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Evaluation of intracranial physiological calcifications in computed tomography

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Abstract

Introduction: Intracranial physiological calcifications are not related to any pathological conditions, rather they are due to the normal deposition of calcium or iron in the different parts of the brain. Computed Tomography (CT) scan is superior to all other modalities in terms of sensitivity in the detection of intracranial physiological calcifications. The objective of the study was to evaluate the frequency and location of intracranial physiological calcifications and also study them according to age and gender.

Materials and methods: A retrospective cross-sectional study with a purposive sampling technique was conducted from November 2020 to February 2021 at the Department of Radiology and Imaging. CT scan images of every age group were reviewed from the base of the skull to the vertex excluding images with intracranial pathologies, injuries, artifacts, contrast enhancement and the patients with follow-up scans. Data were analyzed using SPSS version 25. Descriptive analysis was primarily preferred accompanied by inferential statistics.

Results: Out of 412 patients, 60.7% were male and the mean age was 41.16 ±19.915 years. The total number of calcifications was 795. 92.8% of patients showed calcifications. Males had a higher number of calcifications. The highest number of calcifications was seen in the age group 21-30. The highest calcification was seen in the pineal gland (76%) followed by the choroid plexus (70.4%) and the lowest in the caudate nucleus (0.38%). The earliest age of calcification was 8 years. There was a significant relationship between the increase in age

and the increase in calcification ($p<0.05$). There was also a significant difference between male and female calcifications ($p<0.05$).

Conclusion: This study can be useful for clinicians to differentiate normal physiological intracranial calcifications from pathological calcification which will reduce misinterpretation of the calcifications.

Introduction

Intracranial calcification denotes the presence of calcification (calcium and/or iron) within the brain vasculature and parenchyma [1]. Intracranial 'physiological' calcifications are not related to any pathological conditions, but they look like pathological calcifications. So, the knowledge of the location, extent and frequency of physiological calcification is very essential [1,2,3]. Exact evidence of the relationship between aging and intracranial physiologic calcification is unknown to date but it is believed that the incidence of intracranial physiological calcification usually increases with an increase in age [4].

Computed Tomography (CT) scan is the modality of choice for imaging calcifications because of its high spatial resolution [5]. However, window level, width, slice thickness and many other parameters used during the CT scan greatly impact the calcification's detectability [6].

The studies suggest that the intracranial physiological calcifications are found commonly in the areas like pineal gland, basal ganglia, choroid plexus, Falx cerebri/ tentorium cerebelli, dura, lens, sagittal sinus, petroclinoid ligament, cavernous part of the internal carotid artery, habenula, arachnoid granulations and other non-defined areas [6,7]. According to the literature, most of the calcifications are found in the choroid plexus and pineal gland followed by a lesser number in other regions and the calcifications below five years of age are very rare and if present, should be suspicious of underlying pathology [7,9]. If the size of pineal gland calcification exceeds 1 cm in diameter or it is present in children below 9 years, it can be thought to be due to a neoplastic tumor [9,10]. But this presumption is also being ruled out due to the invention of very high detectability of CT scanners [7].

In addition to the information suggested by the literature, this study aims to find the physiological calcifications present in people from all over Nepal who visit the Radiology and Imaging Department of the hospital for diagnosis. Patient flow in this hospital is of diverse nature which makes the study more open and the results more precisely represent the population of Nepal.

Methods

Data collection

This is a retrospective, descriptive cross-sectional study. Data was collected from the Department of Radiology and Imaging over four months, from November 2020 to February

2021. A purposive sampling technique was adopted. Data collection was done after a thorough questioning of patient about their disease conditions and assessing medical reports to strengthen the exclusion criteria. A total of 412 non-contrast CT scans of the head were included in the study after fulfilling all the inclusion criteria.

