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ORIGINAL ARTICLE

Anatomy of vertebral artery hypoplasia and its relationship with clinical implications: a systematic review and meta-analysis of prevalence

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Abstract

Purpose The vertebral artery (VA) is a vital branch of the subclavian artery, coursing through the transverse foramina of the cervical vertebrae, and playing a crucial role in irrigating the posterior region of the arterial cerebral circle, also known as the Polygon of Willis. Among the various possible alterations that can affect the VA, vertebral artery hypoplasia (HAV) emerges as a significant variant. This study aims to discern the anatomical features of HAV and its correlation with the clinical conditions of the posterior cerebral circulation.

Methods The databases Medline, Scopus, Web of Science, Google Scholar, CINAHL, and LILACS were searched until January 2024. Two authors independently performed the search, study selection, and data extraction. Methodological quality was evaluated with an assurance tool for anatomical studies (AQUA). Pooled prevalence was estimated using a random effects model.

Results A total of 24 studies met the established selection criteria, with a total of 8847 subjects. In this study, 6 articles were included for the meta-analysis with a total of subjects. The average prevalence of VAH reported in each study was 11% (95% CI 10–12%); the studies had a heterogeneity of 41% based on the funnel plot and a low risk of bias.

Conclusion The prevalence of VAH is low, but in the presence of this condition, the changes are mainly in diameter rather than morphological. If it is present, some clinical safeguards must be taken to avoid complications such as stroke.

Keywords Vertebral artery · Encephalic irrigation · Vertebral artery hypoplasia · Variation anatomical · Vascularization brain · Clinical anatomy

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Abbreviations

VA	Vertebral artery
VAH	Vertebral artery hypoplasia
sVAD	Spontaneous vertebral artery dissection

Introduction

The vertebral artery (VA) are muscular vessels that are branches of the subclavian artery and end in an anastomosis at the lower limit of the pons, forming the basilar artery; this route runs through the transverse foramen of the first to sixth cervical vertebrae [1]. These arteries are responsible for blood circulation to the back of the brain [2] and constitute the main blood supply system for structures such as the brain's occipital lobe, cerebellum, brainstem, and upper part of the spinal cord [3]. Topographically, the VAs are divided into 4 portions. The first section moves along the dorsal part from its origin until it enters the foramen of the sixth cervical vertebra. From here, we continue with the second segment, which is located within the transverse foramina from the sixth to the second cervical vertebra. The third part is the extracranial distal portion, which is short and sinuous, passes through the transverse foramen of the atlas, and then bends posteriorly and medially, running posteriorly to the lateral mass of the atlas; then, it makes a sharp turn, perforates the dura mater of the spinal cord, and enters the skull through the foramen magnum. Finally, the fourth segment is intracranial and ends when the vertebral arteries fuse at the lower edge of the pons to form the basilar artery [3].

One of the conditions that can present as a variant is vertebral artery hypoplasia (VAH). This condition has no consensus definition, with definitions varying by the study; however, the main descriptions include a VA with a diameter less than 2.0 mm [4]; a diameter less than 3.0 mm and a length difference greater than or equal to 1:1.7 [5]; and a VA with a diameter less than 3.0 mm, a maximum blood flow systolic velocity less than 40 cm/s, and a resistance index value greater than 0.75 [6]. The literature has reported that the prevalence of VAH varies according to the population studied, fluctuating between 2.34 and 26.5% in European [7, 8] and Indo-Asian [9–11] groups; this wide range may be attributed to the lack of consensus in the definition of VAH. Unilaterality is observed in 26.5% of cases, while bilaterality is recorded in 1.6% [11]. Otherwise, in terms of laterality, the presence of a hypoplastic right vertebral artery reaches 6.2% of the population, and 4.5% for the left one [12]. In many cases, VAH can go unnoticed, as it can present in its asymptomatic form [10, 13]. However, it is important to consider that this condition can predispose patients to develop posterior circulation strokes [14–16], ischemic strokes [16], VA atherosclerosis [11, 15, 17], and ipsilateral spontaneous vertebral artery dissection (sVAD) [18, 19].

The objective of this systematic review and meta-analysis was to identify the anatomical characteristics and prevalence of VAH and its relationship with alterations in the irrigation of the posterior cerebral region and the cerebral arterial circle (of Willis).

Methods

Protocol and registration

This systematic review and meta-analysis were performed and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20]. The registration number in the International Prospective Register of Systematic Reviews (PROSPERO) is CRD4202222466.

Eligibility criteria

Studies on the presence of VAH and its association with any clinical condition were considered eligible for inclusion if the following criteria were met: (1) population: samples from cadaveric dissections or live images of VAH; (2) results: prevalence of VAH variants and their correlation with pathologies of the neck region and the brain territory that is supplied by the VA, and classification and description of anatomical variants based on normal anatomy and classifications and descriptions proposed in the literature; (3) studies: research articles, research reports, and original research published in English in peer-reviewed journals and indexed in the reviewed databases. On the contrary, the exclusion criteria were the following: (1) population: animal studies; (2) studies that analyzed variants of the venous system outside the renal region; (3) studies: letters to the editor or comments.

