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Visual Acuity, Perimetric and Optic Disc Findings at Presentation in Pituitary Macroadenoma: A Retrospective Indonesian Series

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ABSTRACT

Background: Pituitary macroadenoma compresses the optic chiasm, and the resulting visual loss becomes irreversible once retinal ganglion cells die. No Indonesian series describes their visual status at first specialist contact.

Methods: Retrospective review of consecutive pituitary macroadenoma patients at a West Sumatran referral hospital, July 2022 to October 2025, reported per STROBE. Proportions carry 95% Wilson intervals, tested against published benchmarks with Holm adjustment. Because the records give marginal rather than patient-level data, unidentified associations were bounded by enumerating every contingency table consistent with the observed margins.

Results: Seventeen of 18 patients were eligible (34 eyes); 11 (64.7%) were female and 11 (64.7%) aged 21–40 years, neither differing detectably from an even split ($p = 0.332$). Under every admissible eye pairing at least 13 of 17 (76.5%) had an eye below 6/18 versus a 25% benchmark ($p < 0.001$, $h = +1.082$). All 17 had an abnormal field versus a 70% benchmark ($p = 0.003$, $h = +1.159$): bitemporal hemianopia in 10 (58.8%), generalised depression in 7 (41.2%). Optic atrophy affected 9 (52.9%), papilloedema none. All seven with generalised depression had optic atrophy, versus 2 of 10 with bitemporal hemianopia (risk difference +80.0 pp, 95% CI +32.9 to +94.3; $p = 0.002$). Four of 17 tests survived Holm adjustment; others were unidentified, their odds ratio bounds spanning the null.

Conclusion: This cohort presented with markedly advanced visual compromise, optic atrophy being established in over half, without detectable demographic difference from international series. Unexplained visual complaints warrant early perimetry and fundoscopy.

1. Introduction

Pituitary adenoma is among the most common intracranial neoplasms, and its recorded incidence has risen steadily over recent decades. A 30-year population-based analysis places the incidence at approximately 4 per 100,000 person-years, with the increase attributable largely to incidental detection through expanded neuroimaging rather than to any change in tumour biology.¹ Nationwide Korean data confirm a comparable burden in an Asian population and add excess cardiovascular mortality to the long-term cost of the disease.² Population series spanning more than four decades show the age distribution extending well into adolescence and young adulthood,³ and registry analyses consistently recover a female excess among detected cases.⁴ For a neuro-ophthalmology service, however, the relevant denominator is not adenoma incidence but the incidence of the visual syndrome the tumour produces. Compressive optic neuropathy occurs at roughly 1 per 100,000 person-years, and its visual outcome depends heavily on the condition of the anterior visual pathway at the moment of diagnosis rather than on the tumour's dimensions alone.⁵

The clinical route into care is determined largely by whether the tumour secretes. Non-functioning macroadenomas grow silently and declare themselves only through mass effect, and contemporary natural-history data show that their presentation is markedly gender-specific: women are more often detected earlier through endocrine symptoms, while men more often reach care later, through visual failure.⁶ Analyses of presentation across pituitary neuroendocrine tumour subtypes confirm this divergence,⁷ and pituitary function is frequently already impaired by the time a non-functional macroadenoma is first identified.⁸ Distinguishing prolactinoma from non-functioning adenoma at presentation remains consequential because the two carry entirely different first-line treatments, and practical discriminators have been derived for exactly this purpose.⁹ Prolactin-secreting tumours constitute the largest share of functioning adenomas, and their symptoms differ sharply by sex: hyperprolactinaemia produces early and unmistakable manifestations in premenopausal women but vague, easily dismissed complaints in men.¹⁰ The consequence is documented directly in male macroprolactinoma series, where tumours are larger at diagnosis and hypogonadism more often irreversible.¹¹

Pituitary apoplexy represents the acute alternative pathway, presenting abruptly with visual loss and ophthalmoplegia rather than insidiously.¹²

What the ophthalmologist actually measures — acuity, visual field and the optic disc — sits at a specific and rather late point on this trajectory. Tumour morphology independently influences visual field outcome after surgery,¹³ and acuity at presentation remains the dominant prognostic variable in non-functioning adenoma.¹⁴ The most consequential methodological insight of the past five years, however, is that acuity and perimetry are late markers of chiasmal compression. In 184 patients with non-functioning pituitary neuroendocrine tumours, critical flicker fusion laterality detected compressive optic neuropathy in tumours too small to have produced either acuity loss or a field defect.¹⁵ Structural retinal imaging has since become the principal prognostic tool. Magnetic resonance parameters outperform optical coherence tomography for predicting field recovery in some series,¹⁶ but preoperative macular ganglion cell-inner plexiform layer thickness predicts complete postoperative field recovery with an area under the curve of 0.725 (95% CI 0.655–0.795) at a 77.25 μm cut-off,¹⁷ and optical coherence tomography predicts visual outcome as far out as five years.¹⁸ Two meta-analyses and a systematic review now support its role in sellar and para-chiasmal disease,^{19–21} and it is increasingly recommended as a routine part of the preoperative workup.²² The clinical meaning is unambiguous: a pale disc and a depressed field are not merely descriptive findings but markers of ganglion cell loss that has already occurred and will not reverse.

Decompression recovers a great deal of vision when it is performed in time. A recent single-arm meta-analysis and the earlier landmark systematic review both place postoperative visual improvement in the region of four-fifths of operated patients.^{23,24} What separates those who recover from those who do not is consistently the preoperative state of the anterior visual pathway rather than tumour size alone.²⁵ Prognostic modelling has advanced rapidly, from delta-radiomics of the optic chiasm²⁶ through the simple and highly transferable measure of preoperative chiasm volume²⁷ to validated multivariable prediction models²⁸ and machine-learning radiomics,²⁹ and a five-year retrospective cohort confirms the same hierarchy of predictors.³⁰ The therapeutic message is therefore a temporal one: the window in which surgery restores vision closes as retinal ganglion cells die, and no refinement of operative technique recovers what has already been lost.

Against this background, Indonesia published its first national consensus for pituitary adenoma diagnosis in 2025.³¹ That document defines the intended diagnostic pathway, but it is not accompanied by published data describing how patients actually reach it. International benchmarks exist for the endocrine management surrounding surgery,³² and cohort data define the

course of macroadenomas managed conservatively,³³ yet the descriptive layer beneath all of this is missing across much of Southeast Asia: the state of the visual system at the moment patients first present. Without it, there is no way to know whether a national diagnostic pathway is being reached early enough to preserve sight. This study therefore characterised best-corrected visual acuity, perimetric pattern and optic disc status at the time of diagnosis in patients with pituitary macroadenoma attending a provincial referral centre in West Sumatra. One constraint is stated at the outset: the records contain no interval between first visual symptom and presentation, so any conclusion about lateness here is inferred from severity rather than measured. A secondary aim was methodological: to apply partial identification — enumerating every dataset consistent with the observed marginal distributions — in order to establish which associations a record-based series of this kind can legitimately support, and to report explicitly and quantitatively which it cannot.

2. Methods

Study design

This was a retrospective, single-centre, record-based observational study with a cross-sectional analysis of findings recorded at the time of diagnosis. It is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.³⁴ No intervention was administered and no patient was contacted; the study examined data generated in the course of routine clinical care.

Ethical approval

This study received ethical approval from the CMHC Research Center Ethics Committee, Indonesia (Approval No. 2025/0142). The study was a retrospective analysis of anonymised hospital medical records; no patient was contacted, no intervention was administered, and no identifiable patient information is reported. Individual informed consent was waived in accordance with institutional policy governing retrospective record-based research. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Setting and participants

The study was conducted in the neuro-ophthalmology outpatient clinic of Dr. M. Djamil General Hospital, Padang, West Sumatra, Indonesia, the tertiary referral centre for the province. The sampling frame comprised all patients recorded with a diagnosis of pituitary macroadenoma who attended that clinic between July 2022 and October 2025. Total sampling was used: every patient in the frame who met the eligibility criteria was included, and no sampling procedure was applied.

Patients were eligible if the diagnosis of pituitary macroadenoma had been established by a consultant

neuro-ophthalmologist on the combined basis of history, ophthalmological examination and neuroimaging by contrast brain computed tomography, magnetic resonance imaging, or both, and if the record contained age, sex, presenting complaint, complete ophthalmological status, fundus examination and perimetry. Patients were excluded if they had a coexisting optic nerve disorder capable of independently producing a field defect, specifically glaucoma or non-arteritic anterior ischaemic optic neuropathy; if media opacity prevented assessment of the posterior segment or the performance of perimetry; or if they had retinal disease capable of independently reducing acuity or producing a field

defect. Because a recorded perimetry result was an eligibility requirement, the cohort is conditioned on perimetry having been clinically indicated and performed; patients in whom no field test was ordered could not enter the study, and these are likely to have had milder disease. This conditioning bears on the interpretation of the field findings and is revisited in the Results and Discussion.

