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Original Research

Clinical Characteristics of Patients with Pituitary Adenoma: A Single-Center, Cross-Sectional Study from Surabaya, Indonesia (2016-2020)

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Abstract

Pituitary adenoma (PA) is a benign tumor, accounting for the majority of pituitary tumors. While extensive epidemiological data on PA exists globally, such data is limited in Indonesia. Epidemiological insights are crucial as disease patterns, including PA, can be ethnicity-dependent, and the incidence may differ across countries. This study aimed to address this gap by conducting a cross-sectional study at a primary hospital in Surabaya, Indonesia, involving PA participants diagnosed between 2016 and 2020. The collected data included factors associated with PA and its clinical characteristics. A total of 36 participants with PA were included in the study. The highest incidence of PA was observed in the 50-59 age group (30.55%), with a higher prevalence in males (52.78%). Obesity was common, affecting 69.44% of participants, and 72.22% had macroadenomas. Non-functional PAs were observed in 52.78% of participants, with visual impairment being the most common clinical symptom (61.11%). The prevalence of PA was observed among both premenopausal and postmenopausal women. Interestingly, 58.33% of participants were non-smokers. Further studies with larger sample

sizes and multicentre participation are needed to understand the epidemiology of PA in Indonesia better.

Keywords
Clinical; epidemiology; pituitary adenoma

1. Introduction

Pituitary adenoma (PA) is a benign tumor with slow progression, and the majority of pituitary tumors are PA, accounting for 94.0% of cases. PA is classified into three categories based on tumor size: microadenomas (<10 mm), macroadenomas (10-40 mm), and giant adenomas (>40 mm). In the United States (US), macroadenomas are the most common type of PA, according to the National Cancer Database [1]. Surgery is generally indicated for pituitary adenomas measuring ≥10 mm in diameter, tumors with extrasellar extension or significant mass effect causing compression of surrounding structures, persistent tumor growth despite medical therapy, persistently elevated hormone levels despite pharmacological treatment, or symptomatic lesions, particularly when visual function is compromised or at risk [2].

The epidemiology and clinical characteristics of PA are well documented in the US. The incidence of PA was 2.8 per 100,000 population between 1998 and 2016, with an increasing trend over the study period. The incidence did not differ significantly between sexes but was higher among individuals aged 65-84 years. PA was more prevalent in urban areas than in rural or suburban areas and was also more common among Black and Asian populations [3]. However, comparable epidemiological data from Indonesia remain scarce. To the best of our knowledge, no published studies have described the epidemiology of PA in Indonesia, particularly in Surabaya.

Epidemiological data are essential for developing prevention strategies because they help identify disease risk factors and populations at increased risk based on ethnicity, age, and other demographic characteristics. Such data also contribute to understanding disease etiology by evaluating potential causal factors and support the design of effective preventive interventions. Furthermore, epidemiological studies describe disease distribution across populations, providing evidence for appropriate resource allocation and targeted public health measures. These findings also inform evidence-based health policies aimed at improving healthcare outcomes and optimizing resource utilization [4, 5]. Such information is particularly important for PA because its epidemiology varies among different racial and ethnic groups, with Asians reported to have the second highest susceptibility. Despite this, epidemiological data on PA in Indonesia remain scarce. To the best of our knowledge, this is the first study to describe the clinical and demographic characteristics of patients with PA in Surabaya, Indonesia, thereby providing baseline data for future epidemiological and clinical research.

2. Materials and Method

2.1 Sample Source

Clinical data from participants diagnosed with PA between 2016 and 2020 at Premier Surabaya Hospital were collected between March 16 and May 31, 2022, according to the predefined inclusion and exclusion criteria. Participants were eligible if they had a confirmed diagnosis of PA and received either inpatient or outpatient care at Premier Surabaya Hospital during the study period. Participants with incomplete or unreadable medical records were excluded. Ethical approval for this study was obtained from the Ethics Committee of the University of Surabaya (No. 12.A/KE/I/2022).

2.2 Data Collection

The collected data were anonymized prior to analysis to ensure patient privacy and confidentiality, and were classified into two main categories: factors associated with PA occurrence and PA clinical characteristics. These factors included gender, age, smoking habits, history of hormonal contraceptive use, menopausal status, body mass index (BMI), and obesity status, which were considered due to their potential relevance to PA development. The characteristics of the adenoma were categorized into PA case status, clinical symptoms, tumor size and classification, functional adenoma type based on hormones and endocrine classification, and medical management of participants with PA.