Electronic search

We systematically searched MEDLINE (via PubMed), Web of Science, Google Scholar, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus, and the Latin American and the Caribbean Literature on Health Sciences (LILACS) from inception until January 2024. Our search strategy included a combination of the following terms: "vertebral artery" (mesh), "encephalic irrigation" (no mesh),"vertebral artery hypoplasia" (no mesh), "variation anatomical" (no mesh), "vascularization brain" (no mesh), and "clinical anatomy" (no mesh), using the Boolean connectors AND, OR, and NOT. The search strategies for each database are available in the supplementary material.

Study selection

Two authors (CR and AQ) independently screened the titles and abstracts of references retrieved from the searches. We obtained the full text for references that either author considered potentially relevant. We involved a third reviewer (JV) if consensus could not be reached.

Data collection process

Two authors (MO and AQ) independently extracted data on the outcomes of each study. The following data were extracted from the original reports: (1) authors and year of publication, (2) country, (3) type of study, (4) sample characteristics (sample size, age, distribution, and sex), (5) VAH prevalence and morphological characteristics, (6) statistical data reported by each study, and (7) main results.

Assessment of the methodological quality of the included studies

The quality assessment was performed using the methodological quality assurance tool for anatomical studies (AQUA) proposed by the International Evidence-Based Anatomy Working Group (IEBA) [21]. Data extraction and quality assessment were independently performed by two reviewers (JV and CR). We involved a third reviewer (JSG) if consensus could not be reached. The agreement rate between the reviewers was calculated using kappa statistics.

Statistical methods

The data extracted from the meta-analysis was interpreted by calculating VAH prevalence using JAMOVI software [R Core Team, 2021] [8]. A DerSimonian-Laird model with a Freeman-Tukey double arcsine transformation was used to combine the summary data. In addition, a random effects model was used because the VAH prevalence data was highly heterogeneous. The degree of heterogeneity between included studies was assessed using the chi-square test and the heterogeneity (I^2) statistic. For the chi-square test, the p-value proposed by the Cochrane collaboration was considered significant at 0.10. Values of the I^2 statistic were interpreted with a 95% confidence interval (CI) in the following way: 0–40% might not be important, 30–60% might indicate moderate heterogeneity, 50–90% might represent substantial heterogeneity, and 75–100% could represent a significant amount of heterogeneity [21].

Results

Included articles

A total of 145 articles from different databases met the criteria and search terms established by the research team. The filter was applied to the titles and/or abstracts of the articles in the consulted databases, and the primary criterion for the elimination of duplicates was used. In total, 112 full-text articles were evaluated for eligibility for inclusion in this meta-analysis and systematic review. Eighty-eight studies were excluded because their primary and secondary results did not match those of this review or because they did not meet the established criteria for good data extraction, resulting in 24 articles being included for analysis (n = 8847 patients, images, and cadavers) (Fig. 1).

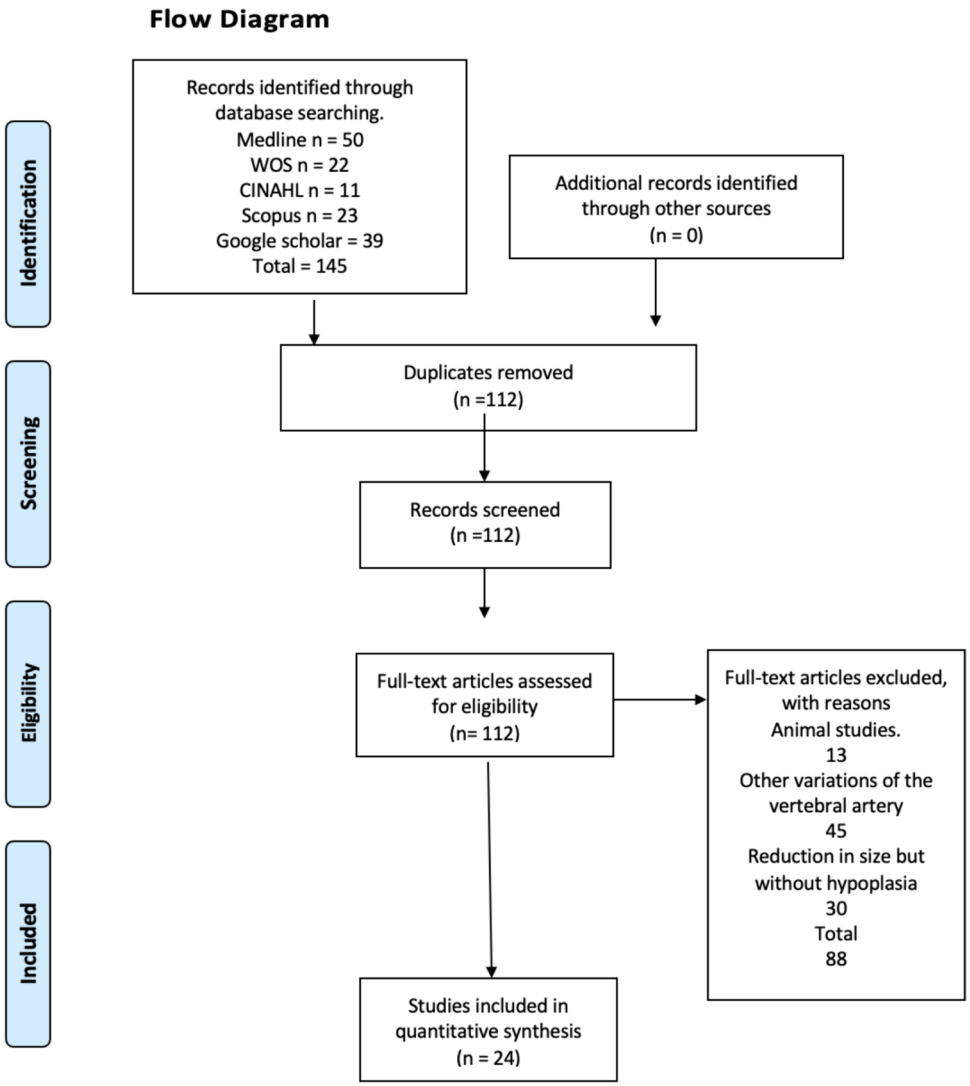
Characteristics of the studies and the study population

