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Magnitude of Intracranial Calcifications, Their Association with Body Mass Index and Anatomical Sites Involved Among Adults in Two Tertiary Level Hospitals in SNNPR Ethiopia: 2022 (Cross Sectional Study)

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Abstract: Background: Intracranial calcification is specifically calcium or calcium compounds deposition within cranial cavity in a brain tissue and or associated structures. Calcification is mineral deposition of any of body tissues notably soft tissue rendering it hard and solid. Unless physiological calcifications which not known to bring health related problem, pathological intracranial calcifications are tremendously notorious cause cognitive, motor, memory, autonomic as well as sensory system diseases and disabilities in affected patients. Objective : The objective of this study was to assess association between intracranial calcifications and their prevalence in two tertiary level health care institutions in SNNPR, Ethiopia. Adult patients who attend these facilities to get CT scan of head. Methods and Materials: The study conducted in two tertiary level healthcare institutions in Wolaita zone, SNNPR of Ethiopia, namely Wolaita Sodo Christian General Hospital and Wolaita Sodo University Teaching and Referral Comprehensive Hospital, which are currently making active use of CT scan for diagnosis of various causes. A systematic sampling technique was used to recruit the predetermined sample size of n = 403. Before the selection of study participants, proportion to size allocations of the sample size for the number of adults undergone CT scan of head in each health institution was performed. Structured questionnaire was prescribed by trained data collectors to get data and Subsequent measurements of height and weight of patients obtained. Data was entered into Epi-data software version 4.4.2.1 and then exported to SPSS version 25 statistical package for analysis. The results are summarized in the form of proportions and frequency tables for categorical variables. Correlation coefficient and odds ratio calculated statistically. Continuous variables Summarized using means, median and standard deviation. P-values computed for categorical variables using Chi-square ($\gamma 2$) test and p value of $P<0.05$ was taken as a statically significant. Results: The overall magnitude of intracranial calcification was 28.3%. Older age (AOR=3.260, 95% CI; 1.671-6.361), Hypertension (AOR=2.353, 95% CI; 1.130-4.901), Kidney disease (CKD) (AOR=2.611, 95% CI; 1.260-5.410), Diabetes Mellitus (AOR=2.523, 95% CI; 1.170-5.442), Stroke (AOR=3.247, 95% CI; 1.053-10.015) and BMI of patient ($\geq$25.0 kg/m^2; AOR=3.247, 95%CI; 1.004-11.202) were significantly associated factors with the ICC formation in brain. Conclusion and recommendation: This study found a magnitude of intracranial calcifications of 28.3% among adults whom underwent CT scan imaging diagnosis of head in WSCGH and WSUTRH for various reasons. Factors that contribute to intracranial calcifications were older age, hypertension, kidney disease (CKD), Diabetes mellitus, Stroke, hemiplegia or paraplegia and higher body mass index level (BMI).

Key words: Body Mass Index · CT scan · Intracranial Calcification · Obesity

INTRODUCTION

In highest order animals like mammals and vertebrate, nervous system is highly specialized system owing to its intricate functional and structural requirements organism needs to survive. Brain and spinal cord constitute central nervous system while spinal nerves constitute peripheral nervous system. Physiologically or functionally nervous system further divides into various categories predominantly being

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classified as autonomic and somatic nervous system depending on control of activities made voluntarily or involuntary [1].

Since it is prominently exposed part of body in humans and some other animals, head is primarily subject to multitude of traumas and injuries that have potential to bring damage to the brain. Furthermore, its confinement within limited area (cranial cavity), which cannot tolerate any increase in mass or pressure that arise due to either pathological or physiological or traumatic processes makes it vulnerable when compared to other parts and structures of human body. An abnormal involvement of little area of brain in cranial cavity or spinal cord and spinal nerves in spinal cavity can end up in profound dysfunctions [2].

Factors that yield to functional and/or structural disruptions of nervous system in general and the central nervous system in particular are related to causes that affect the size of brain tissue and pressure of intracranial cavity. Neoplasms, inflammations, infections, fluid and blood accumulations and calcifications are frequent causes of both anatomical and physiological dysfunctions [3].

Due to the fact that the involvement of small area of brain by any lesion including different forms of calcifications results in profound effect in the normal functioning of nervous system in form of either motor or autonomic nervous system functioning. Notable areas of brain that can result in gross dysfunction of coordination, cognition and memory include basal ganglia, limbic system [4].

Calcification is mineral deposition in any of body tissues notably in soft tissue rendering it hard or solid. Intracranial calcification is specifically calcium or calcium compounds deposition within cranial cavity involving brain tissue and or associated structures. Calcifications that take place external to cranial cavity are called extra-cranial calcifications and those which occur within cranial cavity are called intracranial calcifications [5, 6]. Calcification of tissues can be physiological or pathological. Physiological calcifications commonly include calcification of pineal gland, habenicular, basal ganglia and choroid plexus [6].

The emergence of rapid and effective diagnostic imaging instruments made the study of intracranial calcifications whether they are physiologic or pathologic relatively easy. Computed tomography (CT) is standard imaging instrument in diagnosis and characterization of intracranial calcifications. Magnetic resonance imaging (MRI) though not effective as CT scan for study and diagnosis of intracranial calcification, it has frequently used as important augments to available imaging modalities. Intracranial calcifications are a common radiographic finding and their pathogenesis varies from benign physiological processes to multiple pathological processes, their imaging characterization according to their morphology and location is important to establish a proper differential diagnosis [7].

Although the process of calcification is not clearly understood currently, according to many research findings the underlying cause is closely associated with both physiological and pathological metabolic processes. Metabolism of proteins, fats and carbohydrates plays significant role in the process of formation of calcification apart from cellular calcium metabolism dysfunction [6, 8, 9].

Association of ICCs with nutritional status of body and metabolic processes of nutrients, trace minerals, vitamins and their oxidative respiration is currently ongoing research. Physiological processes of calcium storage and utilization is a major issue surrounding calcification formation. Along with other minerals which are important to normal functioning of organisms, calcium metabolism is to large extent subject to hormonal control. Either hormonal physiological dysfunction in association with excess amount of calcium in the body can lead to deposition of calcium in tissues. To the best of our knowledge, for instance, Hypoparathyroidism is well known phenomena in calcification formation [6, 9, 10].

Abnormal nutritional status either in form of shortage or excess of nutrients is implicated as known cause of many diseases. Even though association between nutritional status of an individual and calcification formation is got some concern among researchers and academicians, there is no definite causation concept. Findings of some studies are even conflicting and paradoxical [11, 12].