2.3 Statistical Analysis

Data were analysed using SPSS software version 24. Categorical variables are presented as frequencies and percentages. Comparisons between groups (e.g., gender vs. obesity, gender vs. smoking history) were performed using the Chi-square test or Fisher's exact test (when expected counts were <5). Continuous variables (age, BMI, maximum tumor diameter) are presented as mean ± standard deviation or median (interquartile range). Group comparisons for continuous variables (e.g., tumor size between genders) were performed using the independent-samples t-test or the Mann-Whitney U test (based on data normality). Correlations between continuous variables (e.g., age and tumor size) were assessed using Pearson or Spearman correlation analysis. All tests were two-sided, and P-values < 0.05 were considered statistically significant.

2.4 Ethics Approval and Consent to Participate

Ethical approval was obtained from the University of Surabaya (12.A/KE/I/2022), and all participants provided informed consent to be included in this study.

3. Results

3.1 Sample Distribution

The characteristics of the 36 participants diagnosed with PA, including age, sex, and BMI, are presented in Table 1 and Table S1. Among the participants, the largest proportion was aged 50-59 years (30.5%), followed by those aged 30-39 years (22.2%) and 40-49 years (19.4%). The least represented age groups were 10-19 years and 70-79 years, each accounting for 2.8% of the sample.

Regarding sex, males comprised a slightly higher proportion of participants (52.8%) than females (47.2%).

Table 1 Demographic Profile.

Variable	Amount (percentage)
Age (years)	
10-19	1 (2.78%)
20-29	2 (5.56%)
30-39	8 (22.22%)
40-49	7 (19.44%)
50-59	11 (30.55%)
60-69	6 (16.67%)
70-79	1 (2.78%)
Total	**36 (100%)**
Gender	
Male	17 (47.22%)
Female	19 (52.78%)
Total	**36 (100%)**
BMI	
Normal	7 (19.44%)
Overweight	4 (11.11%)
Obesity	25 (69.44%)
Total	**36 (100%)**

Based on the Asia-Pacific BMI classification, most participants with PA were classified as obese (69.4%), followed by those with a normal BMI (19.4%) and those who were overweight (11.1%). Participants ranged in age from 16 to 78 years, with a mean age of 48.28 ± 13.88 years and a median age of 50 years. The 95% confidence interval for the mean age was 43.51-53.04 years. BMI ranged from 18.73 to 42.97 kg/m^2, with a mean BMI of 27.18 ± 4.75 kg/m^2 and a median BMI of 26.62 kg/m^2.

3.2 Disease Characteristics

Regarding tumor size, the most common group was 30-39 millimeters, found in 13 participant (36.1%), followed by 10-19 millimeters (19.4%), 20-29 millimeters (16.6%), 40-49 millimeters (13.8%), 0-9 millimeters (11.1%), and the smallest group was 50-59 millimeters (2.78%). Based on these measurements, tumors were classified as microadenomas (11.1%), giant adenomas (16.6%), and for the majority of participants, macroadenomas (72.2%) (Table 2).

Table 2 Disease Characteristics.

Variable	Amount (percentage)
Pituitary Adenoma Size	
Microadenoma	4 (11.11%)
Macroadenoma	26 (72.22%)
Giant adenoma	6 (16.67%)
Total	**36 (100%)**
Endocrine Classification	
Functional	17 (47.22%)
Non-Functional	19 (52.78%)
Total	**36 (100%)**
Based on Secreted Hormones	
Prolactin	10 (58.82%)
GH	3 (17.65%)
ACTH	3 (17.65%)
TSH	1 (5.88%)
Total	**17 (100%)**
Clinical Symptoms	
Visual impairment	22 (61.11%)
Cephalgia	11 (30.56%)
Symptoms due to secreted hormones	6 (16.67%)
Impaired sense of smell	4 (11.11%)
Vertigo	2 (5.56%)
Seizures	1 (2.78%)
Asymptomatic	5 (13.89%)
Management	
EETH	29 (80.56%)
Conservative	7 (19.44%)
Total	**36 (100%)**

In the endocrine classification of the adenomas, the majority of participants had non-functional PA (52.7%), while 47.2% had functional PA. Among those with functional adenomas, prolactin was the most commonly secreted hormone, found in 58.8% of cases. Growth hormone (GH) and adrenocorticotropic hormone (ACTH) were secreted in 17.6% of cases each, while thyroid-stimulating hormone (TSH) was the least frequently secreted, observed in 5.8% of cases (Table 2).

