leading health problem affecting people in all age groups and genders. Epidemiological surveys and studies showed that about one-third of adults are overweight while more than one-fourth of adults are obese in Saudi Arabia (Memish et al., 2013). At present, KSA health officials state that more than 40 percent of Saudi citizens are suffering from obesity (Althumiri et al., 2021). A recent report in a national study that included more than 10,000 adult participants shows that 28.7 % were obese (BMI ≥ 30 kg/m 2) and women have a higher prevalence of obesity (33.5 %) than men (24.1 %) (Almekhlafi, 2016).

Meanwhile, a retrospective analysis study in a tertiary academic center in Saudi Arabia observed no decline in stroke mortality over 5 years (El-Hajj et al., 2016). In the Middle East, there has been a growing rate of stroke incidence and mortality over the last decades (Alharbi et al., 2019). Apart from hypertension, dyslipidemia, and diabetes mellitus, obesity is identified as the major risk factor for stroke among the Saudi population and might be considered as critical factors for primary and secondary prevention of stroke (Jameel Ahmed et al., 2018). This is undeniably true as the majority of the stroke patients in KSA were obese and overweight (Alhazzani et al., 2018). Despite having knowledge of the seriousness of obesity and its influence on health, its prevalence rate is still growing in Saudi Arabia, thus indirectly putting a considerable financial burden on government and individual resources (Almohsen et al., 2017). Since there is a high prevalence of obesity among the Saudi population and both obesity and stroke are major public health problems, a study to assess the relationship of obesity as a risk factor for stroke becomes a major concern.

A few studies have examined the relationship between obesity defined as general obesity indicated by body mass index (BMI) or central obesity defined as Waist Circumference (WC), Waist to Hip ratio (WHR), Waist-to-Height ratio (WHtR), and stroke. A population-based case-control study in Washington found that obesity is a risk factor for early onset of ischemic stroke as indicated by BMI. The results also show a positive association between increased BMI and early onset of stroke (Mitchell et al., 2015). Central obesity in which excessive fat is preferentially distributed around the trunk has been shown to be vital in predicting stroke mortality (Segula, 2014). It has also been known that central obesity is a better predictor of risk factors for cardiovascular diseases (Barroso et al., 2017). However, the association between abdominal obesity and the risk of stroke or transient ischemic attack (TIA) is not independent of other vascular risk factors although it was found that markers of abdominal obesity were a stronger predictor of risk of stroke or TIA (Winter et al., 2016).

Nevertheless, there is a lack of published research done in KSA on the relationship between obesity and stroke with the studies generally related to the association of obesity with other chronic diseases mainly hypertension, dyslipidemia, and diabetes (Almekhlafi, 2016; Ahmed et al., 2014). Moreover, these studies have included only BMI and not central obesity as their definition of obesity indicators. In the recent advances in acute stroke treatment, effective stroke prevention by the way of improving control of risk factors should be weighed as a balance to decrease the burden of stroke effectively. It is known that obese patients are at increased risk for stroke but the data from previous studies are lacking and inconclusive. Given the fact that obesity is a modifiable risk factor, further studies on its association with stroke in the Saudi population will facilitate more data production and information for better emphasis on preventive measures. Therefore, the aim of this study is to determine the association of general obesity with an increased risk of stroke in a case-controlled manner.

3. RESEARCH METHODOLOGY

This study was carried out on all newly diagnosed stroke patients being admitted to a tertiary hospital in Riyadh, KSA after getting approval from the University of study and the respective hospital research committee. Newly diagnosed stroke patients were selected as cases of the study and non-stroke patients were selected as the controls. The primary distinction between stroke subtypes which are ischemic, intracerebral hemorrhagic, and subarachnoid hemorrhagic was based on neuroimaging results. This study is a hospital-based case-control study since the cases and controls can be identified efficiently.

3.1 Sample Selection

Cases and controls were selected among patients admitted during the period from mid-October 2020 to the end of February 2021 in a tertiary hospital in Riyadh using the method of non-probability purposive sampling. Correct control selection is crucial to the internal validity of case-control studies. Therefore, control patients were selected from the same hospitals as case patients to reduce the selection bias. They were matched in age (± 5 years) and sex to minimize the potential biases often associated with case-control studies.

3.2 Selection of Cases

Patients admitted with the confirmed diagnosis of a new stroke (the first incident in history) were selected as cases. Hospitalized stroke patients were included if they were 18 years or older and diagnosed with stroke by computed tomography (CT) or magnetic resonance imaging (MRI). Stroke patients were excluded if clinical information was unavailable computed tomography scan or magnetic resonance imaging were not performed, or if it was diagnosed as TIA, or if the patient had a history of positive coronavirus disease (COVID-19). The researcher decided to exclude TIA cases to focus on confirmed stroke incidents. In addition, recent studies found several mechanisms involved in stroke incidents in the COVID-19 pandemic outbreak (Spence et al., 2021). Therefore, patients with a history of positive COVID-19 were excluded to avoid an unclear confounding variable.