Health associated risks of malnutrition (under nutrition and over nutrition) are common theme in current scientific community. Over nutrition is as equally as health damaging as under nutrition, coupled with modern lifestyle. The role of obesity as contributing factor for intracranial and extra cranial tissue calcification formation is thus being equally viewed to its contribution to diseases like diabetes mellitus and hypertension among others [13, 14].

This current study assessed the association of ICCs formation and nutritional status of adults. Nutritional status is commonly assessed and categorized by world health organization (W.H.O) standardized body mass index (BMI) scale. BMI is technically feasible, easy to understand tool used to assess nutrition status among

humans even though it is inferior to standard laboratory biochemical tests. Despite its shortcomings, BMI is being widely employed for various purposes in connection to health care planning and intervention as well as to decision and policy making.

Statement of Problem: Globally, the prevalence and associated health consequences ascribed to intracranial calcifications tend to differ from one area to another significantly. Periodic reports of world health organization (W.H.O) indicate that neurological disorders and diseases are escalating from time to time. Some forms of intracranial calcifications are intimately related to diseases like Alzheimer's, dementia and Parkinsonism. Alzheimer's disease (AD) is a globally common neurodegenerative disease, which is accompanied by alterations to various lifestyle patterns, such as sleep disturbance. Some forms of ICCs (e.g., bilateral basal ganglia calcifications) are known to culminate in Alzheimer's disease eventually [6, 15, 16].

Increasing trends of Neurological and mental health cases that arise from diverse etiologies put major threat to the health and wellbeing of global population. Neurological disorders contribute to 92 million disability-adjusted life years (DALYs) in 2005 projected to increase to 103 million in 2030 (approximately a 12% increase), with intracranial calcified lesions contributing its share to the problem. While Alzheimer and other dementias are projected to show a 66% increase from 2005 to 2030, there is an estimated 57% decrease in DALYs associated with poliomyelitis, tetanus, meningitis and Japanese encephalitis combined. Neurological disorders included in the neuropsychiatric category contribute to 2% of the global burden of disease, while cerebrovascular disease and some of the Neuro-infections (tetanus, meningitis and Japanese encephalitis) contribute to 4.3% of the global burden of disease in 2005. Thus, neurological disorders constitute 6.3% of the global burden of disease [15, 17].

Intracranial calcifications are directly and indirectly participated in a range of both neuropsychiatric and autonomic dysfunctions. Disorders such as autism spectrum disorder (ASD), Alzheimer Disease, downs syndrome, Attention-Deficit Hyperactivity Disorder (ADHD), cerebral palsy, Sickle Cell Disease (SCD), depression, dyslexia and anxiety are more prevalent. Neurological disorders directly affect the brain and nerve system and causing development disabilities, which has become one of the major health issues worldwide [15, 18]. World statistics have shown that 9.4% of children have diagnosed with ADHD in 2016. The rate of ADHD affected children has increased by more than 50% from 2008 to 2012. According to USA statistics, there is one ASD patient in every 68 adults. In a recent study in Sri Lanka, being a developing country, it is found that 10% of the children involved in the study are suffering from ASD. Another study shows that 1 in every 93 children are affected by ASD in Sri Lanka [19, 20]. Thus, it requires special attention, awareness and treatments of neurological disorders. Some of these disorders are mostly encountered in children and continuing to adulthood that can be a lifelong health problem. Coupled with comparatively shorter access to diagnosis and treatment of neuropsychiatric related morbidities and disabilities, developing and under developed world is under growing need of solution to the situation [8, 21].

Intracranial calcifications that involve some specific areas of brain are known to cause significant diseases and disabilities. In adults, most commonly occurring morbidities and disabilities, that affect motor, memory, cognition and autonomic functioning are Parkinsonism, migraine, dementia and ataxia among others. Dementia, for instance, is a common manifestation with 46.8 million people having this condition worldwide. Dementia mostly appears to result from a combination of factors, including Alzheimer disease (AD), vascular lesions, Lewy bodies and inflammation, which eventually lead to atrophy of the cortex and hippocampus [22, 23].

World Health Organization (WHO) Reported in 2001 [17], figures that show that four of the ten leading causes of disability worldwide are neuropsychiatric disorders, accounting for 30.8% of total disability and 12.3% of the total burden of disease. This latter figure (disability) is expected to rise to 15% by the year 2020. Tumors had 40 %, vascular lesions had 6% and pathological bilateral basal ganglia had 4% and congenital phacomatoses in 2% of patients [17].

On the other hand, obesity that roots from in advert dietary habit currently the major challenge causing a number of both short and long-term health problems. It is in obese and chronically hypertensive and diabetic individuals that most of occlusion of blood vessels occurs due to calcification of arterial walls. Intracranial blood vessel calcification is the major challenge today. The prevalence of overweight was higher, 22.6% in studies published since 2015, 22.4% in studies conducted only in urban settings and 24.4% in studies with small sample size ($\leq$384participants). Similarly, the prevalence of obesity was 6.9% in studies published since 2015, 6.2% in studies conducted only in urban settings, 6.4% in institution-based settings and 9.6% in studies with small sample size [24, 25].

Apart from things mentioned above, there are no sufficient researches nationally (in Ethiopia) that conducted to assess neither magnitude nor prevalence of ICCs and associated factors. Studies conducted elsewhere tried to assess the association between ICC and factors associated but they didn't included BMI as candidate factor. One study conducted in Addis Ababa Tikur Anbessa teaching hospital in Ethiopia [26]. This study had stressed on the incidence of occurrence of pineal gland and choroid plexus but failed to report overall magnitude of ICCs in our setting and the study didn't addressed factors associated with ICCs, including BMI [26].

Present study assessed the association between BMI and ICC, other associated factors and common sites of occurrence of ICCs in adults. The results of this study will shed light on mentioned gaps and will add relevant information to scientific community as whole. The resultant findings of the study hoped to establish overall magnitude of ICCs thereby allowing comparison with other past research findings conducted elsewhere.

Justification of Study: Intracranial calcifications that tend to be pathologic can cause significantly disabling diseases. Diagnosis and treatment of associated diseases is relatively costly in many developing countries including Ethiopia. Adequate scientific information regarding the situation including its prevalence and pattern of occurrence and association with other factors is important to establish preventive and diagnostic as well as screening measures. In addition to this, non-recommendable nutritional health in the form of underweight and overweight currently one of major causes of chronic diseases both in developed and developing countries.