Among the 24 studies included in this review (n = 8847) [4, 5, 10, 13, 14, 16, 19, 20, 22–39], 11 came from Asia with a diverse geographical distribution (n = 3755; 42.4%), 11 from Europe with predominance in Eastern European countries (n = 4880; 55.2%), 1 from North America (n = 39; 0.4%), and 1 from Africa (n = 173; 2%). Topics and articles from Oceania were discarded. Regarding sex, of the total sample of 8847, 4008 (45.3%) were men, 3221 were women (36.4%), and in 4 articles with 1618 subjects (18.3%), sex was not specified. Finally, regarding the laterality of the variant, 961 individuals presented right VAH, 498 presented left VAH, 31 presented bilateral VAH, and finally, 516 did not report the laterality of their sample. Finally, the average VAH diameter reported was 2.3 mm with an SD of 3.23 mm among the studies included in this review (Table 1).

Description of variants

The VAs typically emerges from the proximal portion of the subclavian artery as its first branch. Along their course, they are divided into 4 portions, and the name depends on the VA's anatomical location, such as V1, V2, V3, and V4 [3, 41–43]. Some anomalies could appear in the VA; one of them, which this study addresses, is VAH. This is an anatomical congenital variation [19] that has no consensus definition, but the main descriptions include a decrease in the diameter of the lumen of one or both VAs of 2–3 mm and/or a decrease in blood flow to approximately less than or equal to 30–40 mL/min [9, 22] in the posterior cerebral circulation [6, 23]. This condition could predispose subjects to cerebral circulation problems, the most common being

Fig. 1 Diagram of search



ischemic strokes of the posterior cerebral circulation [19]. In this research about the hypoplastic variation of the VAs, we found no studies that could specifically define a VAH classification; this is due to the different morphometry that the blood vessels present from one individual to another (Fig. 2).

Prevalence

To calculate the prevalence of RV variants in the studies included in this review (Table 2), 4 proportion forest plots were made. For the prevalence of VAH, 6 studies were included [13, 14, 24, 28, 31, 33], which presented a prevalence of 11% (95% CI from 10 to 12%); for the included sample, the heterogeneity was 41% (Fig. 3 and Table 2). For this f sample, the funnel plot graph shows an important asymmetry that presents a p-value of 0.02, which is directly related to this interstudy symmetry (Fig. 4).

Risk of bias of included articles

Twenty-four articles were evaluated with the AQUA Checklist to analyze the risk of bias in 5 domains. For the first domain, which covers the description of the study's objectives and characteristics, all studies presented a low risk of bias. The second domain is the correct reporting of the study design. Twenty-two studies presented a low risk of bias in this domain, and 2 presented a high risk since they did not clearly report their studies' design [10, 20]. For the third domain, which analyzes the study's methodological characteristics, 22 studies presented a low risk of bias, while 2

