Clinical Implications And Embryological Basis Of Median Nerve Variations In Indian Fetuses

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Abstract

Introduction:
The median nerve, a critical structure for upper limb function, presents considerable variability in its formation, directly affecting surgical interventions and regional anesthesia. This study investigated anatomical variations in the formation of the median nerve in Indian human fetuses and explored their embryological foundations. Comprehensive knowledge of these variations is essential to prevent iatrogenic nerve injury during clinical procedures.
Methodology:
Twenty-three aborted human fetuses, aged 16–40 weeks of gestation, were obtained from the Department of Obstetrics and Gynaecology, after parental consent. Following preservation in formalin, bilateral dissections of the pectoral, axillary, and arm regions were performed in the Department of Anatomy. The cords of the brachial plexus and associated vessels were exposed, and the formation of the median nerve was documented.
Results
Anatomical variations in median nerve formation were identified in 21 of 46 upper limbs (45.65%). While a classical two-root "V" formation was observed in 24 limbs (52.17%), the most prevalent variations were three-root formation (19.57%) and low-level formation (13.04%). Less common patterns included communication with the ulnar nerve (4.35%), formation posterior to the axillary or brachial arteries (6.52%), and single lateral cord origin (2.17%). Chi-square analysis indicated no significant association between these variations and gestational age, crown–rump length, gender, side, or plexus fixation pattern ($p > 0.05$).
Conclusion:
Nearly half of the fetal upper limbs examined displayed variations in median nerve formation. These results suggest that such morphological deviations are a common feature of fetal development, likely arising from early embryological signaling differences in the brachial plexus. Awareness of these patterns is essential for clinicians to minimize iatrogenic injury during nerve blocks and surgical interventions.

Key Words: Median nerve, Upper extremity, Brachial Plexus block, Anatomical variation, Human Fetus, Embryology.

Introduction

The median nerve is a major peripheral nerve of the upper limb, originating from the brachial plexus and playing a critical role in motor and sensory innervation of the forearm and hand. Its classical formation involves the union of the lateral and medial cords of the brachial plexus, typically creating a distinctive "V" formation anterior to the axillary artery (1). However, numerous studies have documented considerable anatomical variability in the median nerve's formation, including aberrant roots, unusual branching patterns, and side-specific differences. These variations hold significant clinical importance, particularly during surgical procedures, regional anesthesia, and traumatic injury management, as unrecognized anatomical differences may result in iatrogenic nerve damage or compromised outcomes (2,3).

Despite the research in adult cadaveric specimens (3), data on these anatomical variations within the fetal population—especially among the Indian demographic—remain limited. Understanding the embryological basis for such variability is essential, since deviations in the complex development of the brachial plexus during gestation may account for differences seen at birth and in adulthood. (4). Detailed knowledge of median nerve formation and its variants in human fetuses enhances the anatomical database and supports surgeons and anesthesiologists in preoperative planning and intraoperative decision-making to minimize the risk of complications.

This study aims to investigate the anatomical variability of median nerve formation in Indian human fetuses through meticulous dissection, and to explore the embryological origins of these variations, thereby providing vital insights for clinical and academic applications.

Materials and Methods

The present study was conducted in the Dissection Hall of the Department of Anatomy, SMBT Institute of Medical Sciences & Research Centre (SMBTIMSRC), Nashik, Maharashtra, India. The study was approved by the Institutional Ethics Committee (approval number 1401/SMBT/IMSRC/10/IEC/24/65). Informed written consent was obtained from the parents prior to the inclusion of specimens in the study using Purposive sampling. All procedures were in compliance with the Declaration of Helsinki.

A total of 23 aborted human fetuses, male -14 and female -9 ranging from 16 to 36 weeks of gestational age, were collected from the Department of Obstetrics and Gynaecology. All specimens were preserved in 10% formalin solution soon after collection and stored in appropriately labelled tanks until examination.