Intracranial calcifications have their own share of causing neurological diseases that involve motor, cognitive, memory, as well as disorder of autonomic functions. Information on true magnitude of ICCs plus factors associated with ICC formation is important to measure impact of ICCs on neurological and mental health diseases. It is also mandating issue to find out magnitude of ICCs in our setting, which in turn, will be valuable to concerned bodies like clinicians, academicians and general public as well.

Previous studies conducted on association between ICCs and nutritional status (indirectly with BMI) is very few in number. Thus, it is necessary to conduct present research in order to support, challenge or to compare with findings of past studies. Intracranial calcifications not only limited to affect pineal gland and choroid plexus, which the study in Addis Ababa Tikur Anbessa hospital only addressed the incidence of these two structures and omitted other intracranial structures like basal ganglia, Habenula and hippocampus [26].

Generally speaking, there is paucity of data and literature regarding magnitude of intracranial calcifications and its association with BMI in our setting. Other factors that were indicated and identified by scientific literatures to have association with ICCs were also assessed. Establishing magnitude, pattern and association of ICCs with BMI is necessary to device preventive and diagnostic measures. Comparison also made with existing literature. Feedback information to governmental and to concerned bodies will be given which, in turn, will help for policy revision and inclusion of ICC related health risks in medical routine and to seek early medical attention in case of neurological signs and symptoms of disease. In advert nutritional culture that leads to obesity and eventual health risks will be condemned based on the results of study if any. Screening means, differential diagnoses to rule out suspected neuropsychiatric cases will benefit from the study by giving new insight to clinicians, scientific as well as academic society.

Therefore, it is of paramount importance if association of ICCs and BMI and other associated factors are studied and identified for diagnostic and clinical intervention, including anatomical sites affected by ICCs to provide information to all concerned.

Objectives of the Study

General Objective: To assess the magnitude of intracranial calcifications and its association with body mass index among adults attending two tertiary level health care facilities in SNNPRS Ethiopia, 2022.

Specific Objectives:

- To determine the magnitude of intracranial calcifications among adults attending two tertiary level health care facilities in SNNPRS Ethiopia, 2022
- To assess association between intracranial calcifications and body mass index among adults attending two tertiary level health care facilities in SNNPRS Ethiopia, 2022
- To identify factors associated with ICC among adults attending two tertiary level health care facilities in SNNPRS Ethiopia, 2022
- To establish frequent sites affected by intracranial calcifications among adults attending two tertiary level health care facilities in SNNPRS Ethiopia, 2022.

METHODS AND MATERIALS

Study Setting Characteristics: Sodo Christian general hospital (SCGH) is located at Sodo town, capital the city of Wolaita Zonal administration, which is 320 Kilometers south of Addis Ababa (capital city of Ethiopia). SCGH is a general hospital that has 144 beds in four wards mainly surgical, maternity and medical and pediatrics and orthopedics. The hospital also has an emergency, outpatient, optometry and dental clinic.

Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUCTRH) is located in Wolaita Sodo capital city of Wolaita Zone in SNNPR, 125 km away from Hawassa Capital city of SNNPR and 320 km to south from Addis Ababa capital of Ethiopia. The hospital has catchment of 2 million residents and has 195-bed capacity. There is one government hospital, 2 private hospitals, four health centers and many private higher and medium clinics in the town.

Currently, the hospital serves as a main referral center for the Southern part of Ethiopia serving about 10 million people in the region and surrounding areas. The hospital, which currently has 195 beds went operational since 1960s' and was affiliated to the Wolaita Sodo University. Services delivered by organizing are arranged in to four major departments: Medical, Surgical, Pediatric and Gynecology and Obstetrics departments and other clinics like TB-HIV care unit, ART (Anti-Retroviral Therapy) clinic, Volunteer counseling and testing (VCT), ophthalmology unit, surgical and medical emergency unit, radiology unit, Intensive Care Unit (ICU) unit and Anesthesiology unit.

According to the hospital annual and monthly report, the hospital has about 400 up to 500 daily outpatient visits on average, including approximately 70 daily radiology visits of 30 to 40 cases visiting CT scan imaging room. The radiology department gives services in three main categories. Totally, there are about three specialized professionals and five midlevel personnel in radiology department to provide radiologic services for the clients.

Study Period: This study was conducted from June 2021 to August 2022.

Study Design: Facility based cross sectional study was conducted

Source Population: All patients who underwent CT scan of head in Wolaita Sodo Christian General Hospital and Wolaita Sodo University comprehensive teaching and Referral Hospital.

Study Population: All patients who underwent CT scan of head in Wolaita Sodo Christian General Hospital and Wolaita Sodo University comprehensive teaching and Referral Hospital during study period and fulfill the inclusion criteria were taken as study population.

Inclusion and Exclusion Criteria

Inclusion Criteria: Patients above age of 18 (adults) whom underwent CT scan of head in the mentioned health facilities.

Exclusion Criteria:

- Patients with Glasgow coma scale less than = 8.
- Non ambulatory patients/bed ridden patients
- Cases with unidentified findings and artifacts in CT film

Sample Size Determination: Due to lack of literature results on the same topic area (association between ICC and BMI), p value of 50% (P=0.5) was taken.

By using Table (1), the sample size of this study was calculated as

$$n = \frac{\left(Z(1-\frac{a}{2})\right)^2 \times p \times (1-P)}{d^2} = \frac{(1.96)^2 \times 0.428 \times (1-0.428)}{(0.05)^2} = 384$$

where; n = required sample size d = margin of error 5%. P = proportion of prevalence of ICC = 0.50, Zá/2 critical value for 95% confidence level which equals to 1.96, considering 5% non-response rate (19) added on n, therefore the final sample size was:

$$n = 384 + 19 = 403.$$

Sampling Method: At the beginning the total average of adults (1775) who have been underwent for CT scan of head in one month in two institutions were identified: Wolaita Sodo Teaching and Referral Hospital (994), Wolaita Sodo Christian General Hospital (781). A systematic sampling technique was used to recruit the predetermined sample size (403). Before the selection of study participants, proportion to size allocations of the sample size for the number of adults undergone CT scan of head in each health institution was performed. Finally, from the list, the required number

Table 1: Sample size calculation for magnitude of intracranial calcifications in adult patients whom underwent CT scan of head in two tertiary level health care facilities in SNNPR 2022

