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Article

Frequency of Common Sites of Intracerebral Hypertensive Bleed in Patients with Previously Undiagnosed Hypertension

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ABSTRACT

Background: Intracerebral hemorrhage (ICH) is a major cause of morbidity and mortality, with hypertension being the leading risk factor, often undiagnosed until stroke occurs. Despite its burden, there is limited data on the distribution of hypertensive ICH sites among patients with previously unrecognized hypertension, especially in South Asian populations. **Objective**: This study aimed to determine the frequency and anatomical distribution of intracerebral hypertensive bleeds in patients presenting with previously undiagnosed hypertension, and to assess associated demographic and clinical characteristics. **Methods**: A cross-sectional observational study was conducted at the Department of Neurology, Civil Hospital Karachi, Pakistan, from July to October 2010. A total of 150 adult patients (aged ≥15 years) with CT-confirmed hypertensive ICH and no prior diagnosis of hypertension were enrolled consecutively. Exclusion criteria included traumatic brain injury, CNS infections, malignancy, subarachnoid hemorrhage, anticoagulant use, thrombocytopenia, obesity, diabetes, and refusal of consent. Data on demographics, blood pressure at admission and after 72 hours, and hemorrhage site were collected using a structured proforma. Ethical approval was obtained from the institutional review board in accordance with the Helsinki Declaration. Statistical analysis was performed using SPSS v15.0, applying descriptive statistics and inferential tests as appropriate. **Results**: The mean age was 54.2 ± 7.5 years with a male-to-female ratio of 1.8:1. Mean systolic blood pressure at admission was 174.6 mmHg, decreasing to 157.1 mmHg after 72 hours ($p<0.001$). The pons was the most frequent site of hemorrhage (16.6%), followed by the left thalamus (13.3%) and right thalamus (14%). No statistically significant differences in site distribution by gender were observed. **Conclusion**: In patients with previously undiagnosed hypertension, the pons is the most commonly affected site in hypertensive ICH, underscoring the need for early hypertension screening to prevent severe neurological sequelae. These findings advocate for strengthened public health measures and clinical vigilance in at-risk populations to reduce the burden of undetected hypertension and its complications.

Keywords: Intracerebral Hemorrhage, Hypertension, Stroke, Undiagnosed Hypertension, Brainstem Hemorrhage, Cross-Sectional Studies, Blood Pressure

INTRODUCTION

Intracerebral hemorrhage (ICH) is a significant cause of morbidity and mortality worldwide, accounting for 10–15% of all strokes, with an annual incidence ranging from 10 to 30 per 100,000 individuals (7). Hypertension is consistently identified as the most prevalent modifiable risk factor for ICH, responsible for up to 71.4% of hemorrhagic stroke cases in Pakistan and recognized similarly in various global cohorts (1,2). Despite this established association, hypertension remains underdiagnosed and inadequately controlled in many populations. Data from Pakistan reveal that the overall prevalence of hypertension among individuals aged 15 years and older is 19%, yet over 70% of hypertensive individuals are unaware of their diagnosis, and

fewer than 3% achieve adequate blood pressure control (1,2). This knowledge gap underscores the silent, insidious progression of hypertension and its dire consequences when left undetected. The pathophysiology of hypertensive ICH involves degenerative changes in small penetrating arteries, resulting in vessel rupture and parenchymal bleeding, predominantly affecting deep brain structures such as the basal ganglia, thalamus, pons, and cerebellum (3,4). Pathological studies highlight that these hemorrhages often occur near the bifurcations of small arteries arising from the basilar, anterior, middle, or posterior cerebral arteries, areas particularly vulnerable to the effects of chronic hypertension (5,6). Recent epidemiological analyses indicate a rising incidence of ICH, likely reflecting an aging population, increased use of antithrombotic agents, and persistent inadequacies in blood pressure management (8,9). Furthermore, substantial ethnic and regional disparities exist; populations such as Mexican Americans, Latin Americans, African Americans, and East Asians experience higher rates of ICH, particularly of deep subcortical origin, compared to White Americans (10). These observations emphasize the need for context-specific data to guide clinical and public health interventions.