Among the seven clinical symptom categories, visual impairment was the most common presentation, affecting 22 participants (61.1%), followed by cephalgia (30.5%), hormone-related symptoms (16.6%), asymptomatic presentation (13.8%), and impaired sense of smell (11.1%) (Table 3). Vertigo and seizures were the least common symptoms, reported in 2 (5.5%) and 1 participant (2.7%), respectively. Regarding treatment, most participants (80.5%) underwent endoscopic endonasal trans-sphenoid surgery (EETS), whereas the remaining 19.4% received conservative management (Table 2).

Table 3 Clinical Symptoms of Participants with Pituitary Adenoma (PA).

Clinical Symptoms	Amount (percentage)
Tension type headache	4 (11.1%)
Vision loss	3 (8.3%)
Migraine	1 (2.8%)
Bilateral hemianopsia	11 (30.6%)
Cephalgia	7 (19.4%)
Visus reduction	6 (16.7%)
Palpitations (clinical sign of hyperthyroidism)	1 (2.8%)
Menstrual disorders	2 (5.6%)
Infertility	3 (8.3%)
Nasal obstruction	2 (5.6%)
Acromegaly	1 (2.8%)
Diplopia	3 (8.3%)
Epistaxis	1 (2.8%)
Cold intolerance	1 (2.8%)
Asymptomatic	5 (13.9%)
Vertigo	2 (5.6%)
Seizures	1 (2.8%)

3.3 Analysis of Lifestyle Factors and Their Association with Pituitary Adenoma and Tumor Characteristics

Regarding lifestyle factors, 15 participants (41.7%) were smokers, whereas 21 participants (58.3%) were non-smokers. Obesity was present in 25 participants (69.4%), while 11 participants (30.6%) were non-obese. Among the female participants, 10 (58.8%) reported a history of hormonal contraceptive use, whereas 7 (41.2%) did not. Menopausal status was also evaluated as a potential factor associated with PA. Among the female participants, 9 (52.9%) were premenopausal, while 8 (47.1%) were postmenopausal (Table 4).

Table 4 Lifestyle Factors of the Study Participants.

Variable	Amount (percentage)
Smoking History	
Yes	15 (41.67%)
No	21 (58.33%)
Total	**36 (100%)**
Obesity	
Yes	25 (69.44%)
No	11 (30.56%)
Total	**36 (100%)**
History of Hormonal Contraceptive Use (Female only)	
Yes	10 (58.82%)
No	7 (41.18%)

Total	**17 (100%)**
Menopause (Female only)	
Yes	8 (47.06%)
No	9 (52.94%)
Total	**17 (100%)**

No significant differences were observed between age and gender, tumor size and gender, obesity status and gender, or tumor size and obesity status in PA cases (Figures 1a, 1b, 1c, 1d; Table S2, Table S3).