Eighteen patients were identified in the sampling frame and 17 met the eligibility criteria, yielding 34 eyes for analysis. The reason for the single exclusion is not recorded in the clinical records and is therefore not stated. Participant selection is detailed in Figure 1.

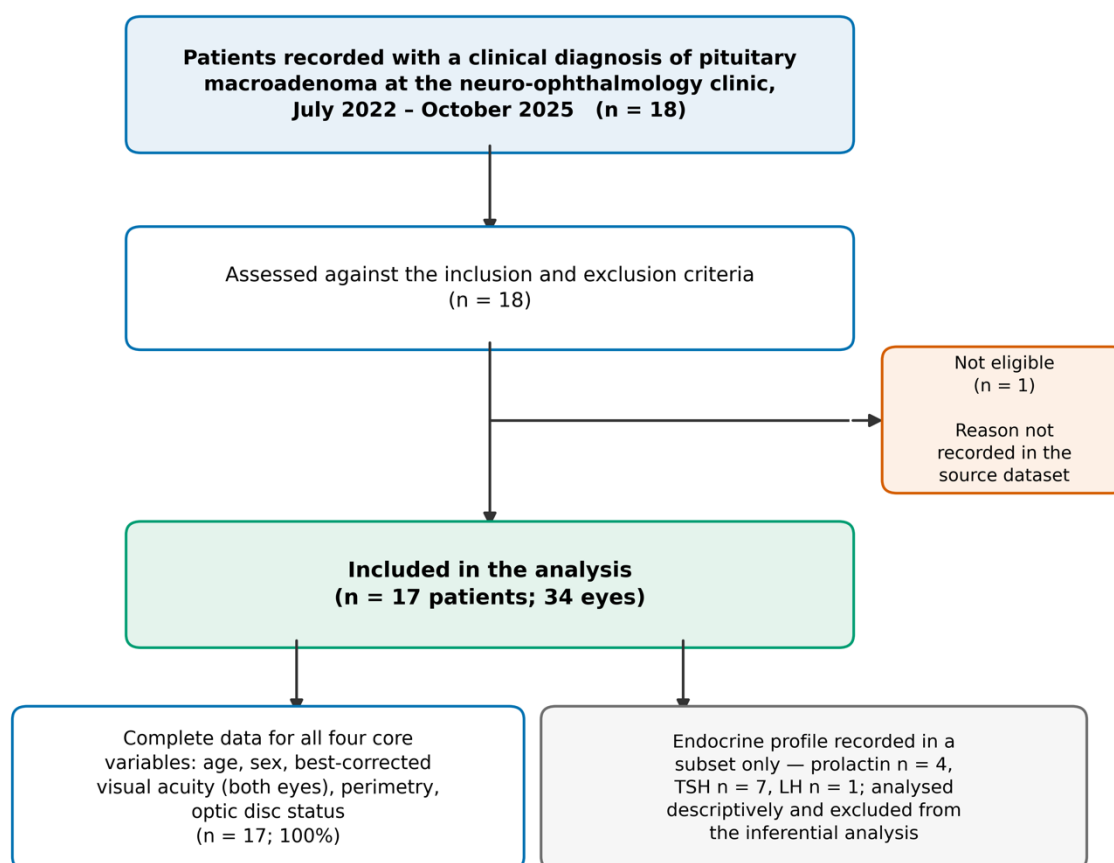


Figure 1. Participant flow. Of 18 patients recorded with a clinical diagnosis of pituitary macroadenoma at the neuro-ophthalmology clinic between July 2022 and October 2025, 17 met the eligibility criteria and were analysed (34 eyes). All 17 had complete data for age, sex, best-corrected visual acuity in both eyes, perimetry and optic disc status. Endocrine testing was recorded for a subset only and was analysed descriptively.

Sample size

No a priori sample size calculation was performed. The study enrolled the complete eligible population of the sampling frame over a 39-month period, so the achieved sample size was determined by disease frequency and referral volume rather than by design. The precision this delivers is stated explicitly rather than left implicit: at $n = 17$ the half-width of a 95% Wilson interval is approximately 21 percentage points for a proportion near 0.50, and at the eye level, with 34 eyes, approximately 15 percentage points; these are Wilson half-widths evaluated at $p = 0.50$, the worst case, at the 95% level. Achieving ± 10 -point precision on

a proportion near 0.50 would require 93 patients and ± 5 -point precision 381 patients. These figures are reported because they define what a series of this size can and cannot establish, and they frame the multicentre design proposed in the Discussion.

Measurements and definitions

All measurements were those recorded at the patient's first attendance, before any treatment. Data were abstracted from the neuro-ophthalmology sub-department records and the hospital medical record.

Pituitary macroadenoma was defined as a benign tumour arising from the pituitary gland with a

maximum diameter of at least 10 mm on computed tomography or magnetic resonance imaging.

Best-corrected visual acuity was measured bilaterally with a Snellen chart at first presentation and categorised, following the categories used in the clinical records, as 6/18 or better, 6/18 to 6/60, worse than 6/60 to 3/60, worse than 3/60 to 1/60, worse than 1/60, and no light perception. These bands correspond to the World Health Organization classification of visual impairment. Acuity is a per-eye measurement and is reported as such throughout.

Perimetry was performed using the Humphrey 24–2 threshold test in patients aged over 18 years whose acuity was at least 1/60, the minimum required for reliable performance of the test. Fields were classified by the reporting neuro-ophthalmologist as within normal limits, bitemporal hemianopia, junctional scotoma, quadrantanopic scotoma, bilateral three-quadrant involvement, or generalised depression. Reliability indices and mean deviation values were not recorded in the clinical records and could not be analysed. Fields were categorised by the reporting clinician against the instrument's own greyscale and probability plots; no numerical threshold was applied, and generalised depression denotes a global reduction in retinal sensitivity across the tested field rather than a defect respecting the vertical meridian. The classification is therefore qualitative and cannot be reproduced from the information recorded, which is treated as a limitation.

Optic disc status was determined by fundus examination and classified as normal, papilloedema, unilateral optic atrophy or bilateral optic atrophy. For analyses of atrophy as a binary variable, unilateral and bilateral atrophy were combined into a single category of any optic atrophy.

Age was recorded in years and grouped into bands of 20 years or younger, 21 to 40, 41 to 60, and 61 or older.

Sex was recorded as male or female.

Endocrine assays were performed in a subset of patients only. The clinical records state that hormone testing was performed in six patients while simultaneously reporting thyroid-stimulating hormone results in seven; these statements are mutually incompatible and the records provide no means of adjudicating between them. Per-assay counts and mean values are therefore reported descriptively, the number of individual patients tested is declared indeterminate, and the endocrine data are excluded from all inferential analysis. Functional versus non-functioning tumour status consequently could not be determined for any patient, and no patient is so classified.

Data handling

All proportions were computed from the recorded counts, using a denominator of 17 for patient-level variables and 34 for eye-level variables. Where a transcribed percentage in the records disagreed with

its own count, the count was treated as authoritative, since counts reconciled exactly with the eligible sample in every instance. No count was altered.

Statistical analysis

Categorical variables are summarised as counts and percentages with 95% Wilson score intervals, which are used in preference to Wald intervals because the latter are unreliable at this sample size and degenerate for proportions at or near 0 and 1. Each clinically meaningful proportion was tested with a two-sided exact binomial test against a benchmark proportion drawn from the published literature rather than against an uninformative null of 0.50, and Cohen's h is reported as the effect size for every such comparison. Associations between categorical variables were assessed with Fisher's exact test, with odds ratios carrying the Haldane–Anscombe correction where a zero cell was present, and Cramér's V as the effect size.

Partial identification. The clinical records provide marginal frequency distributions rather than a patient-level dataset, and cross-classification between variables is available for only two pairs. For those two pairs the records state the joint information explicitly, which, combined with the observed margins, determines the complete contingency table; these are analysed as observed data. For every other pair the joint distribution is unobserved and the association is therefore not identified by the data. No joint distribution was reconstructed, imputed, simulated or assumed in order to produce an estimate. Instead, every non-negative integer contingency table consistent with the observed marginal totals was enumerated exhaustively, and the odds ratio, Fisher exact p-value, Cramér's V and risk difference computed for each. The reported ranges are exact attainable bounds rather than simulation estimates. Where an attainable range spans the null value, the finding reported is that the data cannot identify that association; where a range lies entirely on one side of the null, the conclusion holds for every dataset consistent with the observations and is asserted as robust.