All the patients from ages one to 100 were included in the study. The CT scans of patients having any artifacts, intracranial pathologies and intracranial injuries were excluded from the study. Contrast-enhanced CT scans and angiographic scans were also excluded. Furthermore, exclusion criteria included patients with follow-up CT scans of the head.

All the CT scans were performed on a single machine, the Philips Ingenuity 128-slice multidetector CT scanner. The CT scanner was air calibrated every morning before starting any scans to maintain the technical calibers of the machine in normal standards.

Data analysis

The Non-Contrast CT scans of the patient's brain were thoroughly studied on the workstation in two steps: first in the five-millimeter (mm) slice thickness and second in the thin slices of one mm. The calcification which was visible on both of the steps was only recorded. Verification of the calcification whether it is physiological was done by the group of three consultant radiologists separately as blinded reviewers. The radiologists had minimum one year of clinical experience post their qualification in Doctor of Medicine in Radiodiagnosis. The criteria used for the verification was primarily the size. The threshold of 10mm size was set and the calcification with size greater than 10 mm was stated as pathological. However, the calcification of size smaller than 10 mm was recognized to be pathological in the cases where patient had neurological disorders but no other accompanying intracranial abnormality.

The following areas were visualized to look for calcifications: 1. pineal gland, 2. posterior horn of choroid plexus of lateral ventricle, 3. either of the falx cerebri or tentorium cerebelli, 4. habenula, 5. Globus pallidus, 6. putamen, 7. dentate nucleus of cerebellum 8. superior sagittal sinus and 9. Caudate nucleus. The data was recorded on the data collection sheet.

The data were entered into MS excel and transferred to the SPSS (SPSS 25.0; IBM, Armonk, New York) for analysis. The statistical analysis of the data was accomplished primarily with descriptive statistics. Inferential statistics also accompanied descriptive statistics. The Chi-Square test for trend, independence, and p-value was used to evaluate the association between different variables. The Spearman correlation value was calculated to determine the association between the frequency of pineal gland and choroid plexus calcification.

Ethical considerations

Ethical approval was not required for the study because the study was performed by using the patient data that the patient provided to the hospital and no external intervention was applied on the study. Autonomy and confidentiality of patient identification and data was strictly maintained throughout the study.

Results

A total of 412 samples were taken, of which 250 (60.70%) were male and 162 (39.30%) were female. Of those 412 patients, 380 (92.80%) had calcifications and 32 (7.20%) had no calcifications.

The mean age was 41.16 ± 19.915 and the range 2-91 years. The mean age of males was 40.70 ± 19.782 and the mean age of females was 41.86 ± 20.161. Table 1 shows the comprehensive data about the number of calcifications in each region of the brain in males and females and the values of chi-square and significance (p-value) between the male and female calcifications in different regions of the brain. The samples were divided into ten age groups from zero to 100 with an interval of 10 years as mentioned in Table 2.

Table 1. Number and earliest age of calcification with the significance between male and female calcification in different regions

Region	Male	Female	Total	Earliest age of calcification (Years)	Chi-square	p-value
Pineal gland	198	115	313	8	3.632	0.057
Choroid Plexus	188	102	290	12	7.062	0.008
Falx/Tentorium	65	41	106	11	0.25	0.875
Globus Pallidus	25	18	43	8	1.30	0.719
Putamen	3	3	6	9	0.291	0.590
Superior Sagittal Sinus	11	2	13	9	3.223	0.730
Habenula	5	2	7	9	0.345	0.557
Dentate nucleus	10	4	14	51	0.219	0.640
Caudate nucleus	1	2	3	25	0.947	0.330
Overall	**506**	**289**	**795**	**8**	**4.168**	**0.041**

Table 2. Frequency of the age and sex of the patients

Age (years)	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	91-100	Total
Male	11	24	65	30	44	34	19	17	5	1	250 (60.70%)
Female	4	21	37	20	23	31	7	13	6	0	162 (39.30%)
Sum	15	45	102	50	67	65	26	30	11	1	412

The highest number of patients belonged to the age group 21-30 having 102 members while the age group 91-100 had just one patient recorded. The calcification was not present in patients below eight years. Table 1 shows all the studied calcifications and their earliest age of occurrence.