Confidence interval	Proportion	Power of study	Margin of error
95%	0.50	80	5

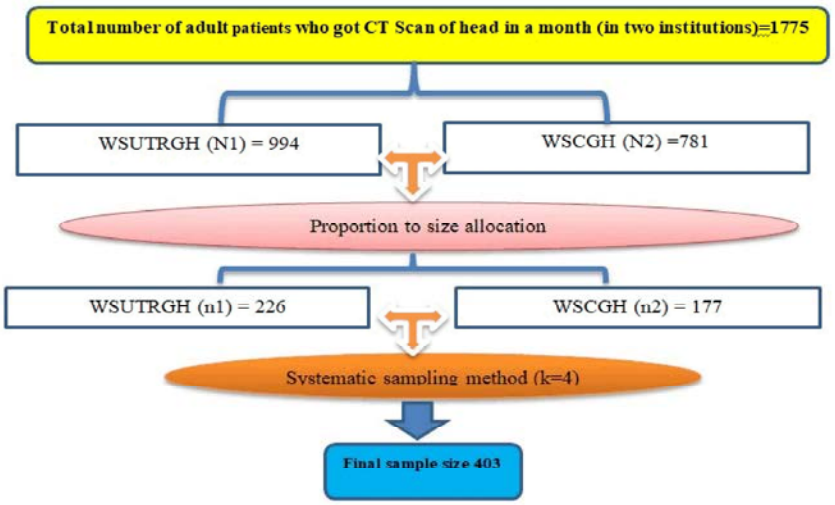

Fig. 1: Schematic representation of sampling technique for patients who underwent CT scan of head in two tertiary level health care institutions in SNNPRS, Ethiopia 2022. [6]

(n=403) of target adults were selected using systematic sampling technique by using interval (K^{th}) calculated from radiology data base in one month that divided for the number of allocated sample to the health facilities which was 4 (four) intervals from each sample unit. Then the study unit was selected every four (4) intervals for face-to-face interview.

Study Variables: Dependent variable

- Intracranial calcification (Yes or No)

Independent variables

- Age
- Sex
- Height
- Weight
- BMI
- Obesity
- Drug use
- Diseases
- Ethnicity
- Socio-economic status, Marital status, educational status

Data Collection Method and Procedure

Data Collection Method and Tool: The questionnaire that assesses basic information and socio-demographic variables was adopted from previous literatures and formulated depending on general objective. The imaging tool at both institutions was CT scan machine of model GE 64 SLICE 2020. Height and weight were measured by precisely calibrated standard weighting scale and measuring tape. Data collectors thoroughly oriented with interview questions, measuring instruments, measurement, Sampling and data collection. Two data collectors (at each Hospital) have collected data and one Advisor assigned to assist and to supervise the research work at the time of data collection.

Data Collection Procedure: Data was collected using structured and pretested interviewer administered interview. The questionnaire consists of socio demographic characteristic and medical history information of participants illegible to inclusion criteria. Each selected study participant interviewed face to face before taking anthropometric measurements. Radiologists in both hospitals read and ensure the findings of CT scan film soon after imaging process. When appropriate, clinical records of patients were reviewed specially for patients with diagnosed chronic diseases. Radiologists read and interpreted CT scan films after imaging. Then data collectors conducted appropriate measurements with standardized measuring instruments. Before measuring weight and height of selected participants, precise calibration of weighting scale and height measuring tool (measuring-tape) performed. Shoes and clothing of selected respondents that likely to affect measured values were avoided. The resultant figures of measurements were rounded to next near digit.

Data Quality Control and Management: To maintain data quality, two days training was given for data collectors and supervisors before data collection. Properly designed interview data collection materials and data extraction

checklist developed including instrumentation and measurement. Senior radiologists read and ensure the findings of CT scan film. Supervision was carried out on daily basis to check completeness, consistency and outliers both by the supervisor and the principal investigator to assure the quality of data. Clinical records of patients were checked and recorded if the need arises. Furthermore, head CT scan images of patients was reviewed from image gallery database by the radiologist when necessary. Pretest was performed in 5% of patients prior to the actual data collection time and all necessary correction was carried provided necessary.

Data Analysis and Interpretation: After data collection completed, data was entered into Epi-data software version and then exported to SPSS version 25 statistical package for analysis. Descriptive statistics were done and summarized by tables, frequencies, percentage, graphs, mean and standard deviation, median and interquartile range.

Binary logistic regression analysis was used to assess the association between ICC and risk factors. Bivariate logistic regression analysis was performed between dependent and each of the independent variables, in sequence. Variables having a p-value of <0.25 in bi-variable logistic regression analysis were a potential candidate for multivariable logistic regression analysis to control confounders in regression models. Variables having a p-value of less than 0.05 in the multivariable logistic regression model were considered as statistically significant. The final model fitness was checked by Hosmer and Lemeshow chi-square test with non-significant p-value (p-value 0.39). The strength and significance of association between the outcome variable and independent variables were reported by using the adjusted odds ratio with 95% CI.

Operational Definitions

Calcification: Deposition of calcium or calcium compounds in body tissue rendering it hard.

Intracranial Calcification: Deposition of calcium or calcium compounds within cranial cavity (brain). In present study, calcified lesion or body of diameter greater than two millimeter was considered as ICC.

Body Mass Index: Indirect measurement or assessment of national status in children and adults which is ratio of weight in kilograms divided by square of height in meters of the individual. Body mass index of <18.5kg/m^2 is categorized underweight, BMI 18.5-24.9kg/m^2 is category normal weight and BMI of ≥25.0kg/m^2 is category of overweight and obese.

Obesity: literally refers to fatness (overweight and obesity) of an individual but technically body mass index greater than 25.0kg/m^2.

CT Scan: Computed tomography scan (advanced, minimally invasive radiologic imaging with 3D visualization of internal organs and structures, but contrast depending on type of tissue).

Ethical Consideration: Ethical approval and clearance were obtained from Arbaminch University School of Medicine and Health science ethical review board. Permission to undertake the study was taken from the officials of health care facilities. Corresponding letters were written to concerned radiologists and staffs involved in radiology unit of both institutions regarding their cooperation and collaboration. Interview was carried out after getting written consent of the Person being interviewed. Before each interview, clear explanation was given about the aim of the Study. Each respondent was assured that the information provided by would be confidential and used only for the purpose of research. Any participants who are not willing to participate in the study were never forced to participate. They informed that all data and sample obtained from them will be kept Confidential by using codes instead of any personal identifiers and is meant only for The purpose of the study.

Dissemination of the Results: The finding of this study will be presented during thesis defense and the result will be submitted to Arbaminch University School of medicine department of clinical Anatomy. Besides, the findings of the study will also be submitted to both of health facilities where this study was conducted and disseminated through publications and presentations in scientific conferences and workshops.

