

## **Prevalence of various anomalies of costal element at cervico-thoracic junction in and around lucknow region of uttar pradesh: A radiological study.**

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### **Abstract**

**Morphological diversities of the costal element at the cervico-thoracic junction adversely affect the positioning of its various neurovascular and soft tissue structures which form the etiological basis of symptoms in many cases of a non-traumatic type of Thoracic Outlet Syndrome (TOS). These rib variants represent disturbances of early organogenesis and are associated with stillbirths, childhood cancers, and several other congenital malformations. The present study aims to document the current prevalence, gender preferences, and laterality associations of various costal anomalies at the thoracic outlet in the reference population.**

**A retrospective cross-sectional analytical study was conducted on 1474 PA skiagrams of the cervico-thoracic region, which comprised 919 males and 555 females of zero days to 73-year age. In 13.02% population, costal element exhibited anomalous development. Anomalies of the costal process of C7 vertebra showed higher(12.20%) prevalence compared to the thoracic first(0.81%). Elongation of the cervical 7 transverse process was most common(10.71%) followed by cervical rib(1.49%), rudimentary first rib (0.54%), and fusion of first and second ribs(0.27%). Cervical 7 costal anomalies showed a significant inclination towards females. No significant association with laterality and sidedness was observed for any of the anomalies. The study highlights a higher prevalence of an elongated transverse process of C7 compared to cervical rib and first rib anomalies in the reference population.**

**Keywords:** Cervico-thoracic junction, Cervical rib, Elongated transverse process, Rudimentary first rib, synostosis.

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### **Introduction**

In the 18<sup>th</sup> century, the cervical rib was identified as a victim in cases of Thoracic Outlet Syndrome (TOS), and in the 19<sup>th</sup> century, the anomalous first rib drew its attention [1]. In the latter part of the 20<sup>th</sup> century, extensive work has been done by the biologists to understand the genetic factors associated with these anomalies. Every vertebra has a costal element that forms a proper rib only in the thoracic region. At other sites, costal process fuses with the so-called transverse process. Prolongation of limb buds carries away the segmental nerves with it, and as the growth of the vertebral column is more rapid than upper limb, spinal nerves assume an oblique course, and now these nerves do not allow the development of ribs in the cervical region [2]. As the development of scleral tissue is preceded by neural or vascular tissues, the rib

abnormalities occur secondary to the erroneous formation of these structures [3]. This explains the presence of the cervical rib in a "prefixed" brachial Plexus with only a small neural contribution from the T1 nerve root. Similarly, in the "postfixed" Plexus with a prominent contribution of the T2 root to the brachial Plexus, the first thoracic rib is often rudimentary [4,5].

Rib development at the Cervico-Thoracic Junction (CTJ) is of special interest because of an evolutionary constraint on the number of cervical vertebrae. All mammals, including humans except the sloth and manatees, have seven cervical vertebrae [6]. This trait is conserved because of the expression of the Hox gene. These genes help in early anterior-posterior patterning of the paraxial mesoderm, hence decides the sequential order of development of the vertebrae. Mutations in the Homeobox are associated with

changes of one body part into the likeness of others, and transition zones are most vulnerable to such mutations [7,8]. Therefore, if a mutation occurs at the CTJ either the seventh cervical vertebra (C7) starts resembling thoracic, and its costal element develops into rib, or the first thoracic vertebra (T1) resembles cervical and shows first rib aplasia or hypoplasia.

Recent studies suggest the role of genes like Pax-1, Myo-D, and SHH in the differentiation of the ribs, which are also involved in the development of other regions. Therefore, rib anomalies are commonly found to be associated with aberrant bronchi, cardiovascular field defects, and neural defects, which most times may cause stillbirths [6,9]. Cervical rib is more prevalent in children with lymphoblastic leukemia, astrocytoma, and germ cell tumor because homeobox genes equally important play a role in tumor suppression and carcinogenesis [10,11]. Polytopic effects of genes associated with rib development make it a constant component of several congenital syndromes [5,12]. Therefore, rib anomalies at CTJ are good phenotypic markers of disturbances in early organogenesis and associated comorbidity of varying degree.