The same procedure was applied to visual acuity, which is recorded as two separate per-eye marginal distributions with no link between a patient's two eyes. All 1,444 joint tables consistent with the two observed margins were enumerated, yielding exact attainable ranges for every patient-level acuity quantity, and an exact McNemar test of the interocular difference in impairment was computed across all admissible pairings. For the multivariable analysis of optic atrophy on sex and age band, the observed age-by-sex distribution makes the admissible space exactly the 24 ways in which nine atrophy labels can be distributed across the four observed cells; all 24 were enumerated and Firth-penalised logistic regression fitted to each, Firth's penalty being required because complete separation is guaranteed at these cell sizes and ordinary maximum likelihood does not converge. All 24

fits converged to a step norm below 1×10^{-9} (median 23 iterations, range 13–35; coefficient standard errors 1.52 to 2.26). Because Wald inference is unreliable under separation even after penalisation, significance was assessed by penalised likelihood-ratio test.

Assumption-based sensitivity analysis. As a secondary analysis, the eye-pairing bounds were recomputed under an explicit assumption of positive interocular dependence, formalised as positive quadrant dependence between the two eyes' acuity severity. This assumption is motivated by the fact that chiasmal compression is a single midline lesion acting on both optic pathways simultaneously, so that severity in the two eyes is expected to be positively rather than independently associated. Results obtained under this assumption are labelled assumption-dependent wherever they appear, and the assumption-free bounds remain the primary reporting throughout.

Benchmark proportions were taken from the studies named in the Discussion and treated as fixed constants; because each is itself a sample estimate, the comparisons understate uncertainty. The benchmark set was assembled after the data were seen, so benchmark testing is exploratory, and where a source gave a range the bound least favourable to the study hypothesis was chosen. Seventeen hypothesis tests were performed in total and the Holm–Bonferroni step-down procedure was applied across that family; adjusted and unadjusted p-values are both reported. For 2×2 tables containing a zero cell the odds ratio is not estimable, so the risk difference with a Newcombe hybrid score interval is the primary measure and exact conditional (Fisher) limits are given for the odds ratio. A misclassification sensitivity analysis was performed by regrading individual patients across the perimetry and optic disc categories and recomputing the exact test. Statistical significance was set at $\alpha = 0.05$, two-

sided, and all p-values are reported to three decimal places. Analyses were performed in Python 3.13 with SciPy 1.16 and NumPy 2.3; the interval estimators, effect sizes, enumeration routines and the Firth-penalised regression were implemented directly from their definitions. The enumeration code is available from the corresponding author so that every reported bound can be reproduced.

3. Results

Participants and demographic characteristics

Eighteen patients with a clinical diagnosis of pituitary macroadenoma attended the neuro-ophthalmology clinic between July 2022 and October 2025. Seventeen met the eligibility criteria and were analysed, contributing 34 eyes; participant selection is detailed in Figure 1. All 17 had complete data for age, sex, best-corrected visual acuity in both eyes, perimetry and optic disc status, so no analysis was affected by missing data.

The demographic characteristics of the cohort are presented in Table 1. Eleven patients (64.7%, 95% CI 41.3–82.7) were female and six (35.3%, 95% CI 17.3–58.7) were male. Eleven (64.7%, 95% CI 41.3–82.7) were aged 21 to 40 years and six (35.3%, 95% CI 17.3–58.7) were aged 41 to 60 years; no patient was aged 20 years or younger, and none was 61 or older. Neither the higher proportion of women nor the concentration in the younger age band was statistically distinguishable from an even split at this sample size, both yielding an exact binomial p of 0.332 with a Cohen's h of +0.299 — the two tests coincide because the counts are identical. Non-detection of a difference at $n = 17$ is not evidence of equivalence: the 95% interval for the female proportion runs from 41.3% to 82.7%, which remains compatible with populations differing appreciably from one another.

Table 1. Demographic characteristics of patients with pituitary macroadenoma at presentation, and the observed age-by-sex cross-classification ($n = 17$).

Characteristic	Category	n	% of 17	95% Wilson CI (%)
Age band	≤ 20 years	0	0.0	0.0 – 18.4
	21 – 40 years	11	64.7	41.3 – 82.7
	41 – 60 years	6	35.3	17.3 – 58.7
	≥ 61 years	0	0.0	0.0 – 18.4
Sex	Male	6	35.3	17.3 – 58.7
	Female	11	64.7	41.3 – 82.7
Age band × sex	21–40 years, male	1	5.9	1.0 – 27.0
	21–40 years, female	10	58.8	36.0 – 78.4
	41–60 years, male	5	29.4	13.3 – 53.1
	41–60 years, female	1	5.9	1.0 – 27.0

Exact binomial test of the female proportion against a 1:1 sex ratio: $p = 0.332$, Cohen's $h = +0.299$; no demographic comparison survives Holm adjustment. Non-detection of a difference at $n = 17$ is not evidence of equivalence. Exact binomial test of the 21–40 year proportion against an even split: $p = 0.332$, Cohen's $h = +0.299$. Neither distribution is statistically distinguishable from an even split at this sample size. The age-by-sex cross-classification is fully determined by the recorded observation that five of the six patients aged 41–60 years were male; it is observed data, not an estimate. Wilson score intervals are used throughout in preference to Wald intervals, which are unreliable at $n = 17$.

Both proportions were, however, consistent with published international series. The female proportion did not differ from the 71.9% reported by Aljabri and

colleagues or the approximately 72% reported by Al-Futaisi and colleagues (both $p = 0.589$, $h = -0.155$ and -0.157 respectively), and the proportion aged under 41

years was almost identical to the 65% reported by Aljabri and colleagues ($p = 1.000$, $h = -0.006$).

The distribution of sex across age bands was recorded explicitly and is therefore reported as observed data rather than as an estimate. Five of the six patients aged 41 to 60 years were male, whereas only one of the 11 aged 21 to 40 years was male (Table 4). The risk difference for male sex in the older band, which is

estimable without correction and is therefore the primary measure, was +74.2 percentage points (95% CI +25.3 to +89.8), with a therefore the primary measure, was +74.2 percentage points (95% CI +25.3 to +89.8). After Holm adjustment across the 17-test family this association did not retain significance (adjusted $p = 0.070$) and is reported as suggestive rather than established.

Table 4. Associations identified by the observed data ($n = 17$).

Association	Contingency table	Risk difference, pp (95% CI)	Odds ratio (exact conditional 95% CI)	Fisher exact p	Holm-adjusted p	Cramér's V
Age band 41–60 years → male sex	21–40 y: 1 male, 10 female; 41–60 y: 5 male, 1 female	+74.2 (+25.3 to +89.8)	32.31 (1.79 – 2586.5)	0.005	0.070	0.742
Generalised depression (vs bitemporal hemianopia) → any optic atrophy	Bitemporal: 2 atrophy, 8 normal; generalised depression: 7 atrophy, 0 normal	+80.0 (+32.9 to +94.3)	not estimable (2.54 – ∞)	0.002	0.034	0.789

These are the only two associations the data identify; each is fully determined by an explicitly recorded cross-classification combined with the observed margins. The risk difference is the primary measure because it is estimable without correction; intervals are Newcombe hybrid score intervals. In the second association the zero cell drives both the unadjusted and the conditional maximum likelihood odds ratio to infinity, so only the exact conditional interval is meaningful, and Cramér's V is correspondingly inflated by that zero cell. Holm-adjusted p -values are computed across the full family of 17 tests reported in this study: the perimetry-by-disc association survives adjustment, the age-by-sex association does not and is reported as suggestive rather than established. A misclassification sensitivity analysis on the perimetry-by-disc association returned Fisher exact p between 0.001 and 0.050 across seven single-patient regading scenarios, but $p = 0.058$ when two patients with generalised depression were regaded as having a normal disc: the association is robust to one misclassification and fragile to two. pp = percentage points.

Best-corrected visual acuity at presentation

Best-corrected visual acuity at presentation is detailed in Table 2, and the distribution across acuity categories is shown in Figure 2. In the right eye, seven patients (41.2%, 95% CI 21.6–64.0) had acuity of 6/18 or better, six (35.3%, 95% CI 17.3–58.7) fell in the 6/18 to 6/60 band, one (5.9%, 95% CI 1.0–27.0) in the worse than

6/60 to 3/60 band and three (17.6%, 95% CI 6.2–41.0) in the worse than 3/60 to 1/60 band. In the left eye the corresponding counts were four (23.5%, 95% CI 9.6–47.3), six (35.3%, 95% CI 17.3–58.7), one (5.9%, 95% CI 1.0–27.0) and six (35.3%, 95% CI 17.3–58.7). No eye had acuity worse than 1/60 and no eye was without light perception.