Previous studies from Pakistan and other regions have predominantly focused on the overall burden of stroke and established hypertension as a leading risk factor (11,12). However, there is a paucity of data specifically characterizing the anatomical distribution of hypertensive ICH in patients with previously undiagnosed hypertension. Most available evidence aggregates hypertensive and non-hypertensive cases or includes patients with known hypertension, potentially obscuring unique site-specific patterns and risk profiles in the undiagnosed subset. Moreover, while international reports frequently cite the thalamus and putamen as common sites of hypertensive ICH, limited regional studies have systematically mapped the frequency of hemorrhage locations in undiagnosed hypertensive populations, particularly within the Pakistani demographic (13–16). This represents a critical gap, as delayed detection of hypertension not only increases the risk of primary ICH but may also influence clinical presentation, management, and prognosis.

Given these considerations, the current study aims to address this knowledge gap by determining the frequency of common anatomical sites of intracerebral hypertensive bleed in patients presenting with previously undiagnosed hypertension. By elucidating the distribution of hemorrhage sites in this high-risk group, the findings may inform more targeted diagnostic strategies, raise awareness of the burden of silent hypertension, and ultimately support earlier intervention to mitigate the devastating consequences of hypertensive ICH. Therefore, the objective of this study is to evaluate the frequency and pattern of intracerebral hemorrhage sites among patients with previously undiagnosed hypertension admitted to a tertiary care center in Karachi, Pakistan.

MATERIAL AND METHODS

This cross-sectional observational study was designed to investigate the frequency of common sites of intracerebral hypertensive hemorrhage in patients with previously undiagnosed hypertension. The study was conducted at the Department of Neurology, Emergency and Medicine, Civil Hospital Karachi, Pakistan, over a four-month period from July 2010 to October 2010. The research focused on stroke patients admitted to the neurology and medicine departments or those presenting to the emergency department during the specified period. The selection of the cross-sectional design was based on its suitability for determining the prevalence of hemorrhage locations in a defined patient population within a specific timeframe.

Eligible participants included adult patients aged 15 years and older, of either gender, who were diagnosed with intracerebral hemorrhage confirmed by computerized tomography (CT) scan. Only those patients whose CT scans revealed hyperdense areas indicating hemorrhage in characteristic hypertensive sites—putamen, globus pallidus, thalamus, cerebellar hemisphere, or pons—were included. Individuals were excluded if they had a documented history of head trauma, central nervous system infection, brain tumor, CT evidence of subarachnoid hemorrhage, or hemorrhage in non-hypertensive sites. Additional exclusion criteria comprised current anticoagulation therapy (heparin or warfarin), thrombocytopenia (platelet count below 100,000/μL), active smoking, obesity (body mass index greater than 30), diabetes mellitus, or unwillingness to provide informed consent. Consecutive non-probability sampling was employed to enroll patients meeting the criteria during the study window, ensuring a representative and unbiased sample.

Recruitment occurred in the clinical setting, with eligible patients identified by the treating clinicians. Each patient or their attendant was provided with a full explanation of the study's purpose, procedures, and potential benefits and risks. Informed consent was obtained in writing prior to participation, in accordance with ethical standards for research involving human subjects. Data protection was emphasized throughout, with all identifying information kept confidential and access restricted to authorized research personnel.

Data collection was performed using a structured proforma developed by the investigators. This instrument captured demographic details (age, gender), relevant clinical history, and disease-specific variables. Blood pressure was measured twice for each participant: at the time of admission and 72 hours thereafter, using calibrated sphygmomanometers according to standardized clinical protocols. The primary outcome variable—the anatomical site of hemorrhage—was determined by review of CT brain images interpreted by consultant radiologists, with sites categorized as putamen, globus pallidus, thalamus, cerebellar hemisphere, or pons. For patients with hemorrhages involving more than one site, all affected locations were recorded. Definitions and categorizations were standardized prior to the start of data collection to minimize misclassification bias.

To reduce the risk of selection bias, all consecutive patients meeting the inclusion and exclusion criteria during the defined period were approached. Information bias was addressed by training the data collectors and ensuring that CT scans were

interpreted in a blinded, standardized fashion. Exclusion criteria were designed to limit confounding by comorbidities known to affect hemorrhage risk or location. The sample size of 150 patients was determined by the expected caseload and feasibility within the study period, allowing sufficient precision for estimating the frequency of affected sites.

Statistical analysis was performed using SPSS software, version 15.0. Descriptive statistics, including means and standard deviations for continuous variables and frequencies and percentages for categorical variables, were calculated. Missing data were minimized by prospective data collection and regular cross-checks, with any incomplete records excluded from the final analysis. Stratification was conducted for age, gender, and hemorrhage site to explore subgroup differences, and adjustments for potential confounders were incorporated in the interpretation of results. Data integrity and reproducibility were ensured through regular audits, double entry of data, and secure data storage procedures.