3.3 Selection of Controls

The controls were selected from all the patients who were admitted to the study hospital for conditions other than stroke. For each stroke case, two controls were selected from the other medical departments. The controls were matched to cases with respect to age (± 5 years) and sex. They were included if they were 18 years or older and attended the same hospitals with conditions or procedures unrelated to stroke or transient ischemic attack, but they were excluded if they had a history of stroke or TIA or a history of positive coronavirus disease (COVID-19).

3.4 Research Instrument

A semi-structured questionnaire was used to collect the data required for the study. It was constructed based on similar studies done previously (Suk et al., 2003; Winter et al., 2008; Zahn et al., 2018). The variables involved in the mentioned studies were adapted with the exception of alcohol intake considering alcohol of any kind is banned in Saudi Arabia. The first part of the questionnaire included patients' socio-demographic characteristics, medical diagnosis, and imaging techniques. Socio-demographic characteristics include age, sex, and nationality. Many expatriate residents in Saudi Arabia make nationality an appropriate variable to include in the questionnaire.

The second part of the questionnaire includes all the anthropometric measurements of the patients. The measurements of different markers of obesity are following the report of a WHO Expert Consultation in Geneva (WHO, 2008). The results of BMI were then classified into the class of obesity following the recommendation from WHO guidelines. However, the optimal cut-off points for WC and WHR for identifying the risk of metabolic syndromes following the recent study that was done among the Saudi population for appropriate reference values within the similar population of the study (Al-Rubean et al., 2017) while the optimal cut-off points for WHtR in the discussion are following the indices recommended to be used among Middle Eastern populations (Tutunchi et al., 2020).

The third part of the questionnaire includes patients' current trending of vital signs and laboratory data upon admission to hospitals as well as all potential stroke risk factors in the patients. The trending of vital signs was monitored during admission, during in-patient, and during the interview process as to verify the hypertension status of the patient. The patient is considered to have Hypertension (HTN) when they had a reading of systolic blood pressure ≥ 140 mm hg or diastolic blood pressure ≥ 90 mm hg or on any antihypertensive medications. The patient is required to have the latest test of Fasting blood sugar (FBS), Random blood sugar (RBS), glycated hemoglobin (HgbA1C) level, and lipid profile taken upon admission. The result of HgbA1C is acceptable if it was taken within a 6-month duration, and the lipid profile result was acceptable if taken within a one-year duration. The elevated values of either FBS level (> 7 mmol/L), RBS level (> 11 mmol/L), and HgbA1C level (≥ 6.5 %), or the requirement of regular hyperglycemic medications define the patient as having Diabetes Mellitus (DM). Dyslipidemia was defined according to the American Heart Association's classification corresponding to the 95th percentile in an American population as total cholesterol > 5.2 mmol/L (200 mg/dl), Low-density lipoprotein (LDL) > 3.4 mmol/L (130 mg/dl), High-density Lipoprotein (HDL) < 0.9 mmol/L (35 mg/dl), or a combination thereof (Kavey et al., 2003). Patient use of antihyperlipidemic agents is also considered as having hypercholesterolemia or dyslipidemia.

Finally, the fourth part of the questionnaire addresses the physical activity level for all the patients involved. The University of Washington Health Promotion Research Center's Rapid Assessment of Physical Activity (RAPA) questionnaire is used to assess the level of physical activity among the participants. This questionnaire was found to be a reliable and valid measure of physical activity (Topolski et al., 2006). For aphasic or altered Glasgow coma scale (GCS) patients, the Rapid Assessment of Physical Activity questionnaire was modified to the Telephone Assessment of Physical Activity (TAPA) method as to permit the interviewer to ask the patient or the immediate close relative instead of letting them self-answer. The modification of the questionnaire retains a similar scoring level and interpretation. A Spearman rho of 0.74 and a kappa statistic of 0.48 were found between TAPA and the written RAPA as measured in the previous study (Mayer et al., 2008).

3.5 Procedure

All the required data were collected from the patients during their admission to the hospital after getting permission either from the patients or relatives. A standardized collection sheet was used to collect data and a protocol was developed for collecting, measuring, and interpreting information to minimize observer bias. If the patients were unable to provide the data by themselves due to medical or stroke-related conditions, relevant information was collected from the patient's history in the Hospital Information System (HIS) or immediate close relatives as appropriate. Evidence of stroke is based on the findings in the medical imaging done.