Table 1 Characteristic included studies

Author	Example Total N	Prevalence	Characteristics of variants	Geographic region	Sex example	Clinical consideration
Acar, 2005 [22]	37 patients	17 patients (45.9%)	Vertebral artery flow volume less than ≈30–40 mL/min, or diameter less than 3 or 2 mm	Turkey	22 men (59.5%) and 15 women (40.5%)	The evaluation of cerebral blood flow that can be used as a diagnostic method, is non-invasive and is easy to apply, is duplex color sonography
Bakalarz, 2022 [23]	240 patients	80 patients (33.3%)	Diameter of the vertebral artery less than 2.0 mm	Poland	104 men (43.3%) and 136 women (56.7%)	In cerebrovascular disease there is a high frequency of VAH. It may be associated with neurological symptoms of the posterior circulation of the brain
Chen, 2010 [24]	1000 patients	95 patients (9.5%)	Diameter of vertebral artery less than or equal to 2.5 mm	Taiwan	582 men (58.2%) and 418 women (41.8%)	Not present
Dinç, 2021 [25]	609 patients	225 patients (36.9%)	Diameter of the vertebral artery with a difference of more than 2 mm (in the V4 segment)	Turkey	368 men (60.4%) and 241 women (39.6%)	Not present
Gaigalaite, 2016 [26]	1109 patients	347 patients (31.3%)	Diameter of the vertebral artery less than 3 mm throughout its entire length	Lithuania	Not present	Age had an influence on the impact of VAH on subsequent stroke/transient ischemic attack and its pathogenic mechanism
Gaigalaite, 2019 [27]	923 patients	146 patients (15.8%)	Diameter of the vertebral artery is less than 2.5 mm throughout its course	Lithuania	527 men (57.1%) and 396 women (42.9%)	Not present
Hu, 2012 [14]	841 patients	91 patients (10.8%)	VA diameter less than 2 mm to less than 3 mm	Chine	577 men (68.61%) and 264 women (31.39%)	VAH is an independent risk factor for stroke due to posterior circulation infarction; however, men with VAH are more likely to suffer this event
Jeng, 2004 [13]	447 patients	52 patients (11.6%)	Vertebral artery diameter less than 0.22 cm or a flow volume less than 30 ml/min	Taiwan	231 men (51.7%) and 216 women (48.3%)	Color doppler ultrasound is effective in the analysis of velocity, diameter and flow volume of the VA, distinguishing congenital variation from steno-occlusion

Table 1 (continued)

Author	Example Total N	Prevalence	Characteristics of variants	Geographic region	Sex example	Clinical consideration
Kavitha, 2014 [15]	15 patients	1 patient (6.7%)	Diameter of the vertebral artery less than 2 mm	India	10 men (66.7%)and 5 women (33.3%)	Partial VAH contributes to acute cerebral ischemia. Arterial variations are etiological factors of various conditions
Miller, 2021 [19]	39 patients	10 patients (25.6%)	Diameter of the vertebral artery less than or equal to 2 mm accompanied by low flow in the posterior cerebral circulation	United States of America	20 men (51.3%) and 19 women (48.7%)	VAH may be a risk factor for decreased cerebral blood flow that could cause stroke and develop cognitive impairment
Min, 2007 [10]	410 patients	98 patients (23.9%)	Diameter of the vertebral artery less than 50% of the contralateral side	Korea	195 men (47.6%) and 215 women (52.4%)	Not present
Mitsumura, 2016 [29]	129 patients	39 patients (31.5%)	VA diameter < 2.5 mm; or < 3.0 mm and a difference in length ≥ 1:1.7; or VA diameter < 3.0 mm, peak systolic velocity < 40 cm/second, and resistance index value > 75	Japan	87 men (67.4%) and 42 women (32.6%)	VAH is an independent risk factor for VA occlusion and posterior circulation ischemia. The analysis of these will be useful for the prevention of ischemic stroke
Oder, 1998 [31]	48 patients	24 patients (50%)	VA diameter is smaller than 3 mm and the Doppler spectrum shows a high resistive pattern	Austria	Not present	Rheological differences between asymptomatic and symptomatic VAH have clinical and research uses in vertebrobasilar occlusive disease
Ogeng'o, 2014 [32]	173 patients	100 patients (57.8%)	VA with internal diameter equal to or less than 2 mm	Kenya	99 men (57.2%) and 74 women (42.8%)	The prevalence of VAH in Kenya is higher than in most populations, and it is more common on the left side and in women
Ozen, 2023 [20]	100 patients	50 patients (50%)	VA diameters between 2 and 3 mm, as well as bilateral AV asymmetry ratio threshold > 1:1.7	Turkey	40 men (40%) and 60 women (60%),	VAH leads to significant changes in the white and gray matter volume of the cerebellum
Park, 2019 [33]	284 patients	29 patients (10.2%).18 (8.7%)	VA diameter ≤ 2.5 mm in segments V1 and V2 and a concomitant diameter asymmetry ratio of ≤ 1:1.7 throughout the AV	Korea	Not present	Evaluation of associated sVAD and VAH should consider dissection subtype and timing

Table 1 (continued)