Dissection was performed bilaterally in the pectoral, axillary, and arm regions. Skin and superficial fascia were reflected to expose the pectoral muscles, which were delicately separated to access the axillary region. The axillary sheath and associated connective tissue were carefully removed to visualize the cords and branches of the brachial plexus with axillary artery. (5)

The median nerve was identified by tracing its usual origin from the lateral and medial cords of the brachial plexus, lateral to the third part of the axillary artery. Special attention was paid to documenting the formation pattern (classical “V” shape or any variations), number of contributing roots, and relationships with adjacent vessels were recorded, along with any accessory roots or communications.

Observations were systematically recorded for both upper limbs of each fetus, yielding a total of 46 limbs.

Inclusion Criteria:

- Aborted fetuses of Indian origin obtained with written parental consent.
- Gestational age between 16–36 weeks.

Exclusion Criteria:

- Fetuses with gross congenital malformations, traumatic injuries to the upper limb, or evidence of decomposition were excluded from the study.

Result

The present study included 46 upper limbs, of which 28 (60.87%) were from male and 18 (39.13%) from female foetuses. Normal median nerve formation was observed in 24 (52.17%) cases, while variations were noted in the remaining cases, the most common being three-root formation Fig -1). (19.57%), followed by low-level formation (13.04%). Other less frequent variations included communication with the ulnar nerve and formation posterior to the axillary and brachial artery (each 4.35% and 2.17%, respectively). Overall, anatomical variations were present in 21 (45.65%) limbs, while 25 (54.35%) showed normal morphology. The majority of brachial plexuses exhibited normal root pattern (C5–T1) in 40 (86.96%) cases, with prefixed plexus (C4–T1 and C3–T1) observed in 6 (13.04%) cases. Both right and left sides were equally represented (50% each). Age-wise distribution showed that the highest number of specimens belonged to the 28–<32 weeks group (34.78%), followed by 36–<40 weeks (21.74%). Similarly, CRL-based grouping revealed the highest frequency in the 26–<30 cm category (34.78%), followed by 34–<38 cm (21.74%). Distribution of study variables shown in table 1. These findings indicate that while normal anatomical patterns predominate, a considerable proportion of variations exist, particularly in median nerve formation, offering valuable insights for clinical practice and embryological understanding.

Table no 1: Distribution of Study Variables (n = 46 Upper Limbs)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Female	18	39.13
	Male	28	60.87
Median Nerve Formation	Normal (N)	24	52.17
	Three-root formation	9	19.57
	Low-level formation	6	13.04
	Communication with ulnar nerve	2	4.35
	Formation Posterior to axillary artery	2	4.35

	Formation Posterior to brachial artery	1	2.17
	Single lateral cord origin	1	2.17
	Missing	1	2.17
Anatomical Variation	Normal (N)	25	54.35
	Variation (V)	21	45.65
Pre/Post Fixation	Normal	40	86.96
	Prefixed	6	13.04
Roots of Plexus	C5–T1	40	86.96
	C4–T1 (Prefixed)	4	8.7
	C3–T1 (Prefixed)	2	4.35
Side	Left	23	50
	Right	23	50
Age Group (Weeks)	20 – <24	8	17.39
	24 – <28	6	13.04
	28 – <32	16	34.78
	32 – <36	6	13.04
	36 – <40	10	21.74
CRL Group (cm)	18 – <22	6	13.04
	22 – <26	8	17.39
	26 – <30	16	34.78
	30 – <34	6	13.04
	34 – <38	10	21.74
Total		46	100

Normal two-root formation of the median nerve (lateral root from the lateral cord and medial root from the medial cord) was observed in 24 limbs (52.17%), whereas 25 limbs (54.35%) were classified as anatomically normal for statistical analysis. Anatomical variation of median-nerve formation was present in 21 limbs (45.65%). The most common variant was three-root formation (Fig.1), identified in 9 limbs (19.57%), followed by low-level formation (Fig.2) in 6 limbs (13.04%). Less frequent variations included communication with the ulnar nerve (Fig.3) in 2 limbs (4.35%), formation below the axillary artery (Fig.4) in 2 limbs (4.35%), formation below the brachial artery (Fig.5) in 1 limb (2.17%), and origin of the median nerve from a single lateral cord (Fig.6) in 1 limb (2.17%).