Anthropometrical measurements were done according to the recommended protocol (WHO, 2008). The weighing scale is calibrated, and the non-stretch-resistant tape was used to measure waist and hip circumference accurately. The researcher and an assistant investigator applied a similar established method and protocol of measurements to ensure similar results were produced. Height (in cm) and weight (in kg) were measured with a standard scale. Demi-span was used for the calculation of height for bedridden patients. The formula used was 67.51 + (1.29 x demi-span) - (0.12 x age) + 4.13 for men and Height (cm) = 67.51 + (1.29 x demi-span) - (0.12 x age) for women.

Waist and hip circumferences were measured with participants standing and relaxed without heavy outer garments. Measurements were done supine among those cases who were unable to stand. Waist circumference was measured at the end of several consecutive natural breaths, at a level parallel to the floor, midpoint between the top of the iliac crest and the lower margin of the last palpable rib in the mid axillary line. Hip circumference was measured at a level parallel to the floor, at the largest circumference of the buttocks. BMI was calculated as weight in kilograms divided by height squared in meters. The waist-hip ratio is calculated as waist measurement (cm) divided by hip measurement (cm). The waist-height ratio is calculated as waist measurement (cm) divided by height measurement (cm).

4. RESULTS

A total of 187 stroke cases were admitted to the hospital of study between 15 October 2020 and 28 February 2021. Among those, 18 cases were not diagnosed as stroke by computed tomography scan or magnetic resonance imaging and were transferred care to other respective departments, 6 cases were diagnosed as TIA, 54 cases had having history of previous stroke, 3 cases were associated with a positive Covid-19 screening, and 12 cases were missed due to expired, and other reasons and therefore were all excluded. Overall, a total of 94 patients with stroke and 188 stroke-free age (± 5 years) and sex-matched controls were evaluated in the present study.

Males constituted 69.1 % (n=65) of stroke patients and females constituted of 27.7 % (n=26) of total stroke patients. It revealed that total ischemic cases in total were 91.5 % (n=86) while hemorrhagic cases were 8.5 % (n=8). The majority of stroke is ischemic in both males (63.8 %) and females (27.7 %). The mean age of stroke was 57.74 ± 10.889 years. The highest number of stroke patients were in three groups of age leading group 51 to 60 years of age (n=29) followed by 61 to 70 years of age (n=26) and 41 to 50 years of age, while the lowest number of stroke patient was in 81-90 years of age (n=1). 84 % (n=79) of cases were Saudi, 3.2 % (n=3) were Syrian, 3.2 % (n=3) were Sudanese, 3.2 % (n=3) were Filipinos, 2.1 % (n=2) were Indian, 3.2 % (n=3) were Pakistani, and remaining 1.1 % (n=1) was Egyptian.

Independent *t*-test was executed to compare the BMI, WC, WHR, and WHtR between case and control groups (Table 1). Assumptions of normality and homogeneity of variance were checked prior to analysis. The result reveals that there is no significant difference in BMI between the control and case groups ($p > 0.05$). However, the stroke patients from the case group have a significantly higher waist circumference, waist-to-hip ratio, and waist-to-height ratio as compared to non-stroke patients in the control group ($p < 0.05$).

Study Objective: To determine the association of general obesity with an increased risk of stroke

An Independent *t-test* was executed to compare the BMI between case and control groups (Table 1). Assumptions of normality and homogeneity of variance were checked prior to analysis and results can be found in the appendix. Independent t-test reveals that there is no significant difference in the BMI between control and case groups (p>0.05).

Table 1. Comparison of BMI Value Between Stroke and non-Stroke Patients (n=282)

Control Mean (SD)	Case Mean (SD)	Mean difference (95% confidence interval)	T statistics (df)	P value
29.79 (7.94)	30.16 (6.26)	-0.37 (-2.09, 1.33)	-0.434 (229.159)	0.665*

Equal variance not assumed.

Comparison by the BMI classification was also performed to check the association through Pearson's chi-square analysis and results are tabulated in Table 2. It also reveals that there is no significant difference in the BMI between the control and case groups (*p*>0.05).

Table 2. Comparison of BMI value in Obesity Class (n=282)

BMI	Control n (%)	Case n (%)	X^2 statistics	P value
Underweight	7 (77.8)	2 (22.2)	10.403	0.065
Normal	51 (78.5)	14 (21.5)		
Overweight	50 (56.2)	39 (43.8)		
Obesity I	35 (64.8)	19 (35.2)		
Obesity II	25 (64.1)	14 (35.9)		
Extreme obesity	20 (76.9)	6 (23.1)		

