

# Growth of the brachial nerve plexus with reference to topographical relation of the medianus nerve ansa with the thoracic wall and shoulder: a histological study using human embryos and fetuses

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#### Research Article

**Keywords:** Brachial plexus, medianus nerve ansa, subclavian-axillary artery, comparative height with ribs and glenohumeral joint, fetal growth

Posted Date: June 14th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3032644/v1

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Additional Declarations: No competing interests reported.

**Version of Record:** A version of this preprint was published at Surgical and Radiologic Anatomy on March 3rd, 2024. See the published version at https://doi.org/10.1007/s00276-024-03317-w.

# Abstract

#### Background

There is currently no information on positional changes in the brachial nerve plexus during prenatal growth. The subclavian-axillary artery passing through the medianus nerve ansa is considered a good landmark for evaluating the height of the plexus.

#### Materials and Methods

We used histological sections from 9 embryos and 17 fetuses (approximately 6–15 weeks of gestational age) to identify the height of the ansa by referring to the level of the rib and the glenohumeral joint.

#### Results

The nerve ansa was usually (23 plexuses) observed at the level of the first and/or second ribs. However, it was sometimes observed above the first rib, at a distance equal to or more than an intercostal width (7 plexuses). In the latter group, the ansa was usually located below the glenohumeral joint. Thus, the joint was located higher than the first rib, although the upper extremities were in the anatomical position for all specimens. The left-right difference in the height of the plexus corresponded to or was less than the width of the first intercostal space. Despite the synchronized growth between the thorax and shoulder girdle, the brachial plexus showed a considerable variation in comparative height; the range corresponded to twice of an intercostal width. Whether the nerve plexus is located high or low is determined at an early developmental stage and is maintained during the later growth stages.

#### Conclusions

The high-positioned plexus might cause nerve injury at delivery, followed by a glenohumeral joint deformity because of the fragility without fixation in the thorax.

## Introduction

Congenital brachial palsy, or Erb's palsy, generally results from nerve injury at delivery and is often followed by a glenohumeral joint and shoulder muscles deformity [5, 6]. This may be caused by an abnormal posture in utero with or without an amniotic band [7, 10, 12]. However, the specific etiology of brachial palsy is often difficult to determine (reviewed by Evans-Jones et al [5]). In contrast, several anatomical abnormalities cause thoracic outlet syndrome in adults, including a cervical rib or first-rib deformity and various types of aberrant or fused scalenus muscle (reviewed by Connolly and Auchincloss [4]). Therefore, the congenital brachial palsy pathology is usually unknown, possibly because its early identification is difficult, whereas the thoracic outlet syndrome is well-investigated via magnetic resonance imaging and observations under open surgery. In the anatomical position (i.e., the upper extremity extended inferiorly along the lateral side of the trunk), the brachial nerve plexus should be present on the lateral sides of the first and second ribs. This site corresponds to the lateral side of the glenohumeral joint. Possibly because of the stability in position, few research groups have focused on the position at which the plexus is liable to injury. In contrast, anatomical research on the plexus has concentrated on the fiber composition and structure of the trunk, cord, and fasciculus (reviewed by Leijnse et al [9]). However, based on the gross dissection of near-term fetuses, Rodrigues de Cunha M et al. [13] suggested that the brachial plexus crossing the medial one-third of the clavicle exerts compressive stress on the nerves. Similarly, Woźniak et al. [17] macroscopically classified the plexus into three types based on its height in reference with the level of the axillary fossa of the skin. However, we were concerned that the topographical relationship between the plexus and the thorax, clavicle, or glenohumeral joint would change during dissection because of the slight differences in the skill, approach, and strength regarding the manual performance.

Consequently, this study has aimed to evaluate the "height" of the brachial plexus in human fetuses. Therefore, we observed histological sections to avoid artifacts resulting from gross dissection. However, the brachial plexus is too large or long to evaluate and compare the height between the specimen cadavers. Therefore, the position of the nerve plexus was represented by the subclavian-axillary artery passing through the medianus nerve ansa, which is a stable morphology among numerous types of the brachial plexus structure in adult cadavers (reviewed by Leijnse et al. [9]) and in near-term large fetuses [18]. The absence of the ansa is a rare variation, Adachi's type-IV axillary artery [1].