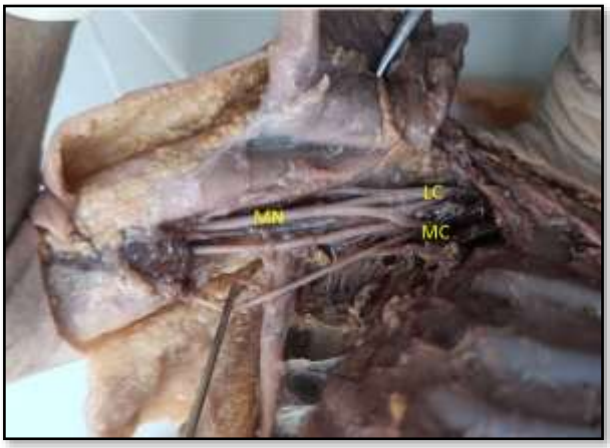

Fig:1 – Formation of MN by Three root

Fig:2 Formation of MN at lower-level than typical formation i.e., lateral to 3rd part of axillary artery

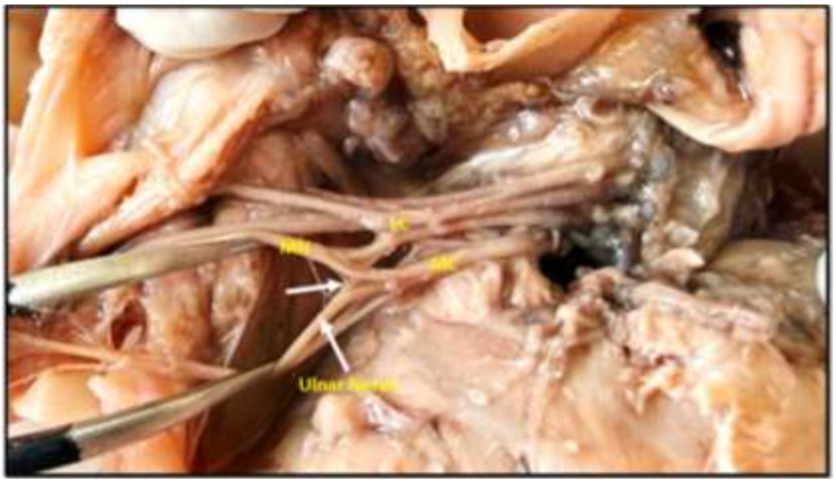

Fig:3 - Communicating Fibres to Ulnar nerve

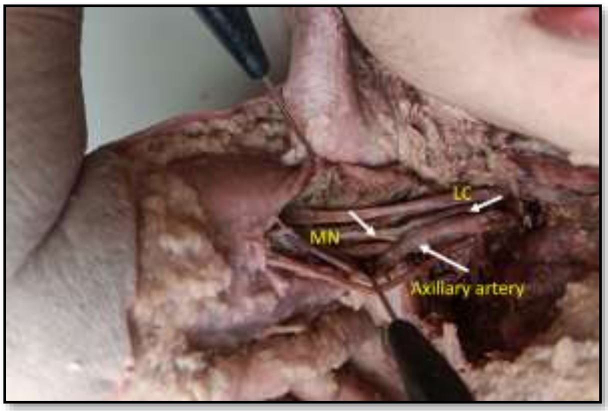

Fig:4 – MN Formation Posterior to Axillary artery

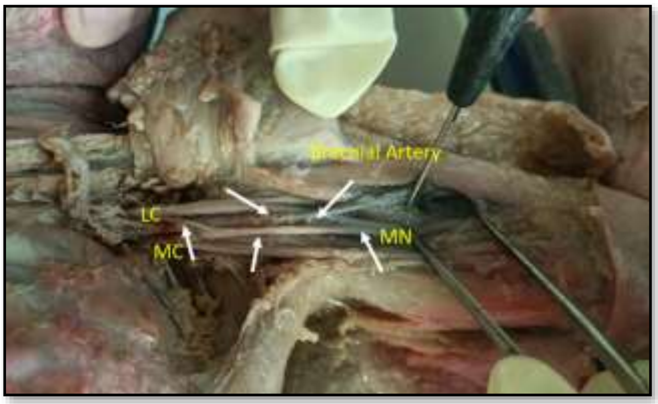

Fig:5 – MN formation Posterior to Brachial artery

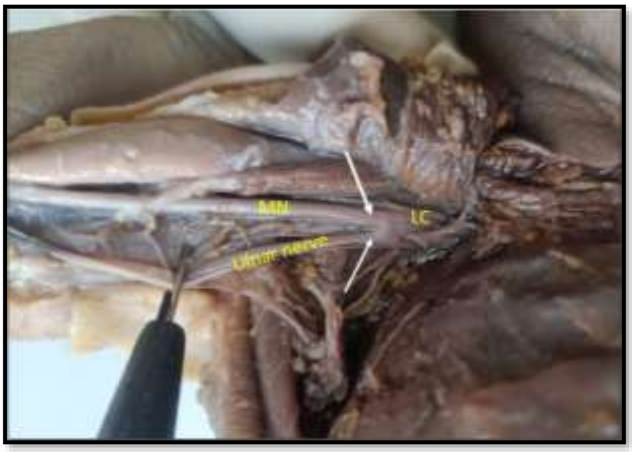

Fig:6 - single root origin (MN arises from lateral cord)

Foot notes: MN – Median Nerve, LC- Lateral Cord, MC- Medial Cord

The distribution of variation across different age groups showed that the highest proportion of variation was observed in the 24–<28 weeks group (66.67%), followed by 36–<40 weeks (50.00%) and 32–<36 weeks (50.00%). In contrast, the 20–<24 weeks and 28–<32 weeks groups showed a higher proportion of normal cases (62.50% each). Overall, variations were present in 45.65% of cases. However, statistical analysis revealed no significant association between age group and variation ($\chi^2 = 1.83$, $p = 0.7665$), indicating that gestational age did not significantly influence the occurrence of variation.

Table 2: Age Group vs Anatomical Variation

Age Group (Weeks)	Normal n (%)	Variation n (%)	Total n (%)	Chi-square test statistics, P val
20 – <24	5 (62.50)	3 (37.50)	8 (100)	Chi-square = 1.83, p = 0.7665