The total recorded calcifications were 795. The maximum incidence of calcification was found in the pineal gland (76%) whereas the minimum incidence was found in the caudate nucleus (0.7%). The age group 21-30 had the highest number of patients (20.1%) (Table 2).

230/412 (55.8%) patients had both pineal gland and choroid plexus calcification whereas 39/412 (9.46%) had none of these two calcifications. Comprehensive data about the comparative study of choroid plexus and pineal gland calcification is given in Table 3. There was a weak positive correlation between the frequency of pineal gland and choroid plexus calcification (the Spearman correlation value = 0.121). The relationship between the pineal gland and choroid plexus calcification was statistically significant (p=0.014).

Table 3. Comparison of Choroid and Pineal calcifications

	Choroid Plexus ✓	**Choroid Plexus ✗**	**Total**
Pineal Gland ✓	230	83	313
Pineal Gland ✗	60	39	99
Total	290	122	412

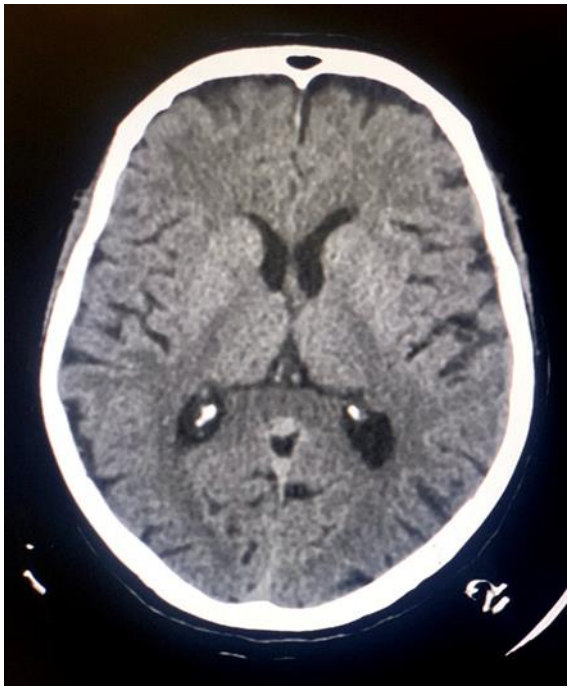

Figure 1. CT head Image with Choroid Plexus calcification in the posterior horn of lateral ventriclect

There was a significant relationship between increasing age and total calcifications ($p<0.05$). Pineal gland and choroid plexus data were analyzed and compared with the data of other studies. The comprehensive and comparative information about the calcification frequency of this study and other studies was stated in Table 4. There was a significant difference between overall occurrence of calcifications in male and female patients ($p<0.05$). There was no significant difference between male and female calcifications in other regions except choroid plexus.

Table 4. Comparison of this study with other studies

Serial Number	Study	Pineal Gland	Choroid Plexus
1.	Kwak R., et al.	67.7%	57.6%
2.	Daghighi, et al.	71%	66.2%
3.	Uduma et al.	46.21%	56.82%
4.	Adeola A., et al.	12.2	-
5.	Guja C., et al.	-	51%
6.	Badal M.J., et al.	75.49%	71.18%
7.	This study	76%	70.4%

Discussion

In this study, the number of calcifications (795) was more than the number of studied patients (412) because a single patient can have calcifications in more than one region. In this study, the age group which had the largest number of patients was 20-30 years (24.8%). The age group having a maximum number of calcifications was also 20-30 years (20.1%). The detailed data about the age group and sex of the patient is shown in table 2. The study done by Badal M.J. et al [6] had the highest number of patients in the age group 31-40 (17.2%) but the highest number of calcifications was found in the age group 51-60 (20.02%). In a similar study done by Uduma et al [19], it was found that 40-49 years age group was the largest studied population, which was also the age group with maximum calcification (35.58%). Daghighi et al. [2] found both the highest number of patients and the highest number of calcifications in the age group 35-44.