Table 2. Best-corrected visual acuity at presentation, reported separately for each eye ($n = 17$ patients; 34 eyes).

Acuity category (Snellen)	WHO-equivalent severity	Right eye (OD)		Left eye (OS)		All eyes	
		n	% (95% CI)	n	% (95% CI)	n	% of 34 (95% CI)
≥ 6/18	No or mild impairment	7	41.2 (21.6 – 64.0)	4	23.5 (9.6 – 47.3)	11	32.4 (19.1 – 49.2)
6/18 – 6/60	Moderate impairment	6	35.3 (17.3 – 58.7)	6	35.3 (17.3 – 58.7)	12	35.3 (21.5 – 52.1)
< 6/60 – 3/60	Severe impairment	1	5.9 (1.0 – 27.0)	1	5.9 (1.0 – 27.0)	2	5.9 (1.6 – 19.1)
< 3/60 – 1/60	Blindness category 3	3	17.6 (6.2 – 41.0)	6	35.3 (17.3 – 58.7)	9	26.5 (14.6 – 43.1)
< 1/60	Blindness category 4	0	0.0 (0.0 – 18.4)	0	0.0 (0.0 – 18.4)	0	0.0 (0.0 – 10.2)
No light perception	Blindness category 5	0	0.0 (0.0 – 18.4)	0	0.0 (0.0 – 18.4)	0	0.0 (0.0 – 10.2)
Any acuity below 6/18	Any visual impairment	10	58.8 (36.0 – 78.4)	13	76.5 (52.7 – 90.4)	23	67.6 (50.8 – 80.9)

Acuity is recorded per eye. The clinical records does not link a patient's right eye to their fellow left eye, so patient-level acuity statements are reported as attainable ranges in Table 5 rather than as point estimates. The eye-level rows are descriptive only and carry no inferential claim, because eyes within a patient are correlated; the primary inferential statement is made at patient level in Table 5, where at least 13 of 17 patients had an eye below 6/18 under every admissible pairing (exact $p < 0.001$ versus a 25% benchmark, Cohen's $h = +1.082$, Holm-adjusted $p < 0.001$). The apparent left-eye predominance was tested by exact McNemar across every admissible pairing of the observed eyes: p ranged from 0.250 to 0.549, so no admissible pairing yields a significant interocular difference. Severity bands follow the categories used in the clinical records, which correspond to the WHO visual-impairment classification.

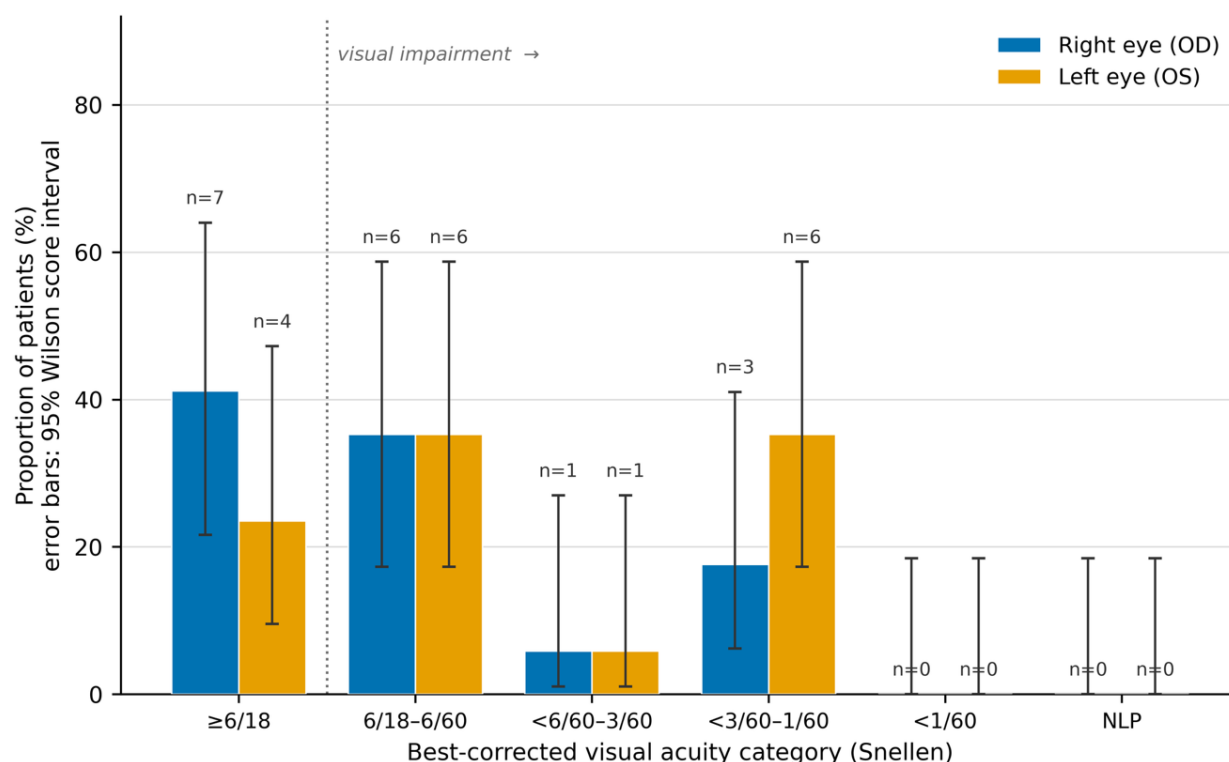


Figure 2. Distribution of best-corrected visual acuity at presentation, by eye ($n = 17$ patients; 34 eyes). Bars show the proportion of patients in each Snellen category for the right eye (OD) and left eye (OS); error bars are 95% Wilson score intervals. Acuity below 6/18 was present in 10 right eyes (58.8%) and 13 left eyes (76.5%), giving 23 of 34 eyes overall (67.6%, 95% CI 50.8–80.9). No eye had acuity below 1/60 and none was without light perception.

Acuity is recorded per eye, and eyes within a patient are correlated because chiasmal compression is a single shared lesion. The primary inferential statement is therefore made at patient level and without any assumption about that correlation: under every admissible pairing of the observed eyes, at least 13 of 17 patients (76.5%, 95% CI 52.7–90.4) had at least one eye below 6/18. Tested against a 25% benchmark this least favourable bound remains highly significant (exact binomial $p < 0.001$, Cohen's $h = +1.082$, Holm-adjusted $p < 0.001$). Descriptively, 23 of all 34 eyes (67.6%, 95% CI 50.8–80.9) were below 6/18; this eye-level figure is reported for completeness only and carries no inferential claim, since it would treat paired eyes as independent observations. The single most common category across both eyes was moderate impairment in the 6/18 to 6/60 band, accounting for 12 of 34 eyes (35.3%, 95% CI 21.5–52.1); this is a plurality rather than a majority and is reported as such.

Because acuity is recorded per eye and the records do not link a patient's right eye to their fellow left eye, the full set of patient-level acuity statements is reported as attainable ranges in Supplementary File 2. Between 13 and 17 patients (76.5% to 100.0%) had at least one eye with acuity below 6/18, between six and 10 (35.3% to 58.8%) had bilateral impairment, and between zero and four (0.0% to 23.5%) had bilaterally normal acuity. The conclusion that this cohort presented with substantial visual impairment holds under every

possible pairing of the observed eyes and does not rest on any assumption.

Left eyes appeared worse than right eyes, with 13 of 17 left eyes and 10 of 17 right eyes below 6/18. This apparent asymmetry was tested by exact McNemar across every admissible pairing of the observed data, yielding p -values ranging from 0.250 to 0.549; an exact Wilcoxon signed-rank test of the ordinal interocular severity difference reached significance in only 15 of the 1,444 admissible pairings (1.0%). No admissible pairing of these data supports an interocular difference, and none is claimed.

Perimetric findings and optic disc status

Perimetric and optic disc findings are summarised in Table 3. As shown in Figure 3, every patient in the cohort had an abnormal visual field: no patient recorded a field within normal limits, and perimetry was performed in all 17. Against a benchmark of 70% abnormal fields, this proportion of 17 of 17 (100.0%, 95% CI 81.6–100.0) was significantly higher (exact binomial $p = 0.003$, Cohen's $h = +1.159$, Holm-adjusted $p = 0.042$), the largest effect size observed in the study. This comparison carries one qualification: a recorded perimetry result was an eligibility requirement, so the cohort is conditioned on a field test having been clinically indicated, whereas the comparator series is not conditioned in the same way. Part of the difference is attributable to that conditioning, and the effect size should be read accordingly.

Table 3. Perimetric findings and optic disc status at presentation, with the observed cross-classification of the two ($n = 17$).