Author	Example Total N	Prevalence	Characteristics of variants	Geographic region	Sex example	Clinical consideration
Sato, 2014 [34]	28 patients	8 patients (28.57%)	VA blood flow of 40 mL/min or lower	Japan	28 women (100%)	VAH is associated with a high risk of subsequent cerebral stroke and thrombosis due to altered blood flow, and vulnerability to distal stenosis
Sauer, 2016 [35]	815 patients	111 patients (13.6%)	VA diameter less than or equal to 2.5 mm or a difference with the contralateral side greater than 1:1.7	Germany	430 men (52.8%) and 385 women (47.2%)	The prevalence of VAH and ischemic stroke ranges between 7.4 and 30%. In addition, it increases susceptibility in young people
Szárazová, 2014 [16]	80 patients	26 patients (32.5%)	VA diameter in the entire course is confined to < 2 mm, or < 3 mm, or there is a difference between the lateral and contralateral vessels ≥ 1:1.7	Slovakia	54 men (67.5%) and 26 women (32.5%)	VAH, together with cerebral risk factors, may be an additional risk cause for posterior circulation stroke
Thierfelder, 2014. [5]	177 patients	59 patients (33.3%)	Vessel diameter ≤ 2.0 mm in the V4 segment and a concomitant diameter asymmetry of ≤ 1:1.7 along the course of the vertebral artery	Germany	Not present	VAH has a 15.6% prevalence in patients with suspected stroke, associated with hypoperfusion of the posteroinferior cerebellar artery in ≤ 42%
Vilimas, 2022 [36]	742 patients	213 patients (28.7%)	Vessel diameter less than 2.5 mm	Lithuania	307 men (41.4%) and 435 women (58.6%)	VAH may be a risk factor for posterior circulation infarction in subjects under 65 years of age
Yang, 2016 [37]	235 patients	38 patients (16.2%)	Diameter < 2 mm or absence of the lateral vertebral artery on digital subtraction angiography	Chine	152 (64.68%) men and 83 (35.32%) women	VAH increases the risk of posterior circulation ischemic stroke in young people, but its impact on clinical outcomes is small
Zhou, 2015 [38]	336 patients	86 patients (25.6%)	VA diameters of 2 to,3 mm or caliber discrepancy ≥ 1:1.7	Chine	177 men (52.68%) and 159 women (47.32%).	The VA is more likely to be ipsilateral to the hypoplastic side when there are VAs with differing diameters Digital subtraction angiography should be used for diagnosis

Table 1 (continued)

Author	Example Total N	Prevalence	Characteristics of variants	Geographic region	Sex example	Clinical consideration
Zhu, 2015 [39]	30 patients	25 patients (83.3%)	Vertebral artery lumen diameter of ≤ 2 mm	Chine	26 men (86.67%) and 4 women (13.33%)	High-resolution MRI allows identifying atherosclerotic plaques and differentiating between acquired atherosclerotic stenosis and VAH

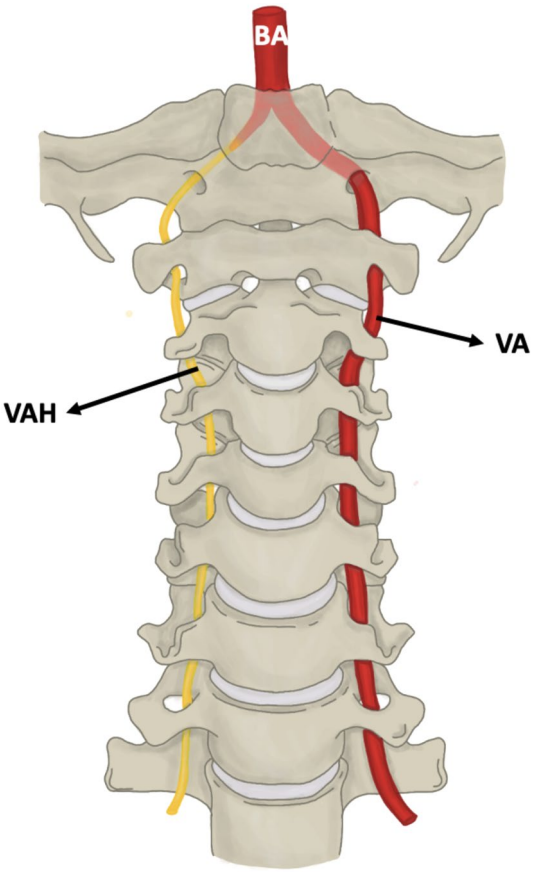


Fig. 2 Representation VAH (In yellow VAH and in red the normal VA) BA: Basilar artery; VA: Vertebral artery; VAH: Vertebral artery hypoplasia (Colour figure online)

Table 2 Prevalence VAH

Author	Total n	Prevalence
Chen et al., 2010 [24]	1000	95 patients (9,5%)
Hu et al., 2012 [14]	841	91 patients (10,8%)
Jeng and Yip, 2004 [13]	447	52 patients (11,6%)
Kavitha et al., 2014 [15]	15	1 patient (6,7%)
Park et al., 2019 [33]	284	29 patients (10,2%)
Sauer et al., 2016 [35]	815	111 patients (13,6%)

presented a high risk since their methodology was unclear [33, 36]. The fourth domain is the correct description of anatomy. Twenty-three studies presented a low risk of bias in this domain, while only one study presented a higher risk since it did not include an anatomical description of the variant but instead merely named it [5]. In the final domain, which involves reporting results, 20 studies presented a low risk of bias, and 4 studies presented a high risk of bias since their results were presented diffusely in tables or discussion sections [10, 24, 25, 30] (Fig. 5).