24 – <28	2 (33.33)	4 (66.67)	6 (100)	
28 – <32	10 (62.50)	6 (37.50)	16 (100)	
32 – <36	3 (50.00)	3 (50.00)	6 (100)	
36 – <40	5 (50.00)	5 (50.00)	10 (100)	
Total	25 (54.35)	21 (45.65)	46 (100)	

Analysis of CRL groups showed that variation was highest in the 22–<26 cm group (75.00%), while the lowest variation was observed in the 18–<22 cm group (16.67%), where most cases were normal (83.33%). Other CRL groups showed nearly equal distribution between normal and variation. Despite these differences, statistical analysis showed no significant association between CRL and variation ($\chi^2 = 5.36$, $p = 0.2524$), suggesting that fetal size, as measured by CRL, does not significantly affect the presence of variation.

Table 3 : CRL (cm) vs Variation

CRL Group (cm)	Normal n (%)	Variation n (%)	Total n (%)	Chi-square test statistics, P val
18 – <22	5 (83.33)	1 (16.67)	6 (100)	Chi-square = 5.36, p = 0.2524
22 – <26	2 (25.00)	6 (75.00)	8 (100)	
26 – <30	10 (62.50)	6 (37.50)	16 (100)	
30 – <34	3 (50.00)	3 (50.00)	6 (100)	
34 – <38	5 (50.00)	5 (50.00)	10 (100)	
Total	25 (54.35)	21 (45.65)	46 (100)	

Among females, 33.33% showed variation, whereas among males, 53.57% showed variation, indicating a relatively higher proportion in males. However, statistical analysis revealed no significant association between gender and variation ($\chi^2 = 1.81$, $p = 0.1786$). This suggests that gender does not have a significant influence on the occurrence of variation.