Assessment	Category	n	% of 17	95% Wilson CI (%)
Perimetry (Humphrey 24–2)	Within normal limits	0	0.0	0.0 – 18.4
	Bitemporal hemianopia	10	58.8	36.0 – 78.4
	Generalised depression	7	41.2	21.6 – 64.0
	Junctional scotoma	0	0.0	0.0 – 18.4
	Quadrantanopic scotoma	0	0.0	0.0 – 18.4
	Bilateral three-quadrant involvement	0	0.0	0.0 – 18.4
	Not performed	0	0.0	0.0 – 18.4
Optic disc	Normal	8	47.1	26.2 – 69.0
	Papilloedema	0	0.0	0.0 – 18.4
	Unilateral optic atrophy	4	23.5	9.6 – 47.3
	Bilateral optic atrophy	5	29.4	13.3 – 53.1
	Any optic atrophy	9	52.9	31.0 – 73.8
Perimetry × optic disc	Bitemporal hemianopia, optic atrophy	2	11.8	3.3 – 34.3
	Bitemporal hemianopia, normal disc	8	47.1	26.2 – 69.0
	Generalised depression, optic atrophy	7	41.2	21.6 – 64.0
	Generalised depression, normal disc	0	0.0	0.0 – 18.4

Every patient had an abnormal visual field. Exact binomial test against a 70% benchmark for abnormal fields in pituitary adenoma: $p = 0.003$, Cohen's $h = +1.159$, Holm-adjusted $p = 0.042$. A recorded perimetry result was an eligibility requirement, so this cohort is conditioned on a field test having been clinically indicated whereas the comparator series is not; part of the difference is attributable to that conditioning. Exact binomial test of any optic atrophy against a 30% benchmark: $p = 0.060$, Cohen's $h = +0.470$; against a 47% benchmark: $p = 0.637$, Cohen's $h = +0.119$. The perimetry-by-disc cross-classification is fully determined by the recorded observation that every patient with generalised depression had optic atrophy; it is observed data, not an estimate.

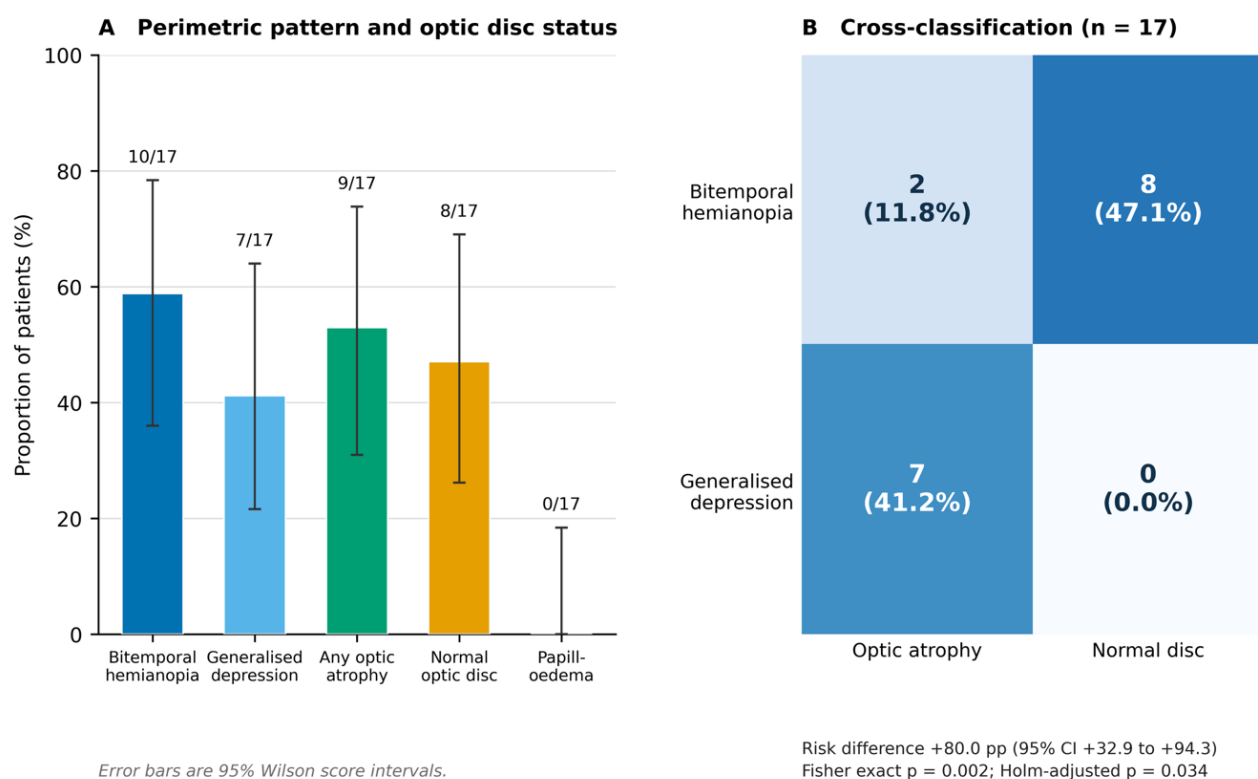


Figure 3. Perimetric pattern and optic disc status at presentation ($n = 17$). **(A)** Proportion of patients in each category, with 95% Wilson score intervals. Every patient had an abnormal visual field and none had papilloedema; the cohort is conditioned on perimetry having been performed, which was an eligibility requirement. **(B)** Cross-classification of perimetric pattern against optic disc status. All seven patients with generalised depression had optic atrophy, whereas eight of the ten with bitemporal hemianopia had a normal disc (risk difference +80.0 percentage points, 95% CI +32.9 to +94.3; Fisher exact $p = 0.002$, Holm-adjusted $p = 0.034$). The odds ratio is not estimable because of the zero cell.

Bitemporal hemianopia was the most frequent pattern, recorded in 10 patients (58.8%, 95% CI 36.0–78.4), followed by generalised depression in seven (41.2%, 95% CI 21.6–64.0). No patient had a junctional scotoma, a quadrantanopic scotoma or bilateral three-quadrant involvement. The proportion with bitemporal hemianopia did not differ from a 70% benchmark for the dominance of this pattern in chiasmal disease ($p = 0.302$, $h = -0.234$).

On fundus examination, eight patients (47.1%, 95% CI 26.2–69.0) had a normal optic disc, four (23.5%, 95% CI 9.6–47.3) had unilateral optic atrophy and five (29.4%, 95% CI 13.3–53.1) had bilateral optic atrophy, giving nine patients (52.9%, 95% CI 31.0–73.8) with any optic atrophy. No patient had papilloedema; the 95% Wilson interval for this proportion excludes any value above 18.4%. The proportion with optic atrophy did not differ from the 47% reported by Deshmukh and colleagues in patients with intracranial tumours ($p = 0.637$, $h = +0.119$), and was higher than a classical estimate of 30% disc pallor without reaching significance ($p = 0.060$, $h = +0.470$). Among the nine patients with atrophy, five (55.6%, 95% CI 26.7–81.1) had bilateral involvement, a proportion indistinguishable from an even split ($p = 1.000$, $h = +0.111$).

Associations identified by the data

The two associations the data identify are given in Table 4. Both are reported as observed because the clinical records state the relevant joint information explicitly, which, combined with the observed margins, determines the complete contingency table.

The second and clinically more informative association is between perimetric pattern and optic disc status, shown in Figure 3B. All seven patients with generalised depression had optic atrophy, whereas eight of the 10 patients with bitemporal hemianopia had a normal optic disc. The odds ratio for optic atrophy in patients with generalised depression relative to those with bitemporal hemianopia is not estimable, because the zero cell drives the unadjusted odds ratio to infinity; the conditional maximum likelihood estimate is likewise infinite, with an exact conditional 95% confidence interval of 2.54 to infinity. The primary measure is therefore the risk difference, which is estimable without correction: +80.0 percentage points (95% CI +32.9 to +94.3, Newcombe hybrid score interval). Fisher exact p was 0.002 (Holm-adjusted $p = 0.034$) and Cramér's V 0.789, the latter inflated mechanically by the zero cell. The direction of the association is clear and it survives multiplicity adjustment, but its magnitude is not estimated with useful precision at $n = 17$.

Because both variables were graded by the same clinician at the same visit without masking, a misclassification sensitivity analysis was performed. The association withstood every single-patient regrade tested, with Fisher exact p ranging from 0.001 to 0.050

across seven reclassification scenarios, but lost significance when two patients with generalised depression were regraded as having a normal disc ($p = 0.058$). The finding is therefore robust to one misclassification and fragile to two, and should be read with that fragility in mind.