RESULTS

Socio Demographic Characteristics: This research was conducted on 403 participants from two tertiary level hospitals in southern Ethiopia namely, Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH). Fortunately, all the study participants (403) are responded (interviewed) making response rate of

Table 2: Socio-demographic characteristics of patients underwent CT scan of head in two tertiary level health care institutions in SNNPRS, Ethiopia 2022

Variables	Category	Frequency (n=403)	Percent (%)	Remark
Age	18-35	124	30.8	
	36-55	157	39.0	
	>55	122	30.3	
Sex	Female	184	45.7	
	Male	219	54.3	
Marital status	Single	137	34.0	
	Married	217	53.8	
	Widowed	38	9.4	
	Divorced	11	2.7	
Educational status	Primary	65	16.1	Meaning level completed
	Secondary	136	33.7	N.F.E: No Formal education
	Diploma	97	24.1	
	Degree	61	15.1	
	Masters and above	10	2.5	
	N.F.E	23	5.7	
	Other	11	2.7	
Religion	Orthodox	121	30.0	
	Catholic	95	23.6	
	Protestant	161	40.0	
	Muslim	26	6.5	
Ethnicity	Wolayta	183	45.4	
	Sidama	46	11.4	
	Gurage	26	6.5	
	Amhara	22	5.5	
	Oromo	27	6.7	
	Other	99	24.6	
Occupation	Civil servant	88	21.8	Current job (at time of interview)
	Merchant	66	16.4	
	Farmer	62	15.4	
	Student	27	6.7	
	Self employed	83	20.6	
	N.G.O	9	2.2	
	Unemployed	17	4.2	
	Other	51	12.7	
Residence	Rural	153	38.0	At least 6 months of stay
	Urban	250	62.0	

100%. The normality of age was checked by histogram and it is skewed to the right; the median (IQR) age of the respondents was 43 (57-33 years). Among a total, 219 respondents (54.3%) were Males and the rest 184 respondents (45.7%) were Females. Married participants account for 217 (53.8%) of study participants. Participants educational status was composed of Primary school completed 65 (16.1%), Secondary school completed 136 (33.7%) and those who holding Diploma were 97 (24.1%).

Ethnic and Religious composition of study respondents comprised of 183(45.4%) Wolaita, 46 (11.4%) Sidama, 26 (6.5%) Gurage, 22 (5.5%) Amhara; and 27 (6.7%) of Oromo were ethnic group. The rest 99 (24.6%) respondents out of 403 study subjects contributed from all other ethnic groups. Out of 403 study participants, 121 (30.0%) were found to be followers of Orthodox Christianity; 95 (23.6%) are Catholic adherents, 161 (40.0%) are Protestant Christianity practitioners and the remaining 26 (6.5%) are Muslim by religion.

Occupational detail or job profile of the research respondents consisted of 88 (21.8%) civil servants, 66 (16.4%) individuals are merchant and 62 (15.47%) are engaged in farming. Unemployed respondents are 17 (4.2%) out of 403 subjects, 83 (20.6%) respondents are self-employed; nine (2.2%) of study participants and the rest 51 (12.7%) are engaged in NGO and other various job types respectively.

With regard to Residence, 153 (38.0%) and 250 (62.0%) participants are dwellers of urban and rural community respectively at the time of interview (Table 2).

Table 3: Health related behaviors of patients underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022.

S.no	Variable (Health related behavior)		Frequency (n=403)	Percentage (%)
1	Smoking	Yes	16	4.0
		No	387	96.0
2	Alcohol intake	Yes	60	14.9
		No	343	85.1
3	Physical exercise	Yes	9	2.2
		No	394	97.8
4	Dietary habit (vegetarian)	Yes	12	3.0
		No	391	97.0
5	Sleep habit >= 8hrs	Yes	368	91.3
		No	35	8.7

Table 4: Past medical history of patients who underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022

Variable	Attribute	Frequency (n=403)	Percentage (%)	Remark
Past Admission	Yes	106	26.3	More than 2 days of hospital stay
	No	297	73.7	
Past Surgery	Yes	25	6.2	Major surgical operation only
	No	378	93.8	
Past Radiology	Yes	16	4.0	-Includes head and body
	No	387	96.0	-Repeats counted
Past traumatic head injury	Yes	13	3.2	-requiring admission
	No	390	96.8	-skull fracture

Health Related Behaviors of Research Respondents: Behaviors that promote or affect health were assessed by using structured questionnaire. Active Smoking and Alcohol intake was responded by 16(4.0%) and 60(14.9%) respondents respectively. Similarly, Dietary habit of being vegetarian was found to be 12(3.0%) participants out of 403-subjects. Nine (2.2%) individuals reported habit of regular physical exercise.

On the other hand, 35(8.7%) of study participants responded of not having recommended daily amount of sleep which is greater than 8 hours per 24 hours.

Past Medical History: According to our data, 106(26.3%) respondents out of 403 have history of past medical (hospital) admission and 25(6.2%) subjects out of 403 study participants have history of major surgical operation in past. Past radiological diagnostic test was conducted on 16(4.0%) respondents and 13(3.2%) respondents report history of Head injury or Trauma (Table 3).

Chronic Disease and Familial Hereditary Illness History: History of chronic (metabolic) and familial hereditary diseases of the participants were assessed across respondents thoroughly using structured questionnaire. Out of total four hundred and three study participants, 41(10.2%) respondents found to have hypertension; another 36(8.9%) individuals have history of Diabetes mellitus. Kidney, heart and liver diseases were reported by 41(10.2%), nine (2.2%), 13(3.2%) respectively. One (0.2%) patient out of 403 participants have history of hypothyroidism and 24(6.0%) had Asthma (Table 4).

Neuro-psychiatric Disease Conditions among Study Participants: Neurological and psychiatric diseases like epilepsy, chronic headache (e.g. Migraine), Depression, Schizophrenia, Stroke and insomnia sought carefully through all research respondents. Among them 10(2.5%) had history of repeated epileptic attack, 8 (2.0%) respondents responded history of chronic headache, 12(3.0%) respondents had history of depression and 18(4.5%) patients had experienced some form of paraplegia or hemiplegia. Among all study participants, 20(5.0%) patients have experienced stroke attacks (Table 5).

Antropho-Morphological and Radiological Findings: Physical measurements like height and weight measured and recorded before CT scan of the selected research respondents. BMI calculation and corresponding classification made by data collectors, then checked and approved by supervisor (investigator) if need arises.

Table 5: Distribution of chronic (metabolic) and Familial hereditary illnesses among patients who underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) Sodo Christian General Hospital (WSCGH); SNNPR Ethiopia 2022.