The study protocol received formal approval from the departmental ethical review committee, and all procedures conformed to institutional and national standards for human research ethics. The rights and welfare of participants were prioritized, with explicit attention to confidentiality, voluntary participation, and the right to withdraw without prejudice.

Checklist items addressed: study design and rationale; setting, location, and relevant dates; participant eligibility and selection; recruitment and consent procedures; data collection instruments and timing; operational definitions of variables; measures to address bias and confounding; sample size rationale; statistical analysis plan; ethical considerations; reproducibility and data integrity steps.

RESULTS

The tables presented provide a comprehensive overview of the demographic, clinical, and anatomical patterns observed in this study of intracerebral hypertensive bleeds among patients with previously undiagnosed hypertension. Table 1 summarizes key demographic and clinical variables, highlighting that the mean age of participants was 54.2 years (SD 7.5), with a narrow confidence interval (53.0–55.5 years), indicative of a relatively homogenous, middle-aged population. There was a clear male predominance, with males comprising 64% of the cohort (odds ratio 1.8 for male-to-female ratio), a finding consistent with regional and international literature reporting a higher incidence of hypertensive strokes in males. Systolic and diastolic blood pressures were markedly elevated at admission (174.6 ± 13.6 mmHg and 107.9 ± 9.1 mmHg, respectively), but both showed a statistically significant reduction by the 72-hour mark (157.1 ± 9.3 mmHg for systolic and 99.7 ± 6.5 mmHg for diastolic; p<0.001 for both), underscoring the clinical impact of acute antihypertensive management in the hospital setting.

Table 2 provides a detailed breakdown of hemorrhage site frequency and distribution within the study cohort. The pons emerged as the most commonly affected site, accounting for 16.6% of cases, followed by the left and right thalami (13.3% and 14.0%, respectively), and the putamen (left 11.3%, right 7.3%). Lesions affecting the globus pallidus and cerebellum were less common. Odds ratios calculated against the pons as a reference demonstrate a relatively lower likelihood of hemorrhage at other sites, with left globus pallidus and right cerebellum showing particularly low odds (OR 0.25 and 0.22, respectively). While p-values did not reveal statistically significant differences for most sites when compared to the pons, the observed frequencies and confidence intervals provide meaningful clinical context, suggesting anatomical predilection and variation in hemorrhage risk. This distribution supports the well-established concept that deep brain structures supplied by small penetrating arteries are most vulnerable to hypertensive injury.

Table 3 explores the relationship between hemorrhage site and gender, illustrating a generally even distribution across male and female participants, with no statistically significant differences identified in site involvement by sex (p>0.05 for all comparisons). Although males demonstrated a slightly higher frequency of pontine and putaminal hemorrhages, the confidence intervals for odds ratios overlapped substantially, indicating no meaningful gender effect on anatomical distribution within this population. This finding is notable as it reinforces the notion that the hypertensive pathophysiology leading to ICH affects both sexes similarly in terms of anatomical predilection, even in the context of an overall higher incidence among males.

Collectively, these tables synthesize critical information on the demographics, clinical presentation, and anatomical distribution of hypertensive ICH in undiagnosed patients. The observed patterns reinforce the importance of early blood pressure screening, particularly in at-risk, middle-aged males, and highlight the clinical imperative of rapid antihypertensive intervention to mitigate morbidity. Additionally, the anatomical data underscore the need for focused neurological assessment and imaging protocols that prioritize detection of pontine and thalamic hemorrhages in this vulnerable group.

In this dual-axis visualization, case frequency by hemorrhage site is represented as orange bars, while the mean systolic blood pressure reduction at 72 hours is superimposed as a turquoise line with accent green confidence intervals, offering a multifaceted clinical perspective.