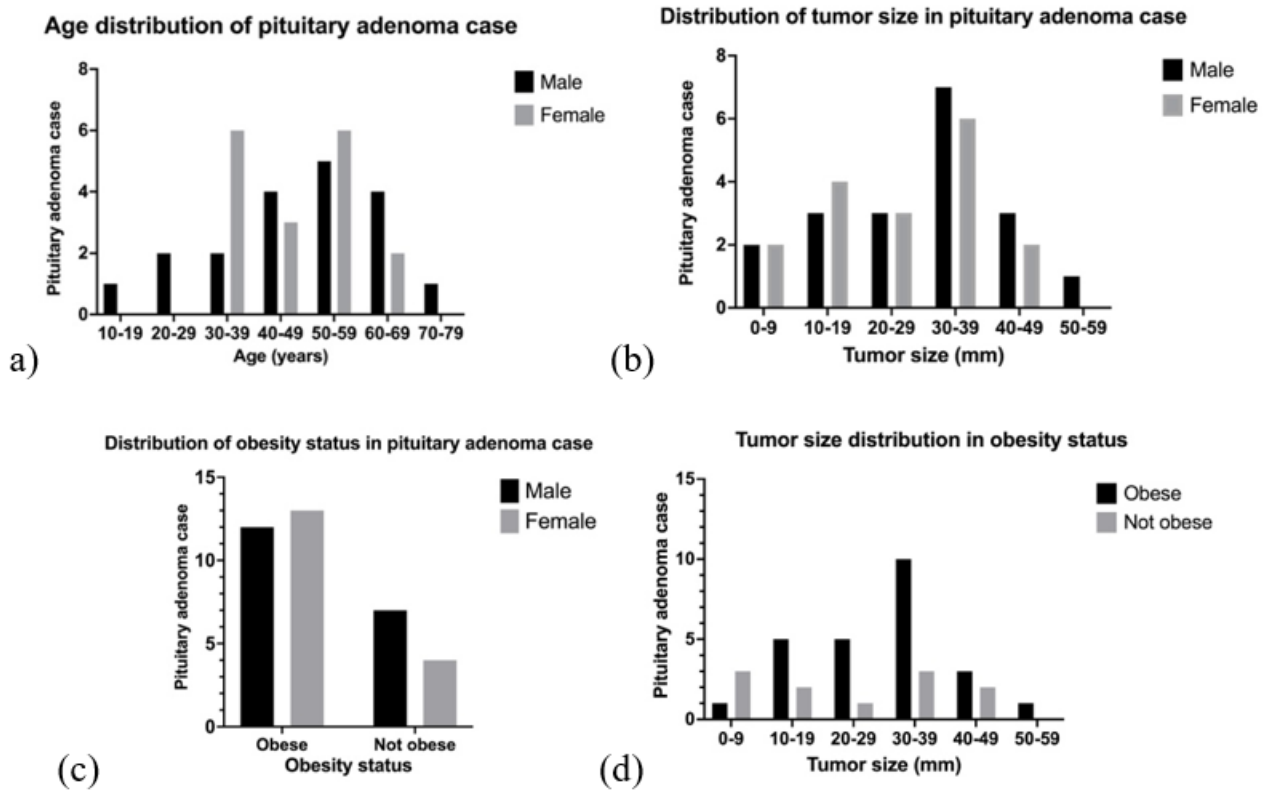

Figure 1 The distribution characteristics of pituitary adenoma cases: (a) age and gender, (b) tumor size and gender, (c) obesity status and gender, (d) tumor size and obesity status.

In terms of tumor size, males had a mean of 28.84 mm, while females had a mean of 24.76 mm (Table S4). For obesity status, the mean tumor size in obese participants was 28.4 mm, compared to 23.55 mm in non-obese participants (Table S5). However, no significant correlations were found between age and tumor size ($p = 0.697$), or between BMI and tumor size ($p = 0.408$) (Figures 1a, 1b; Table S6, Table S7).

4. Discussion

Our study presents epidemiological data on PA in Surabaya. This study included 36 patients diagnosed with PA, with a mean age of 48.28 ± 13.88 years and a slight predominance of female participants. Most patients were middle-aged, particularly those aged 50-59. The majority of participants were classified as obese according to Asia Pacific BMI criteria. Macroadenomas were

the most common tumor type, and non-functional adenomas slightly outnumbered functional adenomas. Among functional adenomas, prolactin-secreting tumors were the most prevalent. Visual impairment was the most frequently reported clinical symptom, and most patients were managed surgically using the EETS approach. Lifestyle factors including smoking, obesity, hormonal contraceptive use, and menopausal status were evaluated. However, no significant associations were identified between demographic characteristics, tumor features, or obesity status.

Due to the uncontrolled, cross-sectional design of this study, the observed proportions of characteristics such as smoking status, contraceptive use, and menopausal status merely describe the distribution within the study cohort. These findings cannot be compared with those of the general population nor used to infer causal relationships with PA. This represents a major methodological limitation of the study.

The age distribution of PA may vary across different populations, potentially reflecting differences in racial or ethnic background. In the United States, the highest incidence of PA has been reported among individuals aged 65-84 years [3], whereas our study, which was conducted in an Asian population, found the highest proportion of patients in the 50-59-year age group. However, given the relatively small sample size of our study, this finding should be interpreted with caution. Larger multicenter studies involving diverse Asian populations are needed to determine whether this age distribution is representative of the broader population.

Regarding weight status, higher BMI in the U.S. is associated with increased PA incidence, with cumulative incidences ranging from 1.33 to 2.28 [6]. Our findings are consistent with this, showing a higher incidence of PA in obese individuals, although the difference was not statistically significant. This contrasts with the commonly held view that obesity in functional PA results from hormonal aberrations [7]. Furthermore, our analysis did not reveal a significant correlation between BMI and tumor size. Similarly, our study found no correlation between age and tumor size. However, a study conducted in Canada reported a positive correlation between these variables [8].