S.Nº	Chronic Diseases		Frequency (n=403)	Percentage (%)	Remark
1	Familial Hereditary diseases	Yes	52	12.9	Physician confirmed diagnoses and record
		No	351	87.1	
2	Hypertension	Yes	44	10.9	Physician confirmed diagnoses and record
		No	359	89.1	
3	Kidney disease	Yes	41	10.2	Physician confirmed diagnoses and record
		No	362	89.8	
4	Heart disease	Yes	9	2.2	Physician confirmed diagnoses and record
		No	394	97.8	
5	DM	Yes	36	8.9	Physician confirmed diagnoses and record
		No	367	91.1	
6	Liver disease	Yes	13	3.2	Physician confirmed diagnoses and record
		No	390	96.8	
7	Endocrine/Hypothyroidism	Yes	1	0.2	Physician confirmed diagnoses and record
		No	402	99.8	
8	Asthma	Yes	24	6.0	Physician confirmed diagnoses and record
		No	379	94.0	

Table 6: Neuro-psychiatric disease conditions among patients whom underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH); SNNPR Ethiopia, 2022

Variable (illness)	Attribute	Frequency (n=403)	Percentage (%)	Remark
Epilepsy	Yes	10	2.5	confirmed
	No	393	97.5	
Chronic headache (Migraine)	Yes	8	2.0	confirmed
	No	395	98.0	
Schizophrenia	Yes	-	-	confirmed
	No	403	100.0	
Depression	Yes	12	3.0	confirmed
	No	391	97.0	
Stroke	Yes	20	5.0	confirmed
	No	383	95.0	
Hemiplegia/Paraplegia	Yes	18	4.5	confirmed
	No	385	95.5	

Out of total 403 research respondents included in the study who undergone CT scan of head, 114(28.3%) have got intracranial calcification irrespective of intracranial location and number (in single or combined manner), making overall prevalence rate of ICC 28.3%. By number of calcifications per person, those with only one calcified center on CT scan film are 75 (18.6%) individuals, those with two calcifications are 33(8.2%) out of 403 and those with three calcifications (persons with three discrete calcifications) are 6(1.5%). There are no participants with four or more calcification on CT scan film. Totally 127 discrete (separate) calcifications are counted (regardless of involved part/calcifications with diameter greater than or equal to 2mm; Figure 2).

Anatomical Sites Commonly Affected by ICCs: Pineal gland calcification alone was found in 41(10.2%) respondents, Choroid plexus alone is calcified in 20 (5.0%) subjects, Basal ganglia calcification found on 12(3.0%) of study participants and that of Habenula is 2 (0.5%) respondents out of 403.

Calcifications that occurred in various combined forms (more than one calcification) are also evident. According to our data, 16(4.0%) of patients have pineal gland and choroid plexus calcification, 10(2.5%) of patients have calcification of pineal gland and basal ganglia. Likewise combined calcifications of both pineal gland and Habenula seen in three (0.7%) of respondents, choroid plexus and basal ganglia calcified in combination in one (0.2%) of patient.

Combined calcifications of three loci in single patient were that of pineal gland, choroid plexus and basal ganglia 5(1.2%) and that of pineal gland, choroid plexus and Habenula account 1(0.2%; Table 6).

BMI Categorization and Distribution among Study Participants: Common WHO BMI classification scheme for adults used to assess BMI of all 403 study subjects. Among them, those subjects with BMI below 18.5kg/m^2 are 32(7.9%), those with BMI of between 18.5kg/m^2-24.9kg/m^2 amount 289(71.7%) and those above BMI of 25kg/m^2 are 82(20.3%) respondents (Table 8).

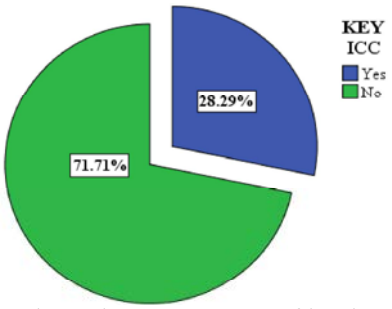

Fig. 2: Magnitude of ICC among patients who underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022. [26]

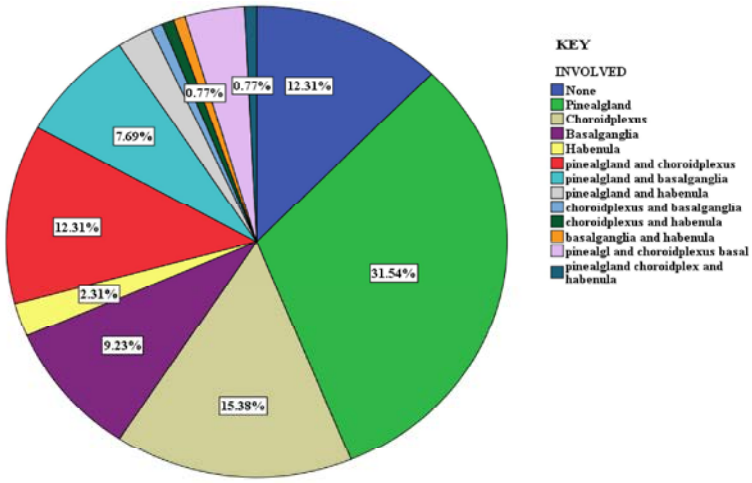

Fig. 3: Frequency of ICC involved (calcified) sites within the brain of patients who underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022 [26].

Table 7: Frequency of ICC involved (calcified) sites within the brain of patients who underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022.

S.№	ICC affected Site		Frequency	Percent (%)	Remark
I	ICC	YES	114	28.3	
		NO	289	71.7	
1	Pineal gland		41	10.2	*
2	Choroid plexus		20	5.0	
3	Basal ganglia		12	3.0	
4	Habenula		3	0.7	2 at a time
5	Pineal gland and Choroid plexus		16	4.0	"
6	Pineal gland and Basal ganglia		10	2.5	"
7	Pineal gland and Habenula		3	0.7	"
8	choroid plexus and basal ganglia		1	0.2	"
9	Choroid plexus and Habenula		1	0.2	"
10	Basal ganglia and Habenula		1	0.2	"
11	Pineal gland, choroid plexus and Basal ganglia		7	1.7	3 at a time
12	Pineal gland, Choroid plexus and Habenula		2	0.5	"
13	Choroid plexus, Basal ganglia and Habenula		2	0.5	"

Table 8: BMI categorization and allocation among patients who underwent CT scan of head at Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022

S.N	BMI category (kg/m^2)	Classification	Frequency (n=403)	Percentage (%)
1	<18.5	Under weight	32	7.9
2	18.5-24.9	Normal weight	289	71.7
3	≥25.0	overweight and obese	82	20.3