Associations the data do not identify

Beyond the two associations above, the data do not identify any association between the recorded variables. For each remaining pair, every contingency table consistent with the observed marginal totals was enumerated exhaustively. In every case the attainable odds ratio range spanned the null: from 0.046 to 91.00 for sex or age band against perimetric pattern, from 0.032 to 49.40 for sex or age band against optic disc status, and from 0.156 to 11.00 for atrophy laterality against perimetric pattern. In each of these the significant tables lay at both extremes of the range, so the data are as compatible with a strong positive association as with a strong negative one. Across all 24 datasets consistent with the observed age-by-sex distribution and the optic atrophy margin, Firth-penalised logistic regression yielded an adjusted odds ratio range of 0.032 to 28.71 for both male sex and the older age band, and only one dataset reached significance. No adjusted estimate is therefore presented as a finding. The full enumerations, together with the assumption-based narrowing of the eye-pairing bounds, are given in Supplementary File 2.

Endocrine findings

Endocrine assays were recorded for a subset of patients only, and the number of individual patients tested cannot be determined from the records. Prolactin was reported for four assays with a mean of 538 $\mu\text{g/L}$, thyroid-stimulating hormone for seven assays with a mean of 1.47 $\mu\text{IU/L}$, and luteinising hormone for a single assay with a value of 1.62 IU/L. Reference ranges, dispersion measures and individual values were not recorded. These figures are presented for completeness only; they were excluded from all inferential analysis, and no tumour in this cohort is classified as functioning or non-functioning.

4. Discussion

Principal findings

In 17 consecutive patients with pituitary macroadenoma attending the neuro-ophthalmology clinic of Dr. M. Djamil General Hospital in Padang, every patient had an abnormal visual field, two-thirds of eyes had acuity below 6/18, and optic atrophy was already established in over half. The female proportion and the age distribution differed detectably neither from published international series nor from an even split. At $n = 17$ such tests establish only that no difference was detected, not that the populations are equivalent, and the interval for the female proportion (41.3% to 82.7%) is wide enough to accommodate real differences. Subject to that caveat, what distinguished

this cohort was not who presented but how far the disease had advanced by the time they did. That contrast is the study's central finding, and it is the one the data support with a large effect size that survives adjustment for multiplicity.

A second finding is mechanistically informative. Perimetric pattern tracked optic disc status closely: every patient with generalised depression had optic atrophy, while eight of the 10 with bitemporal hemianopia retained a normal disc. This is consistent with the two patterns marking different points along a single trajectory rather than two independent phenomena, although a cross-sectional series cannot establish a sequence.

Comparison with the published literature

The proportion of patients with an abnormal visual field is the study's most striking quantitative departure from the literature. In the classical 1,000-case series of ocular manifestations of pituitary adenoma, approximately 70% of patients had a field defect; here every patient did ($p = 0.003$, Cohen's $h = +1.159$). The comparison requires care, because a neuro-ophthalmology clinic population is selected for visual symptoms in a way a neurosurgical series is not, and some of the gap is certainly referral filtering. Two features of the data argue that it is not all of it. First, if severity were purely a selection artefact one would expect enrichment for the most dramatic presentations, yet no patient presented with apoplexy and none had papilloedema: this is a cohort late in chiasmal terms but not catastrophically so, which is a harder pattern for referral filtering alone to produce. Second, contemporary work shows that field defects appear relatively late in chiasmal compression: in 184 patients with non-functioning pituitary neuroendocrine tumours, critical flicker fusion laterality was abnormal in tumours that had produced neither acuity loss nor a field defect, and the prevalence of test abnormality was highest for the *smallest* tumours.¹⁵ If perimetry is a late marker and every patient in a cohort has an abnormal field, the cohort is late. The inference is not airtight, since eligibility here required that perimetry had been performed and this conditions the cohort in the same direction; but the conditioning affects the size of the excess rather than its existence, because a patient reaching a tertiary neuro-ophthalmology clinic with acuity in the 3/60 to 1/60 range has not arrived early on any reading.

The acuity findings point the same way. At least 13 of 17 patients had an impaired eye whatever the true eye pairing ($p < 0.001$, $h = +1.082$ against a benchmark of approximately a quarter), and two-thirds of all eyes were below 6/18. Uvelius and colleagues, reporting long-term acuity outcomes in non-functioning adenoma, identify preoperative acuity as the dominant prognostic variable,¹⁴ and the large endoscopic-surgery series and meta-analyses place postoperative visual improvement at around four-fifths of operated patients^{23,24} — but that figure is an average over

cohorts presenting considerably earlier than this one. The determinant of recovery is consistently the preoperative state of the visual pathway rather than tumour size,²⁵ and in the five-year determinant cohort the same hierarchy holds.³⁰

The optic disc findings are the most direct evidence of established structural loss. Optic atrophy in 52.9% is statistically indistinguishable from the 47% Deshmukh and colleagues reported in patients with intracranial tumours ($p = 0.637$), and higher than a classical 30% disc-pallor estimate without reaching significance ($p = 0.060$, $h = +0.470$). The clinical weight of this figure comes from what optic atrophy predicts. Preoperative macular ganglion cell–inner plexiform layer thickness predicts complete postoperative field recovery with an area under the curve of 0.725 (95% CI 0.655–0.795) at a 77.25 μm cut-off,¹⁷ retinal nerve fibre layer thickness correlates with visual outcome after macroadenoma decompression,³⁵ optical coherence tomography predicts visual outcome at five years,¹⁸ and both pooled syntheses and the primary literature support these relationships.^{19,20,36} Electrophysiological work using RE-PERG demonstrates retrograde optic nerve degeneration in pituitary adenoma directly,³⁷ and microvascular imaging shows that radial peripapillary capillary density and optical coherence tomography angiography parameters carry independent prognostic information.^{38–40} The benefit of relieving compression extends beyond the acuity and field measures used here: pupillometric non-visual function also recovers after chiasmal decompression.⁴¹ A visible pale disc lies at the far end of the process these techniques detect early. Over half of this cohort had already reached it.

The absence of papilloedema in every patient is consistent with the expected natural history and is worth stating positively. Papilloedema in pituitary disease implies hydrocephalus from third-ventricular obstruction, a late and relatively uncommon complication. Its complete absence here, with a 95% interval excluding anything above 18.4%, indicates that however late these patients presented in terms of chiasmal compression, they had not reached the point of raised intracranial pressure. Similarly, no patient presented with apoplexy. The apoplexy literature describes a sharply different clinical picture, with abrupt visual loss and ophthalmoplegia and outcomes that depend strongly on the interval between symptom onset and surgery.^{12,42–47} This cohort represents the insidious pathway in its entirety.

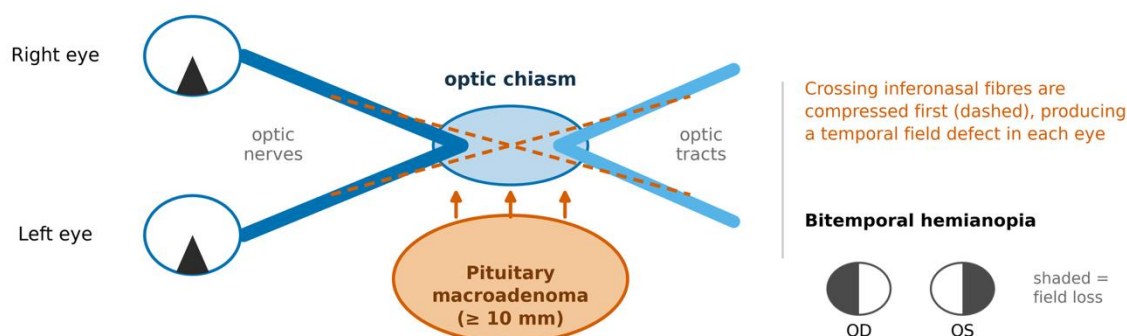
Mechanistic interpretation

The relationship between perimetric pattern and optic disc status observed here has a straightforward mechanistic reading, set out in Figure 4. A macroadenoma extending above the sella compresses the chiasm from below and strikes first the inferonasal fibres that decussate there, producing a temporal field defect in each eye — the classical bitemporal hemianopia. At this stage the insult is predominantly one of conduction block in fibres that remain

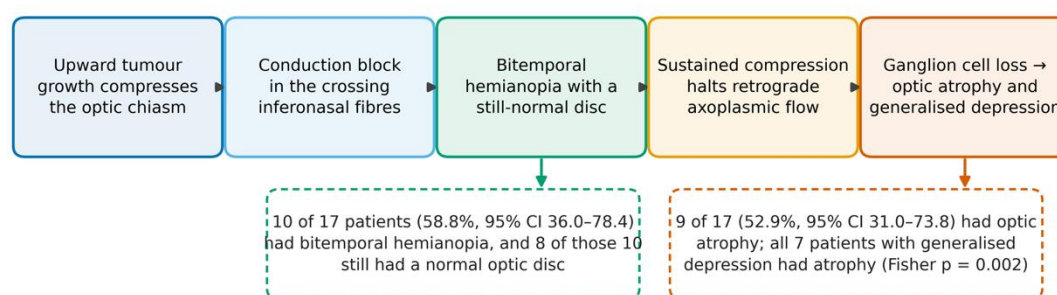
structurally intact, and the optic disc can still appear entirely normal. This is precisely what was observed:

eight of the 10 patients with bitemporal hemianopia had a normal disc.