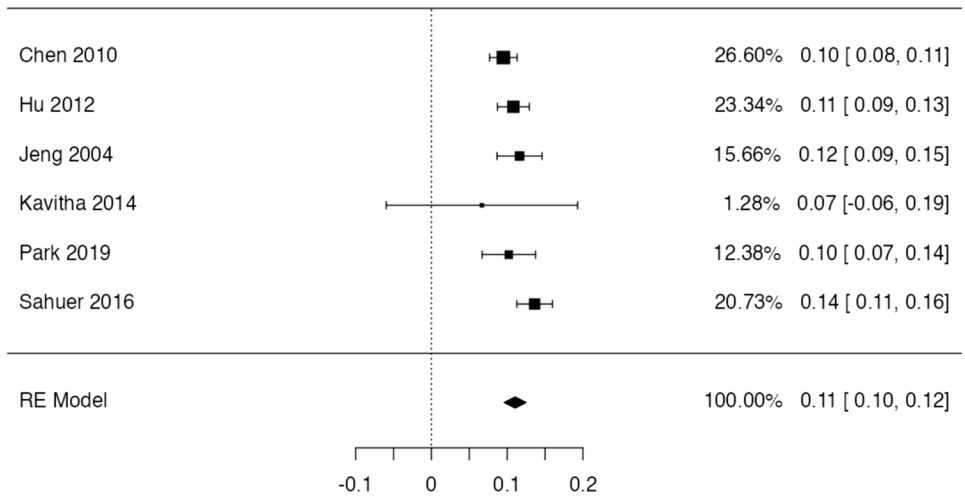


Fig. 3 Forest plot prevalence VAH

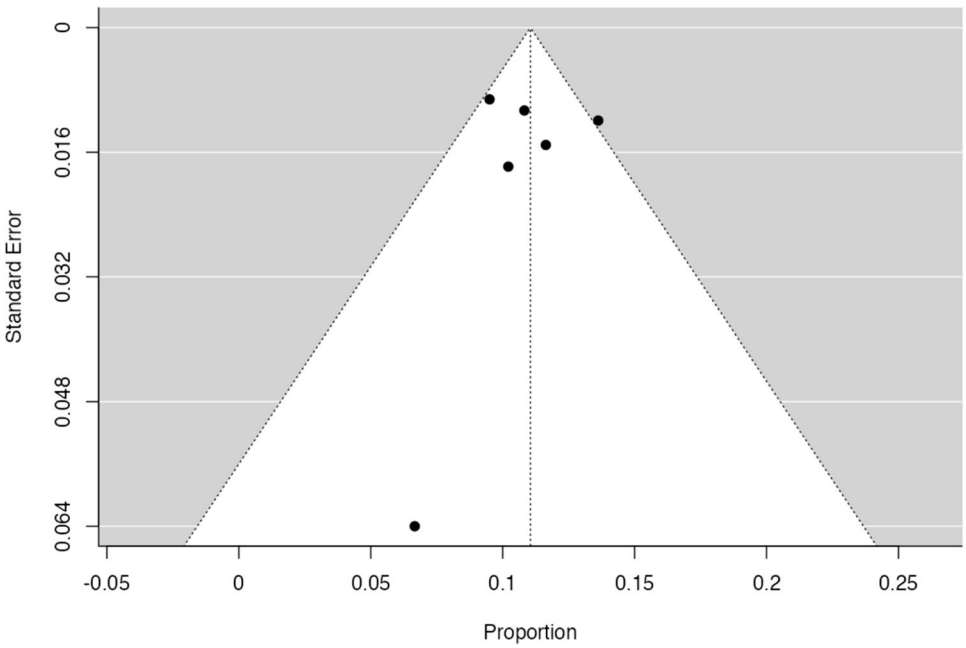


Fig. 4 Funnel plot VA

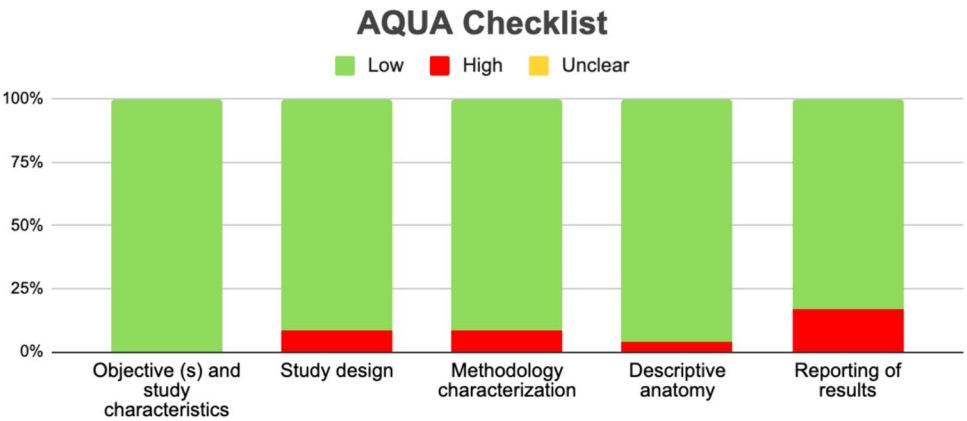


Fig. 5 Risk of bias included studies

Clinical considerations

For the reported clinical correlations, we have found various clinical presentations reported by the articles included in this review, which we will detail below.

Eleven studies [37, 38] mentioned that there is a connection between VAH and cerebrovascular disease, specifically ischemic strokes. Likewise, 2 investigations [14, 27] found that patients with VAH are more susceptible to suffering a stroke due to posterior circulation infarction. Furthermore, 2 research projects [33, 39, 40] reported an association between sVAD and VAH. Also, 1 study [30] indicated that alteration of the dynamic regulation of blood flow could increase the risk of thrombosis.

It should be noted that 1 study [10] pointed out that VAH could increase the risk of developing cognitive impairment due to decreased cerebral blood flow. One study [32] found that VAH leads to significant changes in cerebellar white and gray matter volume. In addition, 1 study [23] mentioned that the coexistence of VAH with a greater frequency of neurological presentations is associated with the posterior arterial circulation of the brain, especially vertigo.

One study [31] demonstrated that statistically significant rheological differences exist between asymptomatic and symptomatic patients with VAH, which may have several potentially important applications for clinical and research approaches to patients with vertebrobasilar occlusive disease. Moreover, 1 study [28] indicated that morphological variations of the VAs are considered an etiological factor of conditions such as arteriosclerosis, infarction, vascular malformations, transient ischemic attack, and syndromes such as Wallenberg's and medial medullary syndrome. Additionally, 1 study [31] showed that the prevalence of VAH in the Black adult population in Kenya is higher than in the majority of the populations studied; it also differs from other populations in that VAH is more common on the left side and in women.

On the other hand, if we analyze the diagnostic methods and images used, 1 study [39] pointed out that high-resolution magnetic resonance images allow the identification of atherosclerotic plaques and differentiation between acquired atherosclerotic stenosis and VAH. Similarly, 1 study [38] demonstrated that digital subtraction angiography remains the examination method of choice for accurate assessment of VAH and sVAD, particularly for differentiation of these conditions. Also, 1 study [22] mentioned that the evaluation of cerebral