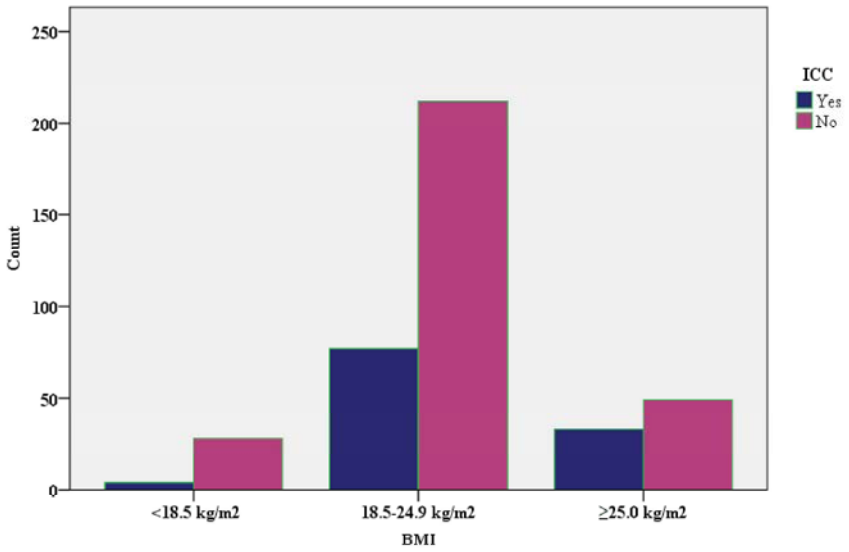

Fig. 4: Distribution and association pattern of ICC and BMI in patients whom undergone CT scan of head in Wolaita Sodo University Comprehensive Teaching and Referral Hospital (WSUTRH) and Sodo Christian General Hospital (WSCGH), SNNPR Ethiopia, 2022 [27].

BMI and ICC Distribution Pattern among Study Participants: Among study participants who are below BMI of 18.9 (underweight) four (12.5%) of participants have intracranial calcification and 77(26.6%) of participants in normal weight BMI rang (18.9-24.5) found to have calcification. Similarly, 33(40.2%) respondents in BMI category of above (pre-obesity to obesity class iii) class have calcification out 43 respondents (Figure 4).

Association between ICC formation, BMI and Other Associated Factors: Bi-variable logistic regression was conducted to identify candidate variables with a p-value<0.25. The identified variables with presence of ICC are: Age, Alcohol consumption, Hypertension, Kidney disease, Diabetes mellitus, Stroke, Hemiplegia/paraplegia and BMI were entered to multivariable binary logistic regression to identify the possible association with intracranial calcification. In the multivariable binary logistic regression analysis, Age of patient, hypertension, Kidney disease, D.M, Stroke attack and BMI were significantly associated factors with formation of intracranial calcification.

This study revealed that, when age increase the likelihood of ICC will also increase. Among the patients that underwent CT scan imaging diagnosis of head in this study, those in the age category of above 55 years of age (late adulthood) are 3.26 times more likely to have ICC than those of young adult (18-35 years of age) individuals (AOR=3.26, 95%CI; 1.67-6.36).

In the same manner, the odds of having ICC were 2.35 times more likely for hypertensive patients compared with their counter parts (AOR=2.35, 95%CI; 1.13-4.90). This study also shown that patients who have chronic kidney disease (CKD) were 2.61 times more likely to be affected by ICC compared to those who have no CKD (AOR=2.61, 95%CI; 1.26-5.41).

It is also evident that according to results of the study, patients with diabetes mellitus (DM) are 2.52 times more likely to get ICC in comparison with non-diabetic counter parts (AOR=2.52, 95%CI; 1.17-5.44). Those patients diagnosed for stroke attack once or more times in their life are 3.25-fold more likely to have intracranial calcification (AOR=3.25, 95%CI; 1.053-10.015).

Body mass index of study participants have also shown significant association with intracranial calcifications. Adults in obese and overweight BMI category (BMI =25.0kg/m^2) were 3.354 more likely to be diagnosed with ICC when compared with those participants who are in underweight Body mass index category ($\leq$18.5kg/m^2). (AOR=3.247, 95%CI; 1.004-11.202). Similarly, those study participants with in normal BMI range (18.5-24.5kg/m^2) shown no increased odds of getting intracranial calcification in contrast to underweight participants (AOR=1.748, 95%CI); (0.972-3.144; Table 9).

Table 9: Bivariate and multivariable logistic regression analysis of ICC formation with predictors for patients who underwent CT scan of head in two tertiary level health care facilities in SNNPRS, 2022.

		ICC				
		YES	NO	COR (95%CI)	AOR (95%CI)	*P*-value
1. Age	18-35	19(15.3)	105(84.7)	1	1	
	36-55	43(27.4)	114(72.6)	1.969(1.192-3.253)	1.759(1.010-3.066)	.046
	≥56	52(42.6)	70(57.4)	4.105(2.239-7.527)	3.260(1.671-6.361)	.001
2. Alcohol	Yes	24(40.0)	36(60.0)	1.874(1.060-3.313)	1.492(0.794-2.803)	.214
	No	90(26.2)	253(73.8)	1	1	
3. Hereditary diseases	Yes	21(40.4)	31(59.6)	1.879(1.029-3.433	1.150(0.571-2.319)	.695
	No	93(26.5)	258(73.5)	1	1	
4. HPN	Yes	26(59.1)	18(40.9)	4.448 2.328 8.498	2.353(1.130-4.901)	.022
	No	88(24.5)	271(75.5)	1	1	
5. Kidney disease (CKD)	Yes	22(53.7)	19(46.3)	3.398(1.760-6.561)	2.611(1.260-5.410)	.010
	No	92(25.4)	270(74.6)	1	1	
6. D.M	Yes	20(55.6)	16(44.4)	3.630(1.807-7.295)	2.523(1.170-5.442)	.018
	No	94(25.6)	273(74.4)	1	1	
7. Stroke	Yes	13(65.0)	7(35.0)	5.185(2.012-13.361)	3.247(1.053-10.015)	.040
	No	101(26.4)	282(73.6)	1	1	
8. Hemi/Paraplegia	Yes	10(55.6)	8(44.4)	3.377 1.298 8.790	1.039(0.298-3.618)	.952
	No	104(27.0)	281(73.0)	1	1	
9. BMI	<18.5	4(12.5)	28(87.5)	1	1	
	18.5-24.9	77(26.6)	212(73.4)	1.854(1.111-3.096)	1.748(0.972-3.144)	.062
	≥25	33(40.2)	49(59.8)	4.714(1.513-14.694)	3.354(1.004-11.202)	. 049

NB: P-value with "*" shows statistically significant variables.