Males (60.7%) were more than females (39.3%). Every age group had more males than females except the age group 81-90. The number of calcifications was more in males (63.64%) than in females (36.35%). But, in a similar study done by Daghighi et al. [2], the female population (59.1%) was more than the male (40.9%). Also, the number of calcifications was more in females in that study. Similar results to that of this study were obtained from the study of Kwak R. et al. [14] and Guja C. et al. [21], which noted more calcification in males than females throughout the age range of their studied population.

Out of 412 studied patients, 313 (76%) had pineal gland calcification, 290 (70.4%) had choroid plexus calcification, 106 (25.7%) had falx/tentorium calcification, 43 (10.4%) had globus pallidus calcification, 14 (3.4%) had dentate nucleus calcification, 13 (3.2%) had superior sagittal sinus calcification, 7 (1.7%) had habenula calcification, 6 (1.5%) had putamen calcification and 3 (0.7%) patients had caudate nucleus calcification as described in table 1. Daghighi et al. [2] showed 71% pineal gland calcifications, 66.2% choroid plexus calcifications, 20.1 % habenular calcifications, 7.3% tentorium cerebelli calcification, 6.6% vessels calcifications, 0.8% basal ganglia calcification and 0.9% lens and other structural calcifications out of 1569 studied patients. Out of total recorded calcifications (795), pineal gland had the highest number of calcifications (39.37%) followed by choroid plexus (36.47%), falx cerebri/tentorium cerebelli (13.33%), globus pallidus (5.4%), dentate nucleus (1.77%), superior sagittal sinus (1.63%), habenula (0.89%), putamen (0.75%) and caudate nucleus (0.38%). Detailed data is shown in table 1. In most of the studies, including this study, pineal gland was the region of maximum calcification but in the study done by Uduma et al. [19], choroid plexus was the region of maximum calcification. Table 4 shows the comparison of the calcifications of this study with different other studies (Table 4).

Total basal ganglia calcification in this study was 6.53% (Globus Pallidus = 5.4%, Caudate = 0.38% and putamen = 0.75%). Daghighi et al. [2] had not differentiated the basal ganglia calcifications, rather they found that basal ganglia consisted of 0.8% of total calcifications. Globus pallidus showed the greatest number of calcifications among the basal ganglia structures in this study.

The earliest age of calcification was 8 years and the earliest calcification to appear was pineal gland calcification which is similar to the study by Badal M.J. et al. [6] and Adeloye A. et al. [20]. Uduma et al. [19] found it as 10 & 9 years in two different studies. Also, in this study, Dentate nucleus calcification first appeared at the age of 25 years and caudate nucleus calcification first appeared at 51 years. Table 1 shows the earliest age of calcification of different regions of the brain.

Of the total 412 patients, 230 (55.8%) had both pineal gland and choroid plexus calcifications. 83 (20.1%) had pineal gland calcification but no choroid plexus calcification. 60 (14.6%) had choroid plexus calcification but no pineal gland calcification. 39 (9.5%) had neither choroid plexus nor pineal gland calcification. In the study by Daghighi et al. [2], 50.03% had both pineal gland and choroid plexus calcification (Table 4).

Choroid plexus and pineal gland calcification were found to have a weak positive association with each other with the Spearman correlation value of 0.121 and the p-value significance between them was 0.014 which tells us that the association between these two calcifications is statistically significant. All other calcifications had no statistical significance between their frequencies. The incidence of the co-existence of choroid plexus and pineal gland calcification was greater in males in this study but in the study of Daghighi et al. [2],

the incidence of the co-existence of choroid plexus and pineal gland calcification was more in the females. These kinds of duplicate calcifications were most common and prominent in the age group 21-30 in this study whereas in the study by Daghighi et al. [2], 35-44 was the prominent age group of duplicate calcifications in different areas of the brain. The ratio of Choroid Plexus to Pineal Gland (CP: PG) calcification in this study was 0.93:1, which was 0.94:1 in Badal M.J. et al. [6] study and 1.23:1 in Uduma et al. [19] study.

