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Original Article

Pineal gland calcification within Saudi Arabian populations

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ABSTRACT

Introduction: Pineal gland calcification (PGC) is common among Western populations but is rare among African and Far Eastern populations; yet, no studies to date have examined Arabian Gulf populations for PGC. This retrospective study was conducted to determine the incidence of PGC within a Saudi Arabian population, to investigate the associations between PGC and age, and to examine the effects of age on both the degree of pineal calcification and the size of uncalcified pineal tissue.

Methods: Fifty-four (54) CT brain scans from individuals 2–87 years of age were procured from the Department of Radiology, Security Force Hospital, Riyadh, Saudi Arabia. The scans were performed in both the coronal and sagittal planes.

Results: Pineal gland calcification was identified in 64.8% of individuals examined ($p = 0.047$), with a higher incidence in females ($p = 0.05$); both of these findings were statistically significant. The percentage of PGC was significantly correlated with increased age ($r = 0.36$; $p = 0.04$). Pineal gland calcification was also found to increase rapidly after the second decade of life, as 68.6% of individuals 50+ years of age exhibited PGC. No significant correlations were found between age and the degree of pineal calcification or between age and the amount of uncalcified pineal tissue.

Discussion: Key findings of the present study indicate that high PGC in females was associated with increased age within a Saudi Arabian population. This finding differs from the findings of previous studies and suggests the need for further research in populations of Arabian Gulf nations.

1. Introduction

The pineal gland is a neuroendocrine gland that protrudes from the roof of the third ventricle and lies in the space between the corpus callosum and the superior colliculi in the dorsal aspect of the brain stem.[1] The pineal gland functions primarily to synthesize and secrete the hormone melatonin. Melatonin is involved in the regulation of diverse physiological functions such as circadian rhythms, immune enhancement, and cancer inhibition.[2] Melatonin levels decline with age, and changes in the levels of this hormone are considered a cause of age-related diseases, immune disorders, cancer,[3] and sleep-wake disturbances.[4]

As humans age, the pineal gland displays increased calcified concretions composed predominantly of calcium and phosphorus as well as small amounts of magnesium and strontium.[5,6] This calcification can be observed on computed tomography (CT) scans.

Zimmerman and Bilaniuk[7] suggested that both age and the characteristics of sub-populations are related to the incidence of pineal gland calcification (PGC). Wurtman et al.[8] studied PGC in subjects aged 3–70 years. The results showed that 2% of subjects aged 3–12 years had PGC, while 46% of those aged 13–40, 66% of those aged 40–55, and 72% of those aged 55–70 years of age had PGC. Okudera et al.[9] reported that 70% of people over 30 years of age displayed signs of PGC.

Doyle and Anderson[10] found that 20% of children up to the age of 15 had PGC. This rate dropped to 8% in children under the age of 10, which suggests that pineal calcification is abnormal in children.

The incidence of PGC has been found to vary among different populations.[11] In earlier studies, the incidence of PGC was reported for several populations as follows: 16% in white Americans, 9.7% in African-Americans,[12] 9.9% in Japanese,[13] 19–24% in Indians,[14] and only 5% in Nigerians.[15] However, recent studies have shown a far greater incidence of PGC in the following countries: 68.5% in

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Turkey[11] and 67% in Thailand.[16] However, no studies of Arabian Gulf populations have been conducted.

While pineal calcification is commonly seen in western countries, it is rarely found among African populations.[17] Odeku and Jonota[18] assessed 952 skull radiographs at the University College Hospital, Ibadan, Nigeria and found that, overall, only 5% of subjects studied had PGC and that most cases of PGC occurred in the fifth decade of life. Akano and Bickler[17] conducted a study on populations of other regions of sub-Saharan Africa, with a focus on Gambia, in order to compare their study data with previous data for white Americans and African-Americans from the study by Adelola and Felson.[12] Their results demonstrated a greater incidence of PGC among white Americans compared with African-Americans and Gambians, which may be related to ethnicity and environmental factors.