Table 4: Gender vs Variation

Gender	Normal n (%)	Variation n (%)	Total n (%)	Chi-square test statistics, P val
Female	12 (66.67)	6 (33.33)	18 (100)	Chi-square = 1.81, p = 0.1786
Male	13 (46.43)	15 (53.57)	28 (100)	
Total	25 (54.35)	21 (45.65)	46 (100)	

The right side showed a higher proportion of variation (56.52%) compared to the left side (34.78%), while normal patterns were more common on the left side (65.22%). Although there appears to be a trend toward more variations on the right side, statistical analysis did not show a significant association ($\chi^2 = 2.19$, $p = 0.1389$). Therefore, side does not significantly influence variation in this study.

Table 5: Side (Rt/Lt) vs Variation

Side	Normal n (%)	Variation n (%)	Total n (%)	Chi-square test statisti P value
Left	15 (65.22)	8 (34.78)	23 (100)	Chi-square = 2.19, p 0.1389
Right	10 (43.48)	13 (56.52)	23 (100)	

Total	25 (54.35)	21 (45.65)	46 (100)	

Variation was slightly higher in prefixed plexus cases (50.00%) compared to normal plexus (45.00%). However, the difference was minimal, and statistical analysis showed no significant association ($\chi^2 = 0.05$, $p = 0.8186$). This indicates that the type of plexus does not significantly affect the occurrence of variation.

Table 6: Pre-fixed vs Variation

Pre Fixed / Post Fixed	Normal n (%)	Variation n (%)	Total n (%)	Chi-square test statistic P value
Normal	22 (55.00)	18 (45.00)	40 (100)	Chi-square = 0.05, p = 0.8186
Prefixed	3 (50.00)	3 (50.00)	6 (100)	
Total	25 (54.35)	21 (45.65)	46 (100)	

Thus, the study reveals a significant degree of anatomical variability in the formation of the median nerve among Indian fetuses, with a higher frequency observed on the right side. The most common variation was the presence of three roots for the formation of the median nerve, particularly two arising from the lateral cord. Recognition of these variations is vital for surgeons to avoid intraoperative and diagnostic errors.

Discussion

The present study highlights the significant anatomical variability in the formation of the median nerve in human fetuses, with nearly half of the examined limbs (45.65%) showing one or more morphological variants. This finding underscores the importance of detailed knowledge of median-nerve anatomy for anatomists, anaesthesiologists, and surgeons, given the nerve's critical role in upper-limb function and its close relationship to major neurovascular structures in the axilla and arm.

In this cohort, the classical two-root formation of the median nerve (lateral root from the lateral cord and medial root from the medial cord) was observed in 24 limbs (52.17%), whereas 25 limbs (54.35%) were classified as anatomically normal for statistical analysis. Anatomical variation was present in 21 limbs (45.65%), indicating that such deviations are not rare but rather common in the fetal period. This prevalence is consistent with previous fetal and cadaveric studies that report a wide range of median-nerve morphological variants.(6,7,8)

The three-root formation and single-lateral-cord origin of the median nerve likely represent persistence of transient embryological contributions that normally regress during development. During limb-bud formation, ventral primary rami extend into the mesenchyme and establish dynamic neuro-muscular interactions; alterations in molecular signalling or guidance cues can produce supernumerary roots, low-level formation, or atypical cord origins, reflecting the mosaic nature of brachial-plexus morphogenesis rather than true malformations.(8,9)

The embryological basis for these variations lies in early upper-limb development, where ventral primary rami invade the mesenchyme and contact differentiating mesodermal condensations that give rise to muscle and connective tissue. This early neuro-muscular interaction is essential for normal patterning; disruption in molecular signalling between mesenchymal cells and neuronal growth cones can result in atypical nerve pathways or positions, including median-nerve formation posterior or atypical to the major arteries, likely reflecting altered guidance cues or persistence of transient embryological connections.(10)

Atypical position of the median nerve, including formation posterior to the axillary or brachial artery, has been reported in earlier case-based and cadaveric studies and corresponds to the variations observed in the present study 3 limbs (2 posterior to the axillary artery and 1 posterior to the brachial artery). These positional deviations may alter the expected topographic relationships used in textbooks and atlases, potentially increasing the risk of iatrogenic nerve injury during axillary dissection, vascular surgery, or brachial-plexus block if the clinician adheres strictly to classical descriptions. (11)