A Chiasmal compression by a suprasellar macroadenoma



B Mechanistic cascade and the corresponding findings in this cohort (n = 17)



Dashed boxes give the observed findings of the present series that correspond to each mechanistic stage.

Stages 1, 2 and 4 are mechanisms inferred from the literature; they were not measured in this study.

Figure 4. Mechanism of visual loss in pituitary macroadenoma and its correspondence with the present findings. **(A)** A macroadenoma extending above the sella compresses the optic chiasm from below, striking first the inferonasal fibres that decussate there and producing a temporal field defect in each eye. **(B)** The mechanistic cascade, with the observed findings of this series aligned to the stages they correspond to. Stages 1, 2 and 4 are mechanisms inferred from the published literature and were not measured in this study.

If compression persists, retrograde axoplasmic transport is progressively interrupted, retinal ganglion cells die, and the loss becomes both structurally visible as disc pallor and functionally broader than the original decussating-fibre pattern. Generalised depression across the whole field, rather than a defect respecting the vertical meridian, is what that broader loss looks like on perimetry. Every patient in this cohort with generalised depression had optic atrophy, and none had a normal disc (risk difference +80.0 percentage points, 95% CI +32.9 to +94.3; $p = 0.002$, Holm-adjusted $p = 0.034$).

This finding should be interpreted for what it is. It is a cross-sectional association observed at a single timepoint in 17 patients, not a demonstrated temporal sequence, and the confidence interval around the odds ratio is far too wide to support any quantitative claim. What can be said is that the association is in the direction the mechanism predicts, that it is statistically significant, and that it is consistent with the

independent evidence for retrograde degeneration in this disease.³⁷

One alternative explanation deserves statement. The position of the chiasm relative to the sella varies between individuals — prefixed, central and postfixed variants are all described — and a tumour meeting a prefixed chiasm produces a different field signature from one meeting a postfixed chiasm. The two perimetric patterns observed here could therefore reflect differing anatomy rather than differing timepoints. Chiasm position was not recorded and cannot be recovered from these data, so this explanation cannot be excluded. Subject to that caveat, the observation generates a testable hypothesis: that generalised depression in chiasmal compression marks a later disease stage than bitemporal hemianopia and carries a correspondingly worse prognosis for visual recovery. Distinguishing it from the anatomical explanation requires longitudinal data with structural imaging and recorded chiasm position, which this study does not have.

What a marginal dataset can and cannot support

The methodological contribution of this study is as important as its clinical one, because the constraint it faced is ubiquitous in record-based research from resource-limited settings. The clinical records provided frequency distributions for each variable but cross-classification for only two variable pairs. Reconstructing a patient-level dataset consistent with the margins and analysing it as though it had been observed would yield estimates that are artefacts of the reconstruction rather than measurements.

Enumerating every dataset consistent with what was observed, and reporting the full attainable range of each measure, avoids that. The results are unambiguous. For every unidentified association the attainable odds ratio range spanned the null, typically from around 0.03 to around 50 or 90, with significant tables at both extremes. In the multivariable analysis, exactly one of the 24 admissible datasets produced a significant coefficient for either predictor, and that at $p = 0.037$. These are not statements of low power in the usual sense; they are statements that the data contain essentially no information about the direction of these associations. Reporting them as null results would be wrong, and reporting a point estimate would be worse. The approach also yields positive results that are stronger than a conventional analysis would have been. Because the lower bound of patients with at least one impaired eye is 13 of 17 under every admissible pairing, and because that lower bound is itself significant against a 25% benchmark ($p < 0.001$, $h = +1.082$), the study's central claim about presenting severity is established without any assumption about the data's unobserved structure. A claim that survives every admissible configuration of the unknowns is more robust, not less, than one resting on a single imputed dataset. The assumption-based secondary analysis makes the same point from the other direction: imposing positive interocular dependence, which is biologically near-certain for a midline compressive lesion, narrows the bounds by half to two-thirds but leaves every conclusion unchanged.

Holm adjustment across the 17-test family makes the same point from the opposite direction. Four tests survive it, and they are the four the clinical hypothesis predicted: eye-level and patient-level acuity impairment, universally abnormal visual fields, and the association between perimetric pattern and optic disc status. The concentration of men in the older age band does not survive (adjusted $p = 0.070$) and is accordingly treated as suggestive rather than established, as are the demographic comparisons, none of which is distinguishable from an even split at this sample size.

Clinical and policy implications

The actionable implication operates at the level of referral rather than treatment. Every patient in this series reached a competent neuro-ophthalmology service and received appropriate multidisciplinary

referral; the problem is not what happened after arrival but the condition of the optic nerves on arrival. Over half had irreversible structural loss already visible on fundus examination, and that loss will not be recovered by any operation.

Three practical measures follow. First, unexplained visual complaints in adults of working age — particularly gradual bilateral blurring without an obvious refractive or media cause — warrant formal perimetry and dilated fundus examination rather than repeated refraction. The cost of confrontation testing and ophthalmoscopy is negligible against the cost of a missed chiasmal compression. Second, the male pattern deserves specific attention. Five of the six patients aged 41 to 60 years in this cohort were male (risk difference +74.2 percentage points, 95% CI +25.3 to +89.8, $p = 0.005$, not retained after adjustment for multiplicity), which is consistent with the documented tendency for men to present later because hyperprolactinaemia produces vague symptoms in men and unmistakable ones in premenopausal women,^{10,11} and with gender-specific presentation patterns in non-functioning tumours.⁶ Third, the Indonesian national consensus for pituitary adenoma diagnosis published in 2025 defines a diagnostic pathway;³¹ what these data suggest is that the binding constraint is not the pathway's content but the point at which patients enter it.

What happens after referral is, on the evidence, not the weak link. Decompression reliably improves pituitary function in non-functioning macroadenoma,⁴⁸ recurrence after surgery is predictable from identifiable baseline factors and amenable to surveillance,⁴⁹ and the completeness of resection measurably influences both visual outcome and the need for further surgery.⁵⁰ Where postoperative haematoma occurs, the timing of reoperation determines the visual result.⁵¹ Even the perioperative pathway is now characterised in detail, with preoperative sinusitis shown to affect endoscopic surgical outcomes in real-world cohorts.⁵² Each of these is a refinement applied to patients who have already arrived. None of them recovers a retinal ganglion cell that died before the patient was referred, which is why the leverage in this setting lies upstream of the operating theatre.

At the level of service configuration, optical coherence tomography deserves consideration as part of the routine workup in centres managing these patients. Its prognostic value before decompression is now well established across primary studies, pooled syntheses and preoperative-workup series,^{17–22,35,36} and unlike perimetry it detects ganglion cell loss before the patient notices a deficit. In a setting where presentation is demonstrably late, a test that moves detection earlier has disproportionate value. Where optical coherence tomography is unavailable, preoperative chiasm volume on existing magnetic resonance imaging is a

simple and transferable alternative predictor that requires no new equipment.²⁷

Regional and public health significance

West Sumatra is served by a single tertiary referral centre for neuro-ophthalmology, and patients reach it through a referral chain that begins in district facilities where perimetry is generally unavailable. This series is, to the best of the authors' knowledge, the first description of presenting neuro-ophthalmic status in pituitary macroadenoma from an Indonesian centre. That claim rests on a search of PubMed and Google Scholar conducted in September 2026 combining terms for pituitary adenoma or macroadenoma with terms for visual field, visual acuity, optic atrophy and neuro-ophthalmology, restricted to Indonesia and to Southeast Asia, which returned no comparable series. It fills a gap that the 2025 national consensus document makes conspicuous: the consensus specifies how pituitary adenoma should be diagnosed,³¹ but no published Indonesian data describe the state patients are in when diagnosis finally occurs.

The comparison that gives these findings their regional meaning is with the health systems that generate the international benchmarks. The large surgical series and prognostic-modelling cohorts that define expected visual recovery come predominantly from settings with dense ophthalmic coverage and routine access to automated perimetry and structural imaging.^{23–30} A Tunisian apoplexy series from a comparable middle-income referral context⁴⁷ and a population-based series from Malta⁴² illustrate how differently the same disease presents where the referral chain is longer. The finding here that demography is ordinary but severity is not suggests that the difference lies in health-system transit time rather than in disease biology — a conclusion that, if confirmed across Indonesian centres, would locate the intervention point in primary and secondary care rather than in the tertiary centre.