The purpose of the present study is to determine the incidence of PGC in a new, previously unstudied population and to investigate the association of PGC with age and the degree of pineal calcification (DOC) using the CT scan method.

2. Materials and Methods

In all, 54 CT brain scans of Saudi individuals (F = 29, 47 ± 21 yrs, aged: 2–77; M = 25, 39 ± 22 yrs, aged: 10–87) who were referred to the Department of Radiology at Security Force Hospital (SFH) in Riyadh, Saudi Arabia were obtained for this study. These individuals were admitted to the hospital between August 2013 and February 2014 with complaints of chronic headache. The electronic medical records were reviewed retrospectively to identify patient imaging data and associated medical histories that were relevant to pineal gland calcification. Exclusion criteria included the presence of cysts or tumors of the pineal gland.

The study was approved by the Security Force Hospital Ethics Committee for Human Research, and the study protocol was approved by the Chatham University Institutional Review Board for the Protection of Human Subjects.

A 64-MDCT scanner (GE Light Speed VCT ct99) was used for all imaging examinations. Image slices 5 mm in thickness were used for the assessment of the pineal gland. Imaging processing software that supported the DICOM image analysis function was used to outline the entire pineal gland or a portion of it. However, the area of the outlined region was calculated directly by the software and was reported in square pixels (pix^2). The pineal boundaries were identified on both sagittal and coronal sections so that multiple measurements could be obtained, which allowed for a clearer estimation of the calcified area. The DOC was calculated by taking into account the percentage of the calcified portion and calcification density.

All images were digitally evaluated using a free version of OsiriX v.5.8.2 computer software (www.osirix.viewer.com). The region of interest of each pineal gland was manually traced using the OsiriX quantification tools. Quantitative measurements of the analyzed images were used to estimate total area of the gland (pix^2), the area of calcified tissue (pix^2), and the density of the calcified portion (Hounsfield Units – HU).

The boundaries of the pineal tissue were defined by visual inspection and were manually traced on two views of the sagittal and coronal planes. The radio-opaque calcified portion had irregular boundaries and appeared on the gland region; this was manually traced on two slices that showed the calcification. The larger calcified portion was selected for the measurement.[19] This was done to avoid errors that may have originated from the manual tracing method by visual inspection.

To quantify the DOC, we used the modified method of Kunz et al.[20] The calcified area and the density of the calcified portion were transposed to five-point scales.

The densities of the calcified pineal areas were grouped based on a five-category scale: 0–50 HU = 0; 51–150 HU = 1; 151–250 HU = 2; 251–350 HU = 3; 351–1000 HU = 4. Then, the calcified area was estimated based on a five-category scale according to the percentage of the calcified portion compared with the total area of the gland: 0% = 0; 1–24% = 1; 25–49% = 2; 50–74% = 3; 75–100% = 4. When the score for the density of the calcified portion was added to the score for the calcified area, it was possible to calculate the DOC score. For example, if the density = 360 HU (DEN = 4) and the percentage of calcified portion = 40% (CPP = 2), then DEN(4) + CPP (2) = DOC(6) (Fig. 1).

The estimated areas of the calcified pineal tissue (CPT) and uncalcified pineal tissue (UCPT) could be calculated using the DOC. To estimate the CPT, the total gland area was multiplied by the DOC (e.g., total area = 159 pix^2, DOC = 2/8: 159× 0.25 = 39.75 calcified tissue). The UCPT was estimated by multiplying the total gland area by the DOC–1 (e.g., the total area = 159 pix^2, DOC = 2/8: 159× (1 – 2/8) = 119.25 for uncalcified tissue).