A notable strength of the present study is the systematic statistical evaluation of anatomical variations against key demographic and morphometric parameters. Morphological variations were observed more frequently in the right upper limb (56.52%) than in the left (34.78%), and in male fetuses (53.57%) than in females (33.33%). The observed laterality bias is consistent with earlier reports by Akhthar et al., suggesting possible embryological or genetic influences on asymmetric nerve development. (7) However, rigorous bivariate chi-square analysis revealed no statistically significant association between variation and gender ($\chi^2 = 1.81$, $p = 0.1786$) or laterality ($\chi^2 = 2.19$, $p = 0.1389$). Similarly, although the highest proportion of variation occurred in the 24–<28-week gestational group (66.67%) and the 22–<26 cm CRL group (75.00%), these developmental and morphometric factors did not significantly influence the occurrence of variation ($p = 0.7665$ for age group and $p = 0.2524$ for CRL, respectively). Furthermore, the type of brachial plexus (normal vs. prefixed) showed no significant association with median-nerve variation ($\chi^2 = 0.05$, $p = 0.8186$).

The most common anatomical variation observed was three-root formation of the median nerve, present in 19.57% of limbs (9 cases). This finding aligns with the variable incidence rates reported in global studies: Uysal et al. described this variant in approximately 5% of cases, Jyoti et al. in 17%, Budhiraja et al. in 22.4%, and Chitra and Anandhi in 2.7%. These differences likely reflect ethnic and methodological diversity, but the consistent report of supernumerary roots across populations suggests that three-root formation is a relatively common anatomical variant. Embryologically, such supernumerary roots may represent persistent ventral-ramus contributions that normally regress during development, underscoring the complex, mosaic nature of brachial plexus formation and the inherent plasticity of peripheral nerve patterning in the fetal period. (12,13,14,15)

The brachial plexus demonstrates distinct topographic relationships with the scalene muscles during early gestation (before 20 weeks), whereas after 28 weeks its morphology and spatial arrangement closely resemble those of the adult plexus. (16)

Out of 46 upper limbs dissected, 32 were aged 28 weeks and above, 14 of which exhibited anatomical variations closely resembling adult-type configurations. These late-gestational variants mirror patterns observed in the adult population and should be taken into account when interpreting or predicting morphological diversity in clinical and surgical practice.

This study also suggests that the observed variants are naturally occurring developmental configurations rather than malformations linked to the assessed demographic and biometric factors. Nevertheless, the relatively small sample size limits the power to detect subtle yet biologically relevant associations, and larger multicentre fetal-anatomy studies may be required to explore putative relationships with genetic or environmental factors.

Limitations and Recommendations for Future Research

This cohort remains relatively small and geographically confined. The study relied on gross dissection alone, without adjunct histological evaluation or advanced imaging techniques, which may limit the resolution of finer fascicular and microanatomical details. Future research should aim to include larger, multi-center fetal populations and incorporate molecular, histological, and advanced imaging modalities to further elucidate the developmental mechanisms underlying these anatomical variations. Longitudinal studies correlating fetal median-nerve patterns with adult neuroanatomy would also be highly valuable for refining surgical approaches and regional anaesthetic techniques.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this study.

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Ethical Considerations

The study was approved by the Institutional Ethics Committee of National Institute of Medical Sciences & Research, Nims University Rajasthan Jaipur, (NIMSUR/IEC/2024/870) and SMBT IMS & RC, Nashik, Maharashtra (1401/SMBT/IMSRC/10/ IEC/24/65). Fetuses were obtained from the Department of Obstetrics and Gynecology with informed consent from legal guardians. All procedures adhered to the Declaration of Helsinki.

Declaration of AI use

During the preparation of this manuscript, the primary author used Perplexity AI to improve grammar and phrasing. The tool provided suggestions to enhance clarity, coherence, and correctness. All content was reviewed and edited by the authors, and the primary author takes full responsibility for the final version.

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