In functional PA, our data revealed a higher prevalence of prolactinomas (58.8%), comparable to findings in Iceland, where prolactinoma is the predominant type [9]. The high prevalence of obesity observed in our cohort may be partially explained by the predominance of prolactinomas, the most common functional pituitary adenomas characterized by elevated circulating prolactin levels [10]. Larger prolactinomas are generally associated with greater prolactin secretion, potentially exacerbating their metabolic effects. Mechanistically, hyperprolactinemia disrupts metabolic homeostasis by affecting both the liver and adipose tissue. In the liver, it upregulates prolactin receptor expression, promotes hepatic steatosis, enhances the activity of the lipogenic transcription factor carbohydrate-responsive element-binding protein (ChREBP), and alters the sterol regulatory element-binding protein-1c (SREBP-1c) response to refeeding. In adipose tissue, hyperprolactinemia promotes adiposity while reducing the expression of these lipogenic transcription factors. Collectively, these alterations impair glucose metabolism, leading to glucose intolerance, hyperinsulinemia, insulin resistance, and ultimately obesity [11]. These findings underscore the importance of routine metabolic assessment and comprehensive metabolic management in patients with pituitary adenomas, particularly those with prolactinomas.

In terms of tumor size, our results align with U.S. data, which indicate that macroadenomas are the most common type of PA [1]. Tumors larger than 2.2 cm are often associated with visual impairment [12]. Although headache was not previously correlated with tumor size two decades ago [13], two studies have since reported a link between headaches and macroadenomas [12, 14].

Concerning clinical symptoms, our study found that visual impairment was the most frequently reported complaint, followed by headaches. This aligns with previous data showing that headaches were reported in 48.5%-87.2% of cases [15, 16] and that visual impairment was observed in 52.9%-74.0% of cases [17, 18].

Smoking is generally recognized as a lifestyle factor associated with malignancy. However, in our study, only a small proportion of participants reported a history of smoking. This finding is consistent with previous studies that have shown no significant association between smoking and PA. Interestingly, smoking has even been reported as a potential protective factor in some studies [19]. Regarding contraceptive use, our data show a higher prevalence of contraceptive use among women with PA. This finding contrasts with previous reports from the United States, which found no association between contraceptive use and PA and reported that non-use of contraceptives was linked to an increased risk of PA [20]. This discrepancy may be due to the small sample size in our study.

In terms of menopausal status, previous studies have reported an increased risk of PA among menopausal women [21]. However, in our study, a higher proportion of participants with PA were non menopausal. This discrepancy may be attributed to ethnic differences, although further investigation is required. These studies would provide a more comprehensive understanding of the epidemiology of PA, which is essential for improving prevention, diagnosis, and management of PA-associated health conditions.

Our study has several limitations. First, selection bias may be present due to the single-center retrospective design, which may primarily represent patients with more severe disease who attend this hospital. Second, the small sample size and the absence of a control group limit the generalizability of the findings. Third, note that recall bias (e.g., for hormonal contraceptive use) and incomplete data may affect results. A prospective design would strengthen findings. Finally, the lack of molecular or genetic data prevented further exploration of underlying mechanisms.

5. Conclusion

Our study provides an overview of the epidemiology of PA in Indonesia, particularly in Surabaya. Although no statistically significant associations were identified, likely due to the relatively small sample size, our findings provide important baseline epidemiological data for this population. We hope these findings will encourage future multicenter prospective studies with larger sample sizes, standardized data collection, appropriate comparison groups, and molecular investigations to further characterize the epidemiology and risk factors of PA and to improve our understanding of its underlying biological mechanisms in the Indonesian population.

Author Contributions

Tasya Fabiola Alim, Valentinus Besin, and Mariana Wahjudi: conceptualized the idea for the article, conducted the literature search, and performed the data analysis. Tasya Fabiola Alim: drafted the manuscript. Valentinus Besin and Mariana Wahjudi: critically revised the work and performed the editing. Tasya Fabiola Alim: Give the final approval of the version to be published. All authors have read and approved the published version of the manuscript.

Competing Interests

The authors have declared that no competing interests exist.

Data Availability Statement

Data attached to the supplementary materials and data the authors generated as part of their study.

AI-Assisted Technologies Statement

I would like to confirm that AI was used solely for basic grammar correction and language refinement in the manuscript. No AI tools were involved in generating scientific content, data interpretation, analysis, or conclusions.

Additional Materials

The following additional materials are uploaded at the page of this paper.

1. Table S1: Characteristics of participants in pituitary adenoma cases.
2. Table S2: Distribution of Risk Factors by Gender.
3. Table S3: Distribution of Tumor Size by Obesity Status.
4. Table S4: Risk Factor Association Based on Gender.
5. Table S5: Association Between Tumor Size and Obesity Status.
6. Table S6: Correlation of Age and Tumor Size.
7. Table S7: Correlation of BMI and Tumor Size.

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