Congenital rib anomalies can be categorized into three major classes: numerical aberrations resulting in supernumerary or aplasia of ribs; segmentation errors leading to fusion and bridging of ribs, and re-segmentation anomalies giving rise to bifid ribs [13]. Anomalous development of the costal element at CTJ may present with complete or incomplete Cervical Rib (CR); the elongated transverse process of seventh cervical vertebra (ETP of C7); Rudimentary or Floating or Hypoplastic First Rib (RFR); Variable degree of synostosis or bridging of cervical, first and second ribs; bifurcated or forked first rib and central defects bridged by ligament bands.

The involvement of CR in the etiology of TOS makes it popular despite the fact that other anomalies are equally important in deranging structural topography at the outlet [14]. Though isolated case reports of bony anomalies other than CR are plenty, studies stating their prevalence in our population are missing. Considering the phenotypic significance of costal anomalies at CTJ and their under-reporting from the reference population, the present study aims to observe the prevalence of various anomalies at the thoracic outlet.

## **Methodology**

The present research was a retrospective cross-sectional analytical study. The census method was used to collect data in the current study, where 4056 digital x-rays of the cervico-thoracic region in the PA view were got during the study period, among which only 1474 digital X-rays were found suitable to incorporate in the present study, as per inclusion and exclusion criteria. The radiographs included 919 males and 555 females in the age range of zero days to 73 years. The study was conducted at the data bank of

the radiology department over six months.

## **Inclusion and exclusion criteria**

Radiographs were studied carefully to document the prevalence of anomalies of the costal element of C7 and thoracic first vertebra. Radiographs in which the concerned area was not clear for any pathology were discarded.

## **Diagnostic criteria for the anomalies**

For each anomaly, criteria were pre-defined and independent observations were done by three observers. Finally, all positive cases were reanalysed and confirmed by an expert radiologist for overall prevalence, gender, and laterality association. The following criteria were used for the identification of various anomalies [14].

- The transverse process of the Cervical 7 (C7) vertebra is oriented transversely, whereas that of Thoracic 1 (T1) is directed laterally and upwards.
- Cervical rib: If a rib articulates with the C7 vertebra by a well-defined joint or originates from its transverse process. The anterior end of such a rib may form a joint with the first rib (synostosis or pseudoarthrosis) or if short may remain free.
- Elongated or enlarged transverse process of C7 vertebra (also known as transversomegaly/apophysomegaly): If the transverse process of 7th cervical vertebra projects beyond the lateral end of the transverse process of T1 vertebrae provided the head of the patient is not turned sideways.
- Rudimentary or floating or hypoplastic first rib: A rib articulating with the first thoracic vertebra with the tapering anterior end not reaching to the sternum. Such a rib may join the second rib.
- Synostosis of first and second ribs: Fusion of shafts or anterior ends of first and second ribs.
- Bifurcation of the first rib or bifid first rib or forked rib: Anterior end of the first rib dividing into two and articulating via two separate costal cartilages with the sternum.

Ethical clearance was obtained by the institutional committee. The data were entered first in MS excel 2016, and the anomalies were statistically analyzed by using IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0, IBM Corp., Armonk, NY. Groups were compared by using Pearson Chi-square test of independence, and Fisher's exact two-tailed test was applied. The results were statistically significant at  $P < 0.05$ .