In this study, the male-to-female ratio of the pineal gland and choroid plexus calcification was 1.72:1 and 1.84:1 respectively. They were 1.91:1 and 1.86:1 respectively in the study by Badal M.J. et al. [6] and 1.44:1 and 1.42:1 respectively in the study by Uduma et al. [19]. Male to female ratio in the calcification of Falx cerebri/ tentorium cerebelli, Globus pallidus, Superior sagittal sinus, habenula, putamen, dentate nucleus and caudate nucleus were 1.59:1, 1.39:1, 5.5:1, 2.5:1, 1:1, 2.5:1 and 1:2 respectively.

In this study, 70.8 percent of the total calcifications were in patients between 20-60. If I compare this study with that of Badal M.J et al. [6], they found, 67.9% of the total calcifications in the patients aged 20-60, which of slightly less than this study but approximately equal. There was a significant difference between male and female calcifications (p-value = 0.041 and chi-square value = 4.168 at df =1). Also, in the study of Badal M.J. et al. [6], the result was similar (p-value = 0.0331 and chi-square value = 6.841 at df =2).

There was a statistically significant relationship between the increase in age and the increase in calcification in this study (p = 0.000 and chi-square value = 179.989 at df 78). Badal M.J. et al. [6] also found the relationship between age and calcification to be statistically significant ((value of chi-square was 83.352; degree of freedom 1) with p-value < 0.0001.) Also, there was a significant relationship between the increase in age and the increase in the frequency of pineal gland and choroid plexus calcification ($p<0.05$). But the relationship between the increase in age and the increase in the frequency of calcification in other regions was statistically insignificant ($p>0.05$).This study elaborately evaluated all the intracranial physiological calcifications in the brain, their percentages, and their comparison with other studies. Knowledge of physiological calcifications and their extent and amount in the brain can help us to differentiate them from pathological causes. Although physiological calcification does not accompany any pathological cause and they can occur in different people varying in numbers according to their age, sex, ethnicity, geographical region, and nutrition [2], they are very essential parameters required to diagnose the pathological calcifications properly. If physiological calcifications are not understood and known properly, they could mimic pathology and lead to misdiagnosis which can be clinically inappropriate and sometimes dangerous too, as in surgical cases [2].

This study was successful in excluding the patients with intracranial pathologies, intracranial injuries and post-operative patients but was unable to exclude the patients with hypertensive disorders because proper data on the hypertension of the patient was unavailable and was not feasible to obtain in the OPD settings of the Radiology and Imaging Department of the Hospital. The Na-K imbalance and parathormone imbalance in the body can also result in an increased amount of calcification in the brain – a factor that could not be considered in this study. Further studies can be done by obtaining patient history thoroughly which includes blood reports including Na+, K+ and Parathormone values. This will give a more detailed and precise result of physiological calcifications by excluding all the possible pathological causes. Size measurement, shape assessment and symmetricity evaluation of choroid plexus calcification are necessary and are recommended for future studies.

Conclusion

The data of this study can be helpful for clinicians and radiologists to compare it with the calcifications they encounter during the evaluation of the pathology. Knowledge of physiological calcifications can help to differentiate them from pathological calcifications which aid in differential and transparent diagnosis. The data suggest that intracranial physiological calcifications increase with the increment in age. This helps to rule out the extent of the calcification that might be present in a healthy person. From this study along with various other comparatively parallel studies, one can generalize the age group, gender and location having the highest frequency of calcification.

Statements and Declarations

Competing Interest: The author declares that there are no conflicts of interest.

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