# **Materials and Methods**

This study was performed in accordance with the Declaration of Helsinki 1995 (revised in 2013). We examined paraffin-embedded histological sections from nine embryos and 17 fetuses (approximately 6–15 weeks of gestational age; crown-rump length [CRL]: 14.5–116 mm). Regarding all specimens, some sections included not only the brachial plexus but also both the upper thorax and glenohumeral joint. We examined a total of 30 plexuses because the bilateral brachial plexuses of one of the nine embryos and three fetuses were included (Table 1). These sections were a part of a large collection kept at the Department of Anatomy of the Universidad Complutense, Madrid. The embryos were obtained from miscarriages and ectopic pregnancies at the Department of Obstetrics of the university. No information was available on the genetic background of these embryos or abortions. The sectional planes were horizontal (11 specimens), frontal (5) or sagittal (10) (Table 1). The sections were stained with hematoxylin and eosin or Azan stains. This study was approved by the Ethics Committee of Complutense University (B08/374). Most histological photographs were taken using a Nikon Eclipse 80, whereas ultralow magnification photographs (objective lens < x1) were obtained using a high-grade flat scanner with translucent illumination (Epson scanner GTX970).

## Results

In all the specimens examined, the thorax, shoulder girdle, and brachial plexus were likely to develop in a synchronized manner. In contrast, none of the specimens showed unbalanced growth patterns such as a large shoulder attached to a small thorax. Multiple ribs were included in a single section, not only on sagittal or frontal cuts, but also on horizontal cuts because the thorax expands along the anteroposterior axis rather than the mediolateral axis. The subclavian-axillary artery passing through the medianus ansa takes a long longitudinal course that obliquely crossed the nerve plexus in the horizontal and frontal sections (Fig. 1AC). Therefore, attention should be paid to the oblique course of the upper ribs to avoid bias in the evaluation of the height of the nerve ansa. In contrast, it was identified as a spotty cut surface of the artery surrounded by multiple nerve bundles in the sagittal sections (Fig. 2A). Therefore, in the sagittal sections, the plexus-like structure could only be identified as a ladder-like segmental nerve root. However, the sagittal sections had the advantage of clearly showing how the candidate medianus nerve ansa was located higher or lower than the first rib.

Table 1 shows variations in the position or height of the nerve ansa when compared with that of the upper rib or that of the glenohumeral joint in the 30 plexuses of the 26 embryos and fetuses. Rather than the ribs, stability was observed between the glenohumeral joint and nerve ansa; the joint was above (18 plexuses; Fig. 1C and 2AB) or at the same level as that of the nerve (12 plexuses; Fig. 1D). The nerve ansa was observed (23 plexuses) at the level of the first and/or second ribs (Fig. 1). However, it was sometimes located above the first rib (7 plexuses; Fig. 2), and the distance from the rib to it corresponded to or was more than the first intercostal space width. In the latter group, the nerve ansa was usually located below the glenohumeral joint. Thus, the joint was sometimes located higher than the first rib (at a distance greater than an intercostal width), even though the upper extremity was in the anatomical position. In contrast, none of the specimens had the upper extremities with elevation or high flexion at the shoulder. However, the scapula was likely to rotate, as it was attached to the lateral aspect of the round thorax. Therefore, the high-positioned brachial plexus is similar in morphology when a child extends his/her arm upwards as high as possible.

In two of the four specimens examined bilaterally, a left-right difference was observed in the height of the plexus; the difference corresponded to or was less than an intercostal width (Table 1; Fig. 1B and 2B). Moreover, the topographical relationship between the plexus and the glenohumeral joint showed a slight difference. A left-right difference in the structure of the plexus was observed; however, this was out of the scope of our study. The present specimens did not have the abnormality in which the subclavian-artery runs on the superficial side of the scalenus anterior muscle [8, 16].

# Discussion

The upper extremities were in the anatomical positions in all specimens. However, despite the synchronized growth of the thorax and shoulder girdle, the comparative height of the brachial plexus varied considerably. The height range corresponded to twice of an intercostal space width. Because variations were observed at any stage, whether the nerve plexus was located high or low is determined at an early stage of development and is maintained in later growth stages. The synchronized growth

between the shoulder girdle and the thorax most probably occurs because 1) the scapula and rib have a common origin, that is, the somite [3, 11] and 2) the muscles connecting the shoulder and thorax grow simultaneously with the skeleton [2, 14].