## **Results**

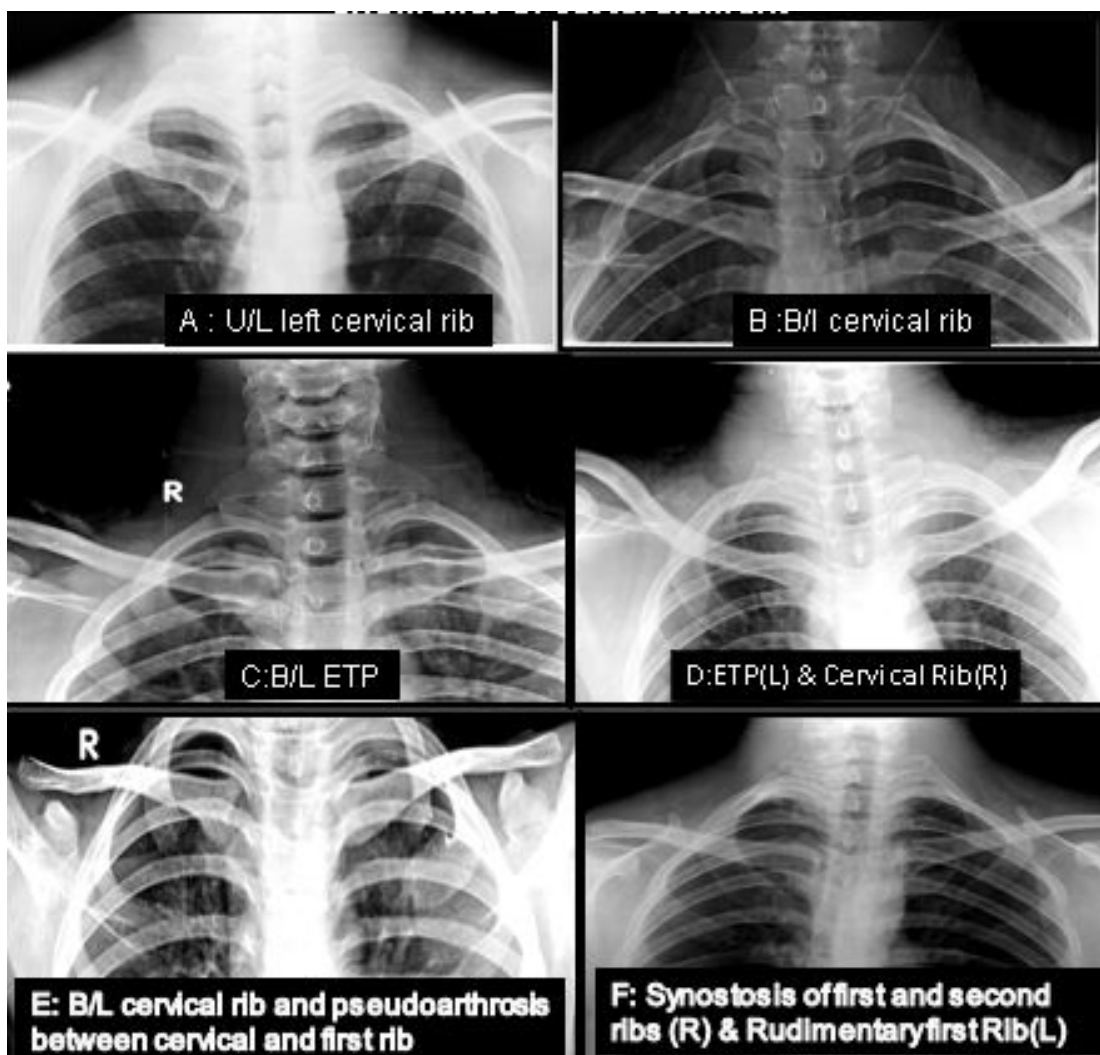
In the present study, 13.02% of subjects exhibited an anomaly of the costal process at the cervico-thoracic junction. Anomalies of the costal process of the seventh cervical vertebra were more usual than that of the first thoracic vertebra. The most frequent anomaly was the

elongated transverse process of C7 vertebra (10.71%) followed by the cervical rib in 1.49% population (Figures 1A-1C). Females were having a significantly higher prevalence (18.20%) of anomalies as compared to males (9.9%). Out of all anomalies, the prevalence of ETP of C7 and the cervical rib was significantly higher in females (Table 1). Anomalies were predominantly unilateral with no preference for right or left (Tables 2 and 3). Gender did not exhibit any significant difference as far as a unilateral or bilateral anomaly was concerned (Table 1). First rib anomalies were less frequent. Only 11 cases were observed of hypoplasia and fusion anomaly, out of which rudimentary first rib was more prevalent (Figures 1D-1F). In the present study, two types of fusion anomalies were observed. In two cases, synostosis between the first and second rib (Figure 1E) and one case, pseudoarthrosis between the cervical and first rib was observed (Figure 1D). Though these anomalies were more commonly observed in males, the difference was not significant statistically. These anomalies were also not found to be associated with sidedness or laterality (Tables 2 and 3). In the present study, first rib anomalies were found to be more common in males as compared to cervical anomalies, which were more frequent in females.