A statistical analysis was performed using SPSS v. 20.0 (IBM Corporation, Armonk, NY, USA). Descriptive values for age were determined separately for males and females. The Chi-square test (X^2) was used to assess the differences in pineal calcification as it related to age and gender. Pearson's correlation coefficient was

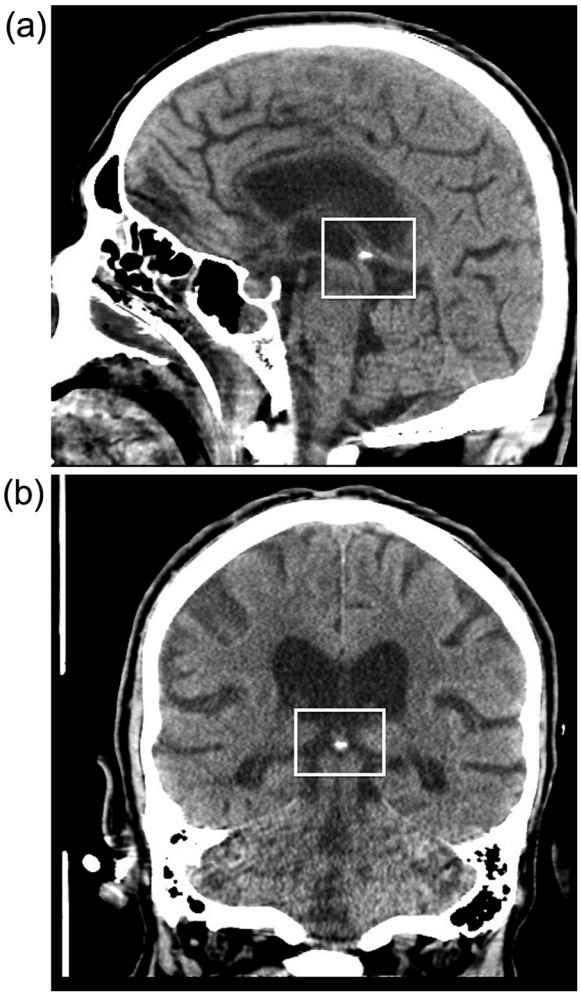

Fig. 1. Coronal and sagittal sections of brain CT scans show pineal gland calcification (PGC). (a) Moderate PGC with a degree score of 4 in a 17-year-old male patient. (b) Moderate PGC is represented on a sagittal section from the same patient.

used to assess the correlation of pineal parameters (DOC, UCPT, CPT) with age. In addition, one-way ANOVA was used to assess the differences in the DOC among the age groups. All results with a p value of ≤ 0.05 were considered statistically significant.

3. Results

In our retrospective analysis of 54 brain CT scans, we found that 35 brain CT scans displayed PGC on either the sagittal or coronal planes (F = 21, age = 53.6 ± 17.7; M = 14, age = 41 ± 25.6).

Overall, the age range of all individuals included in this study (n = 54) was 2–87 years, with an average age of 43.0 ± 21.67. Fig. 2 shows the scan results of PGC incidence by gender. PGC was found more frequently in females (38.9%) than males (25.9%), (X^2; p = 0.05).

Scans were then grouped according to patient age. Table 1 reports the relationship between the incidence of PGC and gender according to age group. PGC was significantly identified in 64.8% of the individuals studied (X^2; p = 0.047). This incidence of PGC increased with age. PGC was first observed in the second decade of life, and 68.6% of the cases of PGC were observed in patients over 50 years of age (Table 1).

A significant correlation was observed between the percentage of PGC and age (r = 0.36; p = 0.04) (Fig. 3). No significant association was noted in the total size of the pineal gland and the age of the patient (ANOVA; p = 0.33). In addition, the DOC score (mean = 4.4) was at the maximum in the 50–65 age group.

A significant correlation was observed between gender and age (X^2; p = 0.02). However, no difference was found in the DOC between genders (X^2 p = 0.32) (Table 2).

Analyses of pineal parameters (DOC, UCPT, CPT) and age indicated no significant correlation between age and DOC (r = 0.22; p = 0.20), CPT (r = 0.189; p = 0.276), or UCPT (r = −0.192; p = 0.270).