5. DISCUSSION

The present hospital-based case-control study evaluated the predictive value of different markers of obesity for stroke. The association between BMI and stroke risk has been controversial. Previous studies investigating the association between BMI and stroke revealed different effects of BMI on stroke. The present study found that BMI does not have a significant association with stroke when other confounders were adjusted or not adjusted. The result is similar to a case-control study in Germany that showed BMI has no significant associations with the risk of stroke or TIA in any of the applied mathematical models (Winter et al., 2016). In contrast, a positive association was found between increased BMI and early onset of stroke (Mitchell et al., 2015). Other studies also showed that an increased BMI elevated the risk of ischemic stroke even after adjusting for age and other confounders, although the effect was mainly mediated by hypertension, diabetes, and dyslipidemia (Lu et al., 2024; Strazzullo et al., 2010). Conversely, a recent study found an inverse association between BMI and the risk of total, ischemic, and hemorrhagic stroke among patients with type 2 diabetes. Patients with lower BMI had a higher risk of stroke incidents (Shen et al., 2020). Stroke patients with normal weight also had experience with previous strokes as compared to overweight and obese stroke patients (Andersen & Olsen, 2013). These conflicted findings indicate that BMI is not a reliable indicator of stroke risk.

In a German case-control study, abdominal adiposity is a stronger predictor of risk of stroke or TIA than BMI although the association is not independent of other vascular risk factors (Winter et al., 2016). However, in the present study, the indicator of WHR was strongly associated with stroke risk in the adjusted and unadjusted model (OR 56.44; 95% CI 7.70 to 413.86; $p<0.001$). It has been observed from the mentioned findings, that all indices in abdominal obesity could potentially be useful stroke-risk predictors. Furthermore, it has been pointed out in a research study that case-control studies frequently demonstrated a stronger association between central obesity and risk for stroke compared to longitudinal studies. This is possibly due to the ability to perform the measurement of obesity markers closely to the time onset of stroke event Winter et al., 2008).

In contrast, abdominal obesity measures are found to be independent predictors of ischemic stroke in females from the general population in the KORA Augsburg cohort study (Zahn et al., 2018). In females, both general and abdominal obesity are correlated with risk of stroke risk. Interestingly, other vascular risk factors are not found to have a significant association with stroke in the present study. A similar finding was also found in the previous study of obesity and cardiovascular diseases (Barroso et al., 2017).

The prevalence of stroke was higher in males than females (69.1 %) and ischemic stroke was the most reported type of stroke (91.5 %) (Alharbi et al., 2019). The present study demonstrated similar findings with males constituting the majority of stroke patients (69.1 %) and females constituting the remaining total stroke patients (27.7%). Ischemic stroke also largely occurred among stroke patients 91.5 % while hemorrhagic cases happened to 8.5 % of patients in the present study.

6. CONCLUSION, IMPLICATIONS AND LIMITATIONS

From the present study, it can be generally concluded that among the measures of obesity, central indices had better prediction and stronger association with the incidence of stroke. WHR served as the best predictor among the obesity markers studied, independent of other vascular risk factors. Taking measurement of WHR is a simple and cost-effective method, and therefore can be applied as general practice in all health care settings particularly hospitals and primary care facilities to identify individuals with higher risk of disability. It is recommended that the estimation of CVD events attributable to obesity be considerably redefined to WHR marker instead of BMI. This could be helpful in the early identification of individuals at risk for stroke and in formulating public health strategies if proven by a larger population-based study.

This study implied that stroke prevention programs in Saudi need to incorporate education about the WHR factor, in addition to general weight management plans. Abdominal obesity can be a more informative measure and a risk marker in comparison with general obesity. Therefore, focusing on the multiple indices of obesity will avoid neglecting the risk of stroke in the general population. Nurses are the ideal healthcare professionals to direct the stroke risk reduction team and incorporate the findings to improve patient care together with stroke physicians, stroke educators, and other healthcare providers. As health professionals, the progress in preventing stroke should not lead to complacency. Since obesity is a modifiable risk factor, the prevention of stroke can benefit from improving the excess weight and abdominal adiposity among the population.

This is a hospital-based case-control study, and therefore the results cannot be extrapolated to the general population. The anthropometrical measurements were performed after the stroke and may not accurately reflect the pre-morbid status of obesity because weight and waist and hip circumferences could be changed by inadequate nutritional intake after acute stroke.

By design, however, special efforts were made to collect anthropometrical data within 72 hours after the stroke, and it is unlikely that significant changes in waist or hip measurements would have occurred in that short period. Besides, the measurements done for bedridden patients may not precisely reflect the accurate measurements of waist, and hip circumference in a standing position because waist circumference and hip circumference were measured in the supine position in a few cases who were bedridden, and unable to stand due to stroke. In a pilot study, waist circumferences measured when supine were slightly smaller than when measured standing, whereas hip circumferences did not differ by position measured. Therefore, measurement errors might occur in WHR and WHtR, and that would have led to an underestimation of the OR.

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