DISCUSSION

This study was conducted to assess the magnitude of intracranial calcification and associated factors among adults who underwent CT scan of head in WSCGH and WSUTRH for various medical conditions.

Overall prevalence of ICC with a 95% confidence interval was 28.3% (23.8% -32.5%). The finding was consistent with the studies conducted in University of Florida Colleges of Dentistry and Medicine (26.96%), but lower than reports of the studies done in University of Southern California, Los Angeles USA (35.2%) and in Tikur Anbessa hospital in Addis Ababa which reported the prevalence in terms of pineal gland and choroid plexus calcifications of around 72.0% for pineal gland (18.8% in this study) and 43.3% for choroid plexus calcifications (11.66% in this study) [26-28]. This perceived difference seems to root from background characteristics of study population and may be lifestyle of population under study.

The magnitude of intracranial calcifications reported in this study was rather higher than the results of studies conducted in Brazil (17.54%) and Beirut in Lebanon (20%). the possible reason in this study might be variation in the study population. The study carried out in Brazil also included subjects under eighteen years of age, which are excluded in this study. In addition to this, life style differences of the study population might be the contributing factor for this different percent of the ICC outcomes [6, 29].

On the other hand, the prevalence of intracranial calcifications reported in present study is lower than the findings of studies that contacted in South Africa (98.2%), Iran (50%) and Cameroon in central Africa (56.82%). This might be due to the variation of study participants; and the study that carried out in South Africa done on larger sample size and on the population entirely much varied socio-demographic background. The study of Iran also employed on the general population including all age groups. Moreover, the study conducted in Cameroon was consists of few study participants (132) in contrast to our study population of 403 [30- 32].

Age is commonly significant variable associated with ICCs. In this study, it is also evident that odds of getting ICCs increase with age. It revealed that participants aged ≥36 years were 1.762 times more likely to have intracranial calcifications than those aged less than 35 years old. Those patients greater than 56 years of age have 3.214-fold probability diagnosed with intracranial calcification than younger adults. This finding is in line with prior research reports as shown by figures of researches of Addis Ababa Tikur Anbessa Hospital in Ethiopia, Cameroon, South Africa and Iran [26, 30, 32].

Hypertensive patients have also elevated risk of getting intracranial calcifications, as in this study. They have 2.277 times more likely chance of affected by ICCs in comparison to non-hypertensive patients. It is also indicated in other studies as significantly associated with ICC, particularly intracranial arterial calcifications. It well established fact that chronic intracranial micro bleeds lead to significant rate in calcification formation. This finding was also reported in previous studies conducted by T.T. de Weert 2009 [33].

Chronic kidney disease (CKD) patients have 2.611 more risk of getting ICC than those did not have the disease (CKD) (AOR=2.611, 95% CI; 1.260-5.410). In France, patients with CKD are mostly affected by intracranial calcifications [34]. Their finding puts the risk of ICC in CKD patients as about 2.6 times higher, which is comparable to finding of this study [35, 36].

Another study published by Romina Maria Uranga *et al.* [37], in their paper 'Complex Interactions Between Obesity, Metabolism and the Brain', found that diabetic individuals like those affected by CKD are too, have more risk of getting intracranial calcifications. In this current research, also, the patients of diabetes mellitus are also found to have 2.523 times more chance of having ICC unlike those whom are non-diabetic (COR= 2.523, 95%CI; 1.170-5.442) [35, 36].

Stroke is also one of factors that associated with risk of ICC formation in those affected by it. In this study it was shown that there is 3.247 times more probability of being affected by intracranial calcification in comparison to no stroke participants (AOR=3.247, 95CI; 1.053-10.015). Works of Romina Maria Uranga *et al*.[37], also support this finding and de Weert *et al.* [33], reported close association of ischemic stroke and intracranial calcifications predominantly that of intracranial arterial calcification (IAC) [35, 36].

Body mass index (BMI) of adults included in this study also associated with carrying some degree risk of intracranial calcification. Those adults in BMI category above 25.0kg/m^2 were 3.354 times more likely to have intracranial calcification in contrast to those below body mass index of 18.5kg/m^2 (underweight) adults (AOR=3.354, 95%CI; 1.004-11.202). Adult study participants with in normal body mass index range (18.5-24.9kg/m^2) have also 1.748 higher risk of intracranial calcification formation than those who are underweight. Even though there are no adequate literatures on this studies topic area at least one study stated that BMI provides a reasonable estimate of body fat and it is more accurate than skinfold measurement [37]. A major problem with obesity is the diverse set of health-associated complications it causes including hypertension, diabetes, increased cardiovascular risk and cancer among others. Another study tried to take into account the effect of body mass index on brain calcification found minimal interaction among the two. It is also stated in other literatures that indeed, there is interplay of various metabolic processes on causation calcification in general and intracranial calcification in general though the process is complex enough to investigate and measure [9, 11, 25, 36, 38].

CONCLUSION AND RECOMMENDATIONS

This study found that a magnitude of intracranial calcifications was 28.3% among adults whom underwent CT scan imaging diagnosis of head in WSCGH and WSUTRH. Factors that contribute to intracranial calcifications were older age, being with hypertension, being with Kidney disease (CKD) and being Diabetes mellitus, patients with history of Stroke attack, hemiplegia or paraplegia and patients with higher Body mass index level (BMI).

Therefore based on the above conclusions the following recommendations can be forwarded are:

- Health care planners should focus on setting a strategy that helps for the delivery of information on the concept of intracranial calcifications. Planning health education delivery method that informs public on prevention and adequate treatment of chronic (metabolic diseases) and nutritional habits that affect health such as obesity thereby addressing prevention of intracranial calcifications.
- Health professionals working in both WSCGH and WSUTRH should aware adults as well as other patients to prevent possible factors that predispose intracranial calcification formation including obesity and other factors discussed in this study. Health education to prevent chronic metabolic diseases and obesity related dangers. Health care professionals also have to screen and diagnose patients at risk intracranial calcifications. They also should give special care in addition to routine care for patients with known risk factors.

- Community health workers should give health education at community and household level for prevention of occurrences of intracranial calcifications as well as dangers associated with improper nutritional habits and avoiding unnecessary weight gain. Awareness creation on early diagnosis and treatment of chronic metabolic diseases like diabetes mellitus, hypertension, chronic kidney diseases (CKD) should be urged.

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