4. Discussion

The results of this study confirm the results of previous studies,[21,22,23] which have indicated that the incidence of PGC increases with age. The incidence of PGC (64.8%) found in this study is in agreement with data from studies conducted in Turkey[11] and Thailand.[16] The finding that PGC is associated with increased age is also consistent with findings from Turkey and Thailand.[11,16] The lack of findings among study participants <10 years of age is in agreement with previous findings that concluded that calcification is rare in those under 10 years of age.[24]

Table 1
The distribution of the individuals according to age and gender and their relationship with pineal gland calcification (PGC) on CT scans.

Age range	No. of individuals with CT scans			No. of cases of PGC on CT scans		
	Females	Males	Total (%)	Female	Male	Total (%)
<20	3	6	9 (16.7)	0	4	4 (44.4)
20-34	4	7	11 (20.4)	2	3	5 (45.4)
35-49	10	3	13 (24.1)	8	1	9 (69.2)
50-65	4	6	10 (18.5)	3	3	6 (60.0)
>65	8	3	11 (20.4)	8	3	11(100)
Total	29 (53.7)	25 (46.3)	54 (100)	21 (72.4)	14 (56.0)	35 (64.8)

Values in the parentheses indicate the percentage of individuals.

In this study, our observation that the incidence of PGC is greater in females than in males is consistent with previous studies on Nigerians in Lagos[15] and Fijians,[14] which found a slight increase in the incidence of PGC in females. In addition, the histological study by Fan[21] included African populations and found a higher incidence of PGC in females. However, our findings differ from those of some other population-based studies that used more recent radiological techniques and showed a higher incidence of PGC in males among primarily white populations.[24,11,16]

The incidence of PGC that has been reported in the literature is population specific. The incidence of PGC was found to be lower in Asian and African populations than in Western populations.[21] Our study demonstrates a relationship between age and PGC in a population that lives in Saudi Arabia. The incidence of PGC within this population increases with age and is more common among females.

Moreover, environmental conditions such as altitude and the intensity of exposure to sunlight might be contributing factors to the development of PGC. Recently, a study conducted in different cities in Turkey based on altitude found that high altitudes >800 m were associated with a decreased risk of PGC.[11] Our study, which was conducted in the central region of Riyadh, Saudi Arabia (low altitude = 620 m), suggests that the high PGC incidence (64.8%) may be associated with this low altitude.

Our study results may be reflective of the influences of ethnicity- and gender-associated stress levels, as higher stress levels are associated with increased PGC. A study based on self-reported data showed that the ratio of stress in Saudi females was

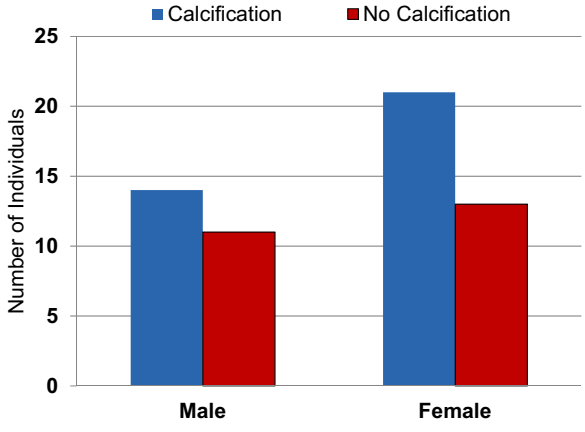

Fig. 2. Distribution of the individuals (n = 54, male = 25, females = 29) according to the presence of pineal gland calcification (PGC). A significant correlation was observed between the presence of PGC and gender (p = 0.05).