There is a second, quieter public health implication. Visual impairment in this cohort clustered in patients aged 21 to 60, which is to say across the entire working-age range. Bilateral impairment affected between 35.3% and 58.8% of the cohort. The economic burden of avoidable visual disability in this age group is borne over decades, and it is avoidable in precisely the sense that matters: the tumour is benign, the treatment is effective, and the only scarce resource is time.

Strengths

The study has four substantive strengths. First, it examined the complete eligible population of a defined sampling frame over 39 months rather than a convenience sample, and the eligibility criteria explicitly excluded glaucoma, non-arteritic anterior ischaemic optic neuropathy, media opacity and retinal disease, so the visual findings are attributable to the chiasmal lesion rather than to competing pathology. Second, data completeness for the four core variables was 100%, so no result is affected by missing-data

assumptions. Third, every proportion is reported with an interval estimate and tested against a specific benchmark drawn from the published literature rather than against an uninformative null, which converts a descriptive tally into a set of falsifiable comparisons. Fourth, and most unusually, the analysis states explicitly and quantitatively which associations the data can and cannot support, using exhaustive enumeration rather than reconstruction, so that no reported estimate depends on an unverifiable assumption about unobserved structure.

Limitations

The sample of 17 patients is small, and the resulting imprecision is severe: the half-width of a 95% Wilson interval is approximately 21 percentage points for a proportion near 0.50, and the confidence intervals around both identified odds ratios span more than two orders of magnitude. The study is single-centre and confined to a tertiary neuro-ophthalmology clinic, so the cohort is selected for visual symptoms and these proportions cannot be read as population prevalences. The absence of patient-level cross-classification is the central analytic limitation. Sex, age band, perimetric pattern and optic disc status are available as marginal distributions, and only two pairs among them are cross-classified in the records; visual acuity is recorded per eye with no link between a patient's two eyes. Every association other than those two pairs is consequently unidentified, which remains a limitation of the dataset.

Four specific variables are absent and their absence is consequential. Tumour size and the extent of suprasellar extension were not recorded, so no dose-response relationship between tumour burden and visual compromise could be examined and no comparison with the chiasm-volume or radiomic prediction literature was possible.^{26,27,29} The duration from first visual symptom to presentation was not recorded, so the central claim that this cohort presented late rests on inference from severity rather than on measurement of an interval. Endocrine profiling was incomplete and internally inconsistent, so no tumour could be classified as functioning or non-functioning, which prevents the stratification that the literature identifies as the principal determinant of presentation route.^{6,9,10} Humphrey reliability indices and mean deviation values were not recorded, so unreliable fields could not be excluded and field severity could not be analysed as a continuous variable. Field classification and optic disc assessment were performed by the treating clinicians as part of routine care, without masking and without a second independent grader, so inter-observer agreement could not be assessed and misclassification cannot be excluded. Diagnosis rested on clinical and radiological grounds without histopathological confirmation, so other sellar and parasellar lesions capable of mimicking macroadenoma, including posterior pituitary tumours,

cannot be formally excluded in every case.⁵³ Optical coherence tomography was not available, so structural loss was assessed by ophthalmoscopy alone — a substantially less sensitive method than the quantitative techniques that dominate the contemporary literature.^{17–22} Finally, the study is cross-sectional: no patient was followed after diagnosis, so the proposed sequence from bitemporal hemianopia with a normal disc to generalised depression with atrophy is a hypothesis consistent with the cross-sectional pattern, not a demonstrated progression.

Two contextual limitations remain. Recruitment opened in July 2022, within a period of disrupted outpatient access and deferred elective referral across Indonesia; this is a plausible system-level contributor to presenting severity that these data cannot quantify, and the distribution of presentations across the study years was not recorded. And although the eligibility criteria required a documented presenting complaint, the abstracted dataset did not carry it forward, so neither the nature of the initial symptom nor the referral source could be analysed; both would have illuminated the care pathway far more directly than severity alone.

Research agenda

Four specific studies follow from these findings, and each is feasible within the Indonesian setting.

The first is a multicentre Indonesian registry of presenting neuro-ophthalmic status in sellar and parasellar tumours. The precision calculation reported in the Methods sets the target directly: 93 patients would deliver ± 10 -point precision on a proportion near 0.50 and 381 patients ± 5 -point precision. At the accrual rate observed here of approximately five patients per year per centre, a 10-centre collaboration would reach the first target within two years. The minimum dataset should be specified in advance to include the patient-level linkage this study lacked: paired right and left eye acuity, perimetric pattern and disc status recorded per patient, maximum tumour diameter and suprasellar extension, a complete anterior pituitary hormone panel with the reference ranges used, and the interval from first visual symptom to first specialist consultation.

The second is a prospective cohort testing the staging hypothesis generated here: that generalised depression marks a later stage than bitemporal hemianopia. This requires perimetry with mean deviation and reliability indices recorded, optical coherence tomography measurement of peripapillary retinal nerve fibre layer and macular ganglion cell–inner plexiform layer thickness at baseline, and visual outcome assessed at six and twelve months after decompression. The comparison group is patients with bitemporal hemianopia and a normal disc; the primary outcome is the proportion achieving complete field recovery, benchmarked against the 77.25 μm ganglion cell threshold already established in the literature.¹⁷ A sample of approximately 120 patients would detect a

25-percentage-point difference in recovery between the two presenting patterns at 80% power.

The third is a diagnostic-delay study measuring the referral pathway directly rather than inferring it. This would trace, for consecutive patients, the interval from first visual symptom to first primary-care contact, from there to first ophthalmological assessment, and from there to neuroimaging, identifying which segment of the chain contributes most delay. Only such a study can convert the present inference from severity into a measured interval and locate the intervention point precisely.

The fourth is an implementation study of a low-cost screening protocol in secondary-care ophthalmology units: confrontation field testing and dilated fundus examination for every adult presenting with unexplained bilateral visual blurring, with defined criteria for onward referral. Where resources permit, preoperative chiasm volume measured on existing magnetic resonance imaging offers a transferable prognostic measure requiring no new equipment,²⁷ and intraoperative visual evoked potential monitoring warrants evaluation in centres performing decompression.⁵⁴

5. Conclusion

Among 17 consecutive patients with pituitary macroadenoma presenting to a provincial Indonesian referral centre, every patient had an abnormal visual field (17/17, 95% CI 81.6–100.0; $p = 0.003$ versus a 70% benchmark, Cohen's $h = +1.159$), at least 13 of 17 had an eye below 6/18 under every admissible eye pairing ($\geq 76.5\%$; $p < 0.001$ versus a 25% benchmark), and optic atrophy was already established in 9 patients (52.9%, 95% CI 31.0–73.8). All three findings survive Holm adjustment across the 17-test family. No demographic difference from published international series was detected, though at this sample size that is non-detection rather than demonstrated equivalence; subject to that caveat, the severity at presentation is more readily explained by delayed arrival than by an unusual patient population. Perimetric pattern tracked optic disc status closely: every patient with generalised depression had optic atrophy, whereas eight of ten with bitemporal hemianopia retained a normal disc (risk difference +80.0 percentage points, 95% CI +32.9 to +94.3; $p = 0.002$), a pattern consistent with the two findings marking different stages of a single process, though differing chiasm anatomy cannot be excluded as an alternative explanation. The practical implication is that unexplained visual complaints in working-age adults warrant perimetry and dilated fundus examination rather than repeated refraction, with particular attention to men aged over 40. A multicentre Indonesian registry recording paired per-patient ophthalmic data, tumour dimensions and symptom duration would resolve the associations this dataset cannot identify; 93 patients would achieve ± 10 -point

precision, a target within reach of a 10-centre collaboration in two years.

Declarations

Ethics approval

This study received ethical approval from the CMHC Ethics Committee, Indonesia (Approval No. 2025/0142). The study was a retrospective analysis of anonymised hospital medical records; no patient was contacted and no identifiable patient information is reported. Individual informed consent was waived in accordance with institutional policy governing retrospective record-based research. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable. No individual patient data, images or identifying details are reported.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Author contributions

CA: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing – original draft, Writing – review and editing. MH: Conceptualization, Methodology, Supervision, Validation, Writing – review and editing.

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Data availability

The aggregated data supporting the findings of this study are contained within the article and its tables. The underlying anonymised records are available from the corresponding author on reasonable request, subject to institutional approval.

Generative AI disclosure

The authors declare that no generative artificial intelligence tools were used in the design, analysis, or writing of this manuscript.

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