**Table 1:** Gender wise prevalence of various anomalies of costal element at cervico-thoracic junction.

Type of anomaly	Gender			P-value <sup>#</sup>
	Male (n=919)	Female (n=555)	% of Total (n=1474)	
Cervical Rib*	9	13	1.49%	0.036
Elongated transverse process of C7 vertebra*	73	85	10.71%	<0.001
Rudimentary first rib**	6	2	0.54%	0.7176
Fusion anomaly of first rib**	2	1	0.27%	1.000
Total anomalies*	91	101	13.02%	<0.001

\*Pearson Chi-square test of independence, \*\*Fisher's exact two tailed test applied. #The result is statistically significant at P<0.05



**Figure 1.** PA radiographs of cervico-thoracic region showing various anomalies of costal element.

**Table 2:** Association of laterality with various anomalies of costal element at cervico-thoracic junction.

Parameter	Side		P-value#
	Unilateral	Bilateral	
Cervical Rib**	Male	8	0.6161
	Female	10	
Elongated transverse process of C7 vertebra*	Male	53	0.274
	Female	68	
Rudimentary first rib**	Male	4	1.000
	Female	1	
Fusion anomaly of first rib**	Male	2	1.000
	Female	1	
Total anomalies*	Male	67	0.435
	Female	80	

\*Pearson Chi-square test of independence, \*\*Fisher's exact two tailed test applied. #The result is statistically significant at P<0.05

**Table 3:** Association of laterality with various anomalies of costal element at cervico-thoracic junction.

Parameter	Side		P-value#
	Male	Female	
Cervical Rib**	Male	2	0.6161
	Female	6	
Elongated transverse process of C7 vertebra*	Male	27	0.274
	Female	26	
Rudimentary first rib	Male	2	1.000
	Female	2	
Fusion anomaly of first rib**	Male	1	1.000
	Female	1	
Total anomalies*	Male	32	0.674
	Female	35	

\*Pearson Chi-square test of independence, \*\*Fisher's exact two tailed test applied. #The result is statistically significant at P<0.05

## Discussion

The prevalence of cervical rib is observed radiologically either in the general population or in patients with symptoms of TOS. Data of such variations are also reported from the cadaveric or surgical studies. Radiological studies, in the last two decades, reflect a 0.6% to 6.2% prevalence of CR among the various populations of the world (Table 4). In India, it was observed that a similar range of prevalence of CR (0.6% to 6%) which reflects its great diversity of geography and demography (Table 5). In the present study, the prevalence of CR was 1.49%. Gupta et al. reported only a 0.6% prevalence of CR from the same geographical area

as that of the existing study [27]. Another study from the southern part of India reported 6% prevalence [32]. Apart from ethnicity, the most probable reason for the difference in the results could be a marked difference in the sample size as well as undefined criteria for the identification of CR.

The studies conducted in certain Muslim populations show a higher prevalence of CR (2.5-6.2%) [15-17,19,26]. Researchers tried to correlate it with the consanguinity. As the lowest prevalence of CR (0.6-0.7%) is also observed in the Muslim population, but from the different geographical area suggests that consanguinity may play a role but alone is not responsible for its higher frequency [22,24]. Factors related to methodologies like sample size, gender, and age of the subjects, criteria for interpretation of CR at one end, and environmental and genetic factors on the other also play a significant role.

The present research included subjects from day zero to 73 years of age in the study. Some researchers excluded childhood subjects from their study and argued that it would be difficult to identify cervical ribs in these subjects because, by this time, it may not fuse with the vertebra [24,33] Whereas, radiological evidence of CR has been found as early as in the 14th week of gestation and also in children of 6-7 years [10,34]. Excluding childhood subjects of the study, the cohort may be responsible for apparent discrepancies of prevalence in different studies.

The identification criteria of CR or its variants also need clarity. In many studies, the prevalence of ETP is not included as a separate entity while documenting CR frequency. The earliest classification of CR by Gruber has included ETP of C7 as one subtype [35]. Later the classification was oversimplified into partial and complete CR in which ETP of C7 was considered as a variant of partial type [5,12,35]. Whereas, according to some authors, when a cervical rib is very short and fuses with the transverse process, it is termed as Elongated Transverse Process or transversomegaly [10,36,37], differentiation between a short or partial or incomplete cervical rib and an elongated C7 transverse process is dependent on being able to visualize the cervical rib as separate from (but articulating with) the transverse process on a radiograph [18].