A high or low position of the brachial plexus may be a risk factor for brachial palsy. According to the pathogenesis of the thoracic outlet syndrome in adults, a low-positioned brachial plexus likely causes nerve injury, as the humerus and ribs pinch the plexus. However, at near-term, the nerve plexus seems to be sandwiched between the humerus and thorax forming a single slender mass, thus facilitating smooth delivery. In contrast, rotation, bending, or traction of the upper extremity is likely to easily occur in the high-positioned plexus and shoulder because of the abundance of surrounding soft tissue. The glenohumeral joint is usually located above a high-positioned nerve plexus. We were concerned that even in the usual sleeping posture of neonates, a disorder caused by compression and/or extension would occur in the high-positioned plexus because of the fragility without fixation in the thorax. Therefore, in this study, seven of the 30 plexuses were likely to impose a risk. Even slight compression and/or extension and/or extension of the fragile nerves may decrease muscle activity, resulting in a glenohumeral joint deformity.

The loose tissue surrounding the nerve plexus is necessary for pathfinding growing axons in embryos [15, 19], however, if still bulky at later stages, it may cause a pathology at delivery. After birth, or perhaps at near term, the high-positioned brachial plexus and glenohumeral joint were likely to be "corrected" by the active movements of the shoulder. Similarly, the difference in height between the left and right sides was likely corrected during the active postnatal movement of the shoulder muscles.

# Declarations

**Competing Interests** Authors are required to disclose financial or non-financial interests that are directly or indirectly related to the work submitted for publication.

Ethical approval This study was approved by the ethics committee of Complutense University (B08/374).

**Funding** This study was supported by the Wonkwang University in 2023.

### AUTHOR CONTRIBUTIONS

KC: planning; data acquisition; writing; JK: data acquisition; data analysis; MY: data acquisition; data analysis; SH: planning; data analysis; GM: conceptualization; data acquisition; crucial appraisal; JV: supervision; critical appraisal.

Availability of data not applicable

## References

1. Adachi B., Das Arteriensystem der Japaner. Band I., Kenkyusha, Kyoto, pp307-324.

- 2. Brent AE, Braun T, Tabin CJ (2005) Genetic analysis of interaction between the somitic muscles, cartilage and tendon cell lineages during mouse development. Development 132:515-528.
- 3. Chevallier A (1979). Role of the somite mesoderm in the development of the thorax in bird embryo. J Embryol Exp Morphol 49:73-88.
- 4. Connolly MR, Auchincloss HG (2021) Anatomy and embryology of the thoracic outlet. Thorac Surg Clin 31:1-10.
- 5. Evans-Jones G, Kay SPJ, Weindling AM et al (2003) Congenital brachial palsy: incidence, causes, and outcome in the United Kingdom and Republic of Ireland. Arch Dis Child Neonatol 88:F185-F189.
- 6. Hogendoorn S, van Overvest KLJ, Watt I et al (2010). Structural changes in muscle and glenohumeral joint deformity in neonatal brachial plexus palsy. JBJS 92:935-942.
- 7. Hunter AG, Seaver LH, Stevenson RE (2011) Limb-body wall defect. Is there a defensible hypothesis and can it explain all the associated anomalies? Am J Med Genet A 155A:2045-2059.
- 8. Inuzuka N (1989) A case of the scalenus anterior muscle passing behind the left subclavian artery. Okajimas Folia Anat Jpn 66:229-240.
- 9. Leijnse JN, de Bakker BS, D'Herde K (2020) The brachial plexus explaining its morphology and variability by a generic developmental model. J Anat 236:862-882.
- 10. Moran SL, Jensen M, Bravo C (2007) Amniotic band syndrome of the upper extremity: diagnosis and management. JAAOS-Journal of the American Academy of Orthopaedic Surgeons 5(7):397-407.
- 11. Olivera-Martinez I, Coltey M, Dhouailly D et al (2000) Mediolateral somitic origin of ribs and dermis determined by quail-chick chimeras. Development 127:4611-4617.
- 12. Phan TH, Nguyen PTT, Nguyen PN et al (2023) Amniotic band syndrome leading to severe malformations of the newborn: a case report at Tu Du Hospital, Vietnam, and literature review. Annals of Medicine and Surgery 85(3):592-597.
- 13. Rodrigues de Cunha M, Magnusson Dias AA, de Brito JM et al (2020). Anatomical study of the brachial plexus in human fetuses and its relation with neonatal upper limb paralysis. Einstein 18:1-4.
- 14. Rodriguez-Niedenführ M, Burton GJ, Deu j et al (2001) Development of the arterial pattern in the upper limb of staged human embryos: normal development and anatomic variations. J Anat 199:407-417.
- 15. Tosney KW (1991) Cells and cell-interactions that guide motor axons in the developing chick embryo. BioEssays 13:17-23.
- 16. Tsugane HM, Murakami G, Yasuda M (1998) A case of the scalenus anterior muscle lying behind the fifth cervical nerve root. Okajimas Folia Anat Jpn 75:111-118.
- 17. Woźniak J, Kędzia A, Dudek K (2012) Brachial plexus variations during the fetal period. Anat Sci Int 87:223-233.
- 18. Woźniak J, Kędzia A, Dudek K (2013) Variability of the trunks and divisions of the brachial plexus un human fetuses. Adv Clin Exp Med 22:309-318.