blood flow using color duplex sonography is non-invasive and easily applicable to all patients, providing a diagnostic method. Likewise, 1 study [13] indicated that color Doppler ultrasound allows the efficient and practical identification and quantification of the diameter, velocities, and flow volumes of the VAs. Because these parameters can be used to precisely define VAH and reference values, they can better differentiate between congenital variation and VA steno-occlusion and guide clinical decision-making.

Discussion

This systematic review and meta-analysis aimed to report the anatomical characteristics and prevalence of VAH, in addition to its association with pathologies in the encephalic and cervical region or, in some special cases, other surrounding structures. Our review's main finding was that the presence of VAH may be related to vascular diseases of the encephalic and cervical regions, giving greater emphasis and care towards possible strokes of the posterior cerebral circulation.

VAH has been sufficiently studied in the literature; however, in our search, we did not find previous systematic reviews or meta-analyses that completely addressed the anatomy of VAH or its correlation with clinical considerations. Therefore, this review is novel and the first with a meta-analysis of this topic. However, we want to mention Klepinowski's 2020 review [18], which indicates that high-riding VA is defined as an internal height of C2 less than or equal to 2 mm and/or a height of the isthmus of C2 less than or equal to 5 mm measured 3 mm lateral to the edge of the spinal canal, by which the ascent is not directly at the level of the lateral masses of C1 but rather ascends close to the spinal segments of C2 and C1 due to the anastomosis between the mentioned vertebrae. This study proposes that we should be paying attention to sudden movements, chiropractic treatment, or surgeries in the region. Although this study makes an important clinical correlation in the upper region of the VA, our study is different because we have only addressed VAH without other predisposing conditions. Another study to which we paid attention is Gottesman's 2012 review [40], which evaluated the symptomatic and imaging characteristics of traumatic or hemorrhagic VA dissections, with the main result that there is no single radiographic sign in the majority of patients with VA dissection, indicating that the best available image is of the Angio CT. Although the VA's size could be associated with a dissection of the VA, this review does not establish any connection to that factor, which is why our study is completely different from it, since we focused specifically on the anatomical and clinical characteristics of VAH.