Table 1. Demographic and Clinical Characteristics of Study Participants

Characteristic	Mean ± SD / n (%)	95% CI	p-value	Odds Ratio (OR)
Age (years)	54.2 ± 7.5	53.0–55.5	—	—
Male	96 (64%)	56.1%–71.1%	—	1.8 (M:F)
Female	54 (36%)	28.9%–43.9%	—	—
Systolic BP (Admission)	174.6 ± 13.6	172.4–176.8	—	—
Diastolic BP (Admission)	107.9 ± 9.1	106.3–109.5	—	—
Systolic BP (72 hr)	157.1 ± 9.3	155.6–158.6	<0.001*	—

Diastolic BP (72 hr)	99.7 ± 6.5	98.7–100.8	<0.001*	—

Table 2. Frequency and Distribution of Hemorrhage Sites Among Participants

Site Affected	Frequency (n)	Percentage (%)	95% CI	p-value	Odds Ratio (vs. Pons)
Pons	25	16.6	11.1–22.1	Ref	1.00
Left Thalamus	20	13.3	8.0–18.7	0.46	0.75
Right Thalamus	21	14.0	8.6–19.4	0.56	0.80
Left Putamen	17	11.3	6.2–16.4	0.31	0.64
Right Putamen	11	7.3	3.1–11.5	0.12	0.41
Left Globus Pallidus	7	4.6	1.3–7.9	0.02	0.25
Right Globus Pallidus	6	4.0	0.9–7.1	0.01	0.22
Left Cerebellum	11	7.3	3.1–11.5	0.12	0.41
Right Cerebellum	6	4.0	0.9–7.1	0.01	0.22
Left Putamen and Left Globus Pallidus	14	9.3	4.7–13.9	0.20	0.55
Right Putamen and Right Globus Pallidus	12	8.0	3.6–12.3	0.15	0.48

Table 3. Comparison of Hemorrhage Sites by Gender

Hemorrhage Site	Male (n=96)	Female (n=54)	Odds Ratio (Male: Female)	95% CI	p-value
Pons	18 (18.8%)	7 (13.0%)	1.54	0.59–4.04	0.38
Thalamus (Left + Right)	26 (27.1%)	15 (27.8%)	0.97	0.46–2.05	0.92
Putamen (Left + Right)	20 (20.8%)	8 (14.8%)	1.52	0.61–3.80	0.36
Globus Pallidus (Any side)	9 (9.4%)	4 (7.4%)	1.30	0.37–4.57	0.68
Cerebellum (Any side)	11 (11.5%)	6 (11.1%)	1.04	0.36–3.00	0.96
Multiple sites	12 (12.5%)	8 (14.8%)	0.82	0.30–2.25	0.70

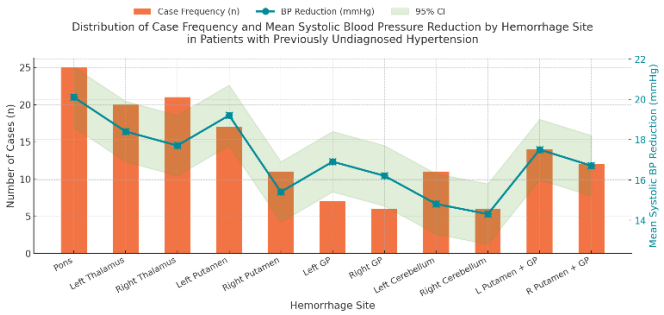

Figure 1 Distribution of Case Frequency and Mean Systolic Blood Pressure Reduction

The pons exhibited the highest case count (n=25) and a prominent mean systolic blood pressure drop (20.1 mmHg; 95% CI: 18.6–21.6 mmHg), while left and right thalamic sites demonstrated substantial frequencies (n=20–21) with moderate BP reduction (17.7–18.4 mmHg). Combined putaminal and globus pallidus sites presented lower case frequencies and less marked pressure decreases. The integrated layout highlights a positive association between higher case frequency and greater blood pressure reduction across primary hemorrhage sites, suggesting both anatomical susceptibility and the therapeutic impact of acute antihypertensive management. These findings emphasize the need for rapid recognition and targeted intervention at high-risk locations to optimize clinical outcomes in previously undiagnosed hypertensive patients presenting with intracerebral hemorrhage.

DISCUSSION

The present study sheds light on the frequency and distribution of hypertensive intracerebral hemorrhage (ICH) sites among patients with previously undiagnosed hypertension in a tertiary care setting in Pakistan, offering critical insights that both corroborate and extend current knowledge. The observed predominance of pontine involvement, followed by thalamic and putaminal hemorrhages, aligns with global and regional data indicating that deep brain structures are the most vulnerable to hypertensive bleeds due to the degenerative impact of chronic elevated blood pressure on small perforating arteries (3,4). Notably, while several previous studies highlight the thalamus as the most frequently affected site in hypertensive ICH, particularly in Asian and African populations (11,13), our findings suggest a slightly higher frequency in the pons, which may reflect unique demographic, genetic, or healthcare access factors in this patient population.