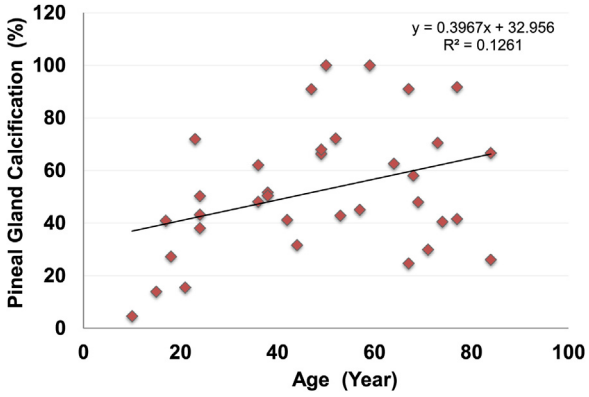

Fig. 3. Correlation between the percentage of pineal gland calcification (PGC) and the age of the individuals (n = 35 age range = 10–84 years); r = 0.36; p = 0.04.

Table 2
The distribution of individuals (n = 54) according to the degree of pineal calcification (DOC) and gender.

Gender	DOC									Total
	0	1	2	3	4	5	6	7	8	
Female	8 (14.8)	0	1 (1.9)	4 (7.4)	5(9.3)	3 (5.6)	6(11.1)	2 (3.7)	0	29
Male	11(20.4)	0	1 (1.9)	3 (5.6)	7(13.0)	2 (3.7)	0	1 (1.9)	0	25

Values in the parentheses indicate the percentage of individuals.

higher than in males and that the rate was higher than that found in the West.[25] Vogel and Jensh[26] suggested that stress increases melatonin synthesis via norepinephrine. Consequently, the production of free radicals and the subsequent neurodegeneration of sympathetic neurons increases. Interruptions in pineal sympathetic innervation and rhythmic melatonin secretion associated with stress may alter different biological activities and cause conditions such as sleep disorders [27]. Mahlberg et al[4] proposed that PGC correlates with the occurrence of sleep disorders and that high DOC scores are associated with sleep disturbances at the time of stress.

Recently, there has been a growing interest in the study of the association of pineal parameters (DOC, UCPT, CPT) and the levels of melatonin in the circulation. The DOC and UCPT may reflect pineal abnormalities that influence melatonin secretion. The study by Mahlberg et al.[19] on patients with Alzheimer's disease confirmed that the DOC serves as a marker of decreased production of melatonin by the pineal gland within an individual. In contrast, the size of UCPT predicts the absolute melatonin levels in the circulation.

Nevertheless, the CPT and the total size of the pineal gland do not provide significant information regarding melatonin secretion.[4,20] The size of the pineal gland, which reaches a mature size at an early age, varies among individuals.[4] Our study supports this as we found no significant association between the size of the pineal gland and age.

The DOC and UCPT are known to be related to age.[19] However, in the present study, no significant correlations were found between age and the DOC and UCPT. This missing association may be due to the small sample size in this study. However, this finding is in agreement with results from the study by Mahlberg et al.[19]

Although the morphology of PGC has been well studied, the mechanism that underlies the development of pineal calcification and the biogenesis of this calcification remain unclear. Recently, the study by Mahlberg et al.[19] found that high DOC scores were associated with Alzheimer's dementia. The DOC concept may lead to an applicable tool that may be used to estimate the capability of the pineal gland to produce melatonin without the need for elaborate or time-consuming diagnostics.

This study has several limitations. Because the hospital was able to provide only 54 CT scans, this review consisted of a small sample size. However, the results echo previous findings regarding age and PGC, but the small sample size may have affected the findings related to the DOC and UCPT. Moreover, because this was a retrospective study, we were unable to include additional and potentially relevant factors such as smoking history, body mass index, and sleep disturbances in this analysis. Future analyses should build on this study by evaluating scans obtained throughout a longer time period and from additional test centers. A more sophisticated study design should be used and should include the level of melatonin secretion and risk factors related to melatonin secretion and PGC.

5. Conclusions

The present study provides new information on a population of an Arabian Gulf country. Study results are limited to these populations, yet they show the prevalence of PGC within a homogeneous population that lives in Saudi Arabia. Our data confirm the findings of previous studies that found that PGC increases with age. Unlike previous studies, we found that the incidence of PGC is greater among females than males. These results suggest the need for further study of PGC in Arabian Gulf populations.

Conflict of interest

We have no conflict of interest to declare.

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