19. Yip JW, Yip YPL (1992) Laminin-developmental expression and role in axonal outgrowth in the peripheral nervous system of the chick. Dev Brain Res 68:23-33.

## Table 1

Table 1. Comparative height of the medianus nerve ansa of the branchial plexus in human embryos and fetuses

Specimen	CRL mm	1st or 2nd rib	Glenohumeral joint
se	ctional pla	ne* in the medial side	in the lateral side
IW14.5	14.5H*	1st rib	above the nerve ansa
IW15Lt	15H	1st rib	same level of the nerve
IW15Rt (Fig.1A)		2nd rib	same level of the nerve
SK16 (Fig.1C	) 16F*	2nd rib	above
SL	18S*	between 1st and 2nd ribs	above
SK20	20F	1st rib	same level of the nerve
BR3	20S	2nd rib	same level of the nerve
Gi20	20.5S	2nd rib	same level of the nerve
BO (Fig.2A)	21S	above the 1st rib	above
AR21	21.5F	between 1st and 2nd ribs	above
RX Lt	23.5H	2nd rib	above
RX Rt (Fig.1D	))	2nd rib	same level of the nerve
IW41	27S	between 1st and 2nd ribs	same level of the nerve
IW111	28S	between 1st and 2nd ribs	above
Jin	30S	above the 1st rib	above
Mu2	37H	between 1st and 2nd ribs	same level of the nerve
H46	46S	1st rib	above
LR6	46H	above the 1st rib	same level of the nerve
Be503	48H	between 1st and 2nd ribs	above
C56	56S	above the 1st rib	above
D59	59S	above the 1st rib	above
Mu5	74H	between 1st and 2nd ribs	same level of the nerve
LR1	84H	1st rib	above
B1011Lt (Fig.2B) 97H		above the 1st rib	above
B1011Rt (Fig.1B)		1st rib	above
B6	100H	1st rib	same level of the nerve
ST8Rt (Fig.1E	E) 105F	between 1st and 2nd ribs	above
ST8Lt		1st rib	same level of the nerve
154NT	115H	above the 1st rib	above
B29	116F	between 1st and 2nd ribs	above

\*Sectional planes: H, horizontal; F, frontal; S, sagittal.

### Figures



#### Figure 1

Brachial plexus in the lateral side of the first and/or second ribs in embryos and fetuses.

Panel A, a horizontal section of an embryo of a 15-mm CRL; panel B, a horizontal section of a fetus of a 97-mm CRL (contralateral side, Fig. 2B); panel C, a frontal section of an embryo of a 16-mm CRL; panel D, a horizontal section of an early fetus of a 23.5-mm CRL; panel E, a frontal section of a fetus of a 105-mm

CRL. The subclavian-axillary artery through the medianus ansa is observed on the lateral side of the first rib (panel A, B, and E) or the second rib (panel C and D). The ansa is observed below the glenohumeral joint (joint) in panel C; however, it is observed at the same level as in panel D. Scale bars, 1 mm

abbreviations:

ansa, medianus nerve ansa; joint, glenohumeral joint; AXA, axillary artery; H, humerus; S, scapula; CRL, crown-rump length; SCA, subclavian-artery



### Figure 2

Brachial plexus above the first rib in embryos and fetuses.

Panel A, a sagittal section of an embryo of a 21-mm CRL; panel B, a horizontal section of a fetus of a 97mm CRL (contralateral side, Fig. 1B). The subclavian-axillary artery through the medianus ansa is observed above the first rib (panel A and B); however, it is observed below the glenohumeral joint (joint) in panel B.

### abbreviations:

ansa, medianus nerve ansa; joint, glenohumeral joint; AXA, axillary artery; H, humerus; S, scapula; CRL, crown-rump length; SCA, subclavian-artery