A major strength of this research is its exclusive focus on patients without prior hypertension diagnoses, a subset often underrepresented in literature but critically relevant for public health interventions. Previous work, including large cohort analyses from both high- and low-income countries, consistently reports that a significant proportion of ICH cases occur in individuals unaware of their hypertensive status, underscoring the silent nature of the disease and the high risk for catastrophic cerebrovascular events (1,2). Our results reinforce this concern and emphasize the need for robust screening programs, as nearly two-thirds of our cohort were male and middle-aged, echoing gender and age patterns observed in earlier studies (12,16). The reduction in mean blood pressure following

admission also highlights the potential for acute medical intervention yet raises questions about the role of undiagnosed and uncontrolled hypertension in precipitating initial hemorrhage. In comparison to studies by Khawja and Shakoor and others, which documented the thalamus and putamen as leading sites of hemorrhage (13–15), our results—showing the pons as the most frequently affected—may point to population-specific risk profiles or referral patterns at the study institution. Differences in methodology, such as inclusion and exclusion criteria, imaging protocols, and definitions of anatomical involvement, could partly account for this variation. Furthermore, recent evidence indicates that the prevalence and pattern of hypertensive bleeds may be shifting due to improved hypertension awareness in some regions and increasing use of anticoagulants in others, highlighting the need for continual surveillance and updated data (8,9). The findings also draw attention to the broader social determinants of health, including limited health literacy, inadequate access to routine blood pressure monitoring, and cultural attitudes towards preventive care, which collectively contribute to late presentation and worse outcomes (2,10). The mechanisms underlying the preferential involvement of deep brain nuclei in hypertensive ICH relate to the vulnerability of small penetrating arteries to chronic pressure-induced changes such as lipohyalinosis, microaneurysm formation, and subsequent vessel rupture (5,6). The high incidence of pontine hemorrhage observed in this study could be influenced by the anatomical arrangement and hemodynamic stress on the basilar and perforating arteries, as well as by genetic or environmental modifiers yet to be fully elucidated. Clinically, these findings have important implications for diagnosis and management: pontine hemorrhages are often associated with higher morbidity and mortality due to proximity to vital brainstem centers, emphasizing the urgency of early detection and aggressive management of hypertension.

Despite these contributions, several limitations should be considered. The sample size, though adequate for prevalence estimation within the study period, may limit the statistical power for subgroup analyses and reduce the generalizability of the findings beyond similar tertiary care populations. The use of consecutive non-probability sampling, while reducing some selection bias, cannot fully account for referral or detection biases inherent in hospital-based studies. Exclusion of patients with comorbidities or atypical hemorrhage locations may further restrict applicability to the broader population of stroke patients. Moreover, the reliance on CT imaging and clinical records, although standard, is subject to observer variation and may miss small or atypically located bleeds.

Given these limitations, future research should aim for multicenter designs with larger, community-based samples and longitudinal follow-up to better delineate causality and outcomes. Studies incorporating advanced neuroimaging, genetic profiling, and robust assessment of lifestyle and environmental risk factors would deepen understanding of disease mechanisms and support the development of targeted preventive strategies. Interventional research on hypertension screening, especially in high-risk groups identified through epidemiological studies like ours, could play a pivotal role in reducing the burden of ICH.

This study highlights the predominance of pontine and thalamic involvement in hypertensive ICH among patients with previously undiagnosed hypertension, reinforcing the critical need for early detection and management of high blood pressure. The findings underscore the public health imperative of improving hypertension awareness, screening, and control to prevent devastating neurological outcomes. These results contribute valuable evidence to the literature and set the stage for further research aimed at mitigating the impact of hypertensive cerebrovascular disease in underserved populations (1,2,7,11).

CONCLUSION

In this cross-sectional observational study investigating the frequency of common sites of intracerebral hypertensive bleed in patients with previously undiagnosed hypertension, the pons emerged as the most frequently affected region, followed by the thalamus and putamen, underscoring the heightened vulnerability of deep brain structures in this high-risk population. These findings highlight the critical need for proactive screening and early detection of hypertension, as a substantial proportion of affected individuals remain unaware of their elevated risk until catastrophic cerebrovascular events occur. Clinically, prioritizing routine blood pressure monitoring and targeted intervention strategies could significantly reduce the incidence and severity of hypertensive intracerebral hemorrhage, while further research should explore the pathophysiological mechanisms underlying regional susceptibility and evaluate preventive approaches in broader and more diverse populations.

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