Regarding the characteristics of the 24 included studies, they came mainly from Asia and Europe, which indicates that the presence of VAH could be more associated with those regions. However, due to the lack of data, we believe that this connection cannot be made, since it could be due to a bias in our search or because not as much research is carried out on the matter in other geographic regions due to lack of resources or other factors. Regarding the sex of the subjects included in the articles, the presence of VAH

was greater in men than in women, but the difference was not great. Therefore, we believe that VAH is not associated with sex according to the data obtained in this study review; however, more studies are needed for this statement to be valid. Finally, regarding the laterality of VAH, there was no difference in presence between the right and left sides, but we can observe that when VAH was present, it was mostly unilateral, since it presented bilaterally in very few cases (only 31). All these considerations must be analyzed when diagnosing, managing, and treating VAH because the clinical behavior could be different depending on individual variation.

Regarding the characteristics of the VA itself and VAH, this anatomical congenital variation does not have an established definition, since this artery has wide interindividual variation; however, VAH is generally considered to have VA lumen diameters of less than 2 or 3 mm, which could be accompanied by a decrease in blood flow to 30 or 40 mL/min. From the studies, it was possible to extract that the predisposition to suffer from posterior cerebral circulation diseases, such as ischemic stroke, is higher in patients with VAH, especially when these indicated values are considerably lower. All these characteristics show that VAH does not yet have a clear definition of an established size, and this should be analyzed from one individual to another, mainly associated with their personal characteristics and genotypes.

Regarding the prevalence of VAH, we were only able to include 6 articles that calculated a prevalence as accurately as possible and whose samples we believe were obtained randomly and not by convenience. Based on those studies, the prevalence obtained for hypoplasia was 11%, as we did not find previous studies that showed a global prevalence. We believe that this could be approximately correct; however, we believe that a 1–10 rate of VAH could be overestimated due to different study-specific factors, and future studies should report this with caution.

Regarding the standard error and the estimated effect of the included studies, it was presented symmetrically in the funnel plot, which is why the publication bias was low for this review. Regarding the bias of the primary studies evaluated with AQUA, the majority of the studies presented a low risk of bias in the 5 domains evaluated, which indicates that the primary studies present a low risk of bias.

Finally, and most importantly, in our review's included studies that reported a clinical connection between the presence of VAH and cerebrovascular disease, we believe that the articles referring to ischemic stroke could be attributed to the decrease in blood flow through the VA associated with hypoplasia. Furthermore, if this is combined with risk factors, such as atheroma that could more easily obstruct the VA, there would be an anatomoclinical connection that explains this association between VAH and stroke. This type of pathology mainly affects the posterior cerebral circulation, since it covers the territory of the basilar artery and the posterior cerebral artery mainly as common trunks and can affect these arteries' irrigation territories by altering their blood flow. Although our study analyzes VAH, we must also take into consideration that the irrigation towards the posterior part of the cerebral arterial circle (of Willis) originates from these arteries, so any alteration, whether in the arteries of the region of the basilar artery or the posterior cerebral artery, could cause an increase in the chances of suffering a cerebrovascular event. Studies such as that of Yang 2016 [37] report that the presence of VAH in the cerebral arterial circle, focused mainly in the posterior region, increases the possibility of a cerebrovascular accident in young patients. On the other hand, Katsano (2013), Mitsumura (2016), and Hsu (2021) [10, 15, 41] report that in the presence of a bilateral VAH, they have a collateral supply in the cerebral arterial circle (of Willis) with a special stroke pattern and an onset of younger stroke; they also report that VAH is more associated with ischemic stroke. Regarding the above, in the presence of VAH, the treating physician must continually monitor the patient to avoid future complications [42–44].

Limitations

This review was limited by the included studies' publication and authorship bias. First, studies with different results that were in non-indexed literature in the selected databases may have been excluded. Second, there could be limitations in the searches' sensitivity and specificity. Finally, the authors personally selected articles. All of this increases the probability of excluding potential cases from countries outside of Asia and North America that are going unreported in the scientific community.

Conclusions

The anatomy of VAH in relation to normal morphology does not present major differences in shape; the difference is only associated with the VA's diameter. This decrease in diameter could reduce the flow to the arteries of the brainstem region, cerebellum, and posterior part of the brain, which could increase the probability of presenting ischemic strokes, in addition to a decrease in collateral flow in the cerebral arterial circle (of Willis) in the middle and anterior regions through the communicating arteries. The above suggests that professionals who treat the cerebral region should be aware of this condition and, in the early diagnosis of asymptomatic patients, follow up regularly to avoid future complications.

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Declarations

Conflict of interest The authors declare no competing interests.

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