The frequency of ETP of C7 is relatively higher than CR and varies from 0.15% to 23% in different studies. (Tables 4 and 5) Zahrani et al. noted its prevalence to be only 0.15% of the Saudi population [15]. A few decades later, Bhokari et al. observed an interim increase in its incidence to 23%. Gulf countries have shown an interim increase in the prevalence of CR also from 1.9 to 3.4%. It was proposed that this increase may be either due to alteration in the population gene pool because of a high rate of consanguinity or higher rate of malignancy in their population [19].

**Table 4:** Comparison of prevalence, laterality, sidedness and gender preference of anomalous cervical costal element of C7 vertebra among different study populations of world.

Authors/Year	Geographical Area/ Population	Number of Subjects	Prevalence %		Laterality/ Sidedness		Gender	
			CR	ETP of C7	CR	ETP of C7	CR	ETP of C7
Zahrani et al [15]	Saudi Arabia	1300	1.9%	0.15%	BL	-	F	-
Gulekon [16]	Turkey	6630	3%	-	ULR	-	39	39
Erken et al [17]	Turkish	1053	6.2%	21%	ULR	ULR	F	M
Merks et al [10]	Caucassian	881	2.2%	-	NM	-	NM	-
J Brevin [18]	London	1352	0.74%	2.21%	UL	-	F	F
Bokhari et al. [19]	Saudi Arabia	1000	3.4%	23%	ULR	ULR	F	F
*Viertel et al. [20]	North America	3404	2.0%	-	UL	-	F	-
**Walden et al. [21]	American	2500	1.2%- 2%	-	-	F	-	39
Ezeofor SN et al. [22]	Nigeria	6571	0.7%	-	BLR	-	F	-
Lalchan S et al. [23]	Nepal	3600	1.1%	-	UL/R	-	F	-
Kolade&Salaem [24]	Nigeria	1520	0.7%;	-	BL	-	F	-
***Davran [25]	Turky	650	3.39%	-	BL	-	M	-
Shinvari et al. [26]	Afghanistan	800	2.5%	-	UL/R	-	F	-

\*CT study, \*\*CT & MRI Study, \*\*\*MDCT Study  
BL=Bilateral; UL=Unilateral, R=Right; L= Left; M=Male; F=Female; NM=Not mentioned

**Table 5:** Comparison of prevalence, laterality, sidedness and gender preference of anomalous cervical costal element among different study populations of India.

Authors/Year	Region of India	No. of study subjects	Prevalence %		Laterality/ Sidedness		Gender	
			CR	ETP of C7	CR	ETP of C7	CR	ETP of C7
Gupta et al. [27]	Lucknow, UP North India	12950	0.6%;	-	BL	-	F	-
Gulekon [16]	Turkey	5000	1.22%	-	UL	-	M	-
Erken et al [17]	Turkish	1871	2.67%	14.96%	UL/R	BL	F	F
Merks et al [10]	Caucassian	1500	0.8%	1.4%	BL	BL	F	F
J Brevin [18]	London	8000	0.79%;	-	BL	-	F	-
Bokhari et al. [19]	Saudi Arabia	100	6%	-	BLL	-	M	-
Present study	Lucknow, UP North India	1474	1.49%	10.71%	ULL	ULR	F	F

BL=Bilateral; UL=Unilateral, R=Right; L= Left; M=Male; F=Female

The prevalence of ETP of C7 observed in the present study (10.71%) is though less than that observed in the Kashmiri population (14.96%) but is starkly more than that observed in the population of Uttarakhand (1.4%). [29,30]. It is claimed that ETP and CR show a genetic transmission of autosomal recessive type and that consanguinity increases the chances of expression of recessive genes [33,38]. The fact that the Muslim community predominates in Kashmir and also in and around Lucknow, so in this situation, when all other parameters are similar, the consanguinity could be one of the potential factors for the high prevalence of ETP.

Cadaveric studies seem to be more promising for providing genuine evidence for most bony anomalies. A prevalence of 2.67% of the CR was reported in the Maharashtra region of India [39]. In another multicentric study on 250

cadavers, reported 1.6% and 9.6% prevalence of CR and ETP of C7, respectively, without significant association with gender and laterality [37]. In the surgical case series of the patients presenting with symptoms of TOS, the prevalence of CR is much higher (up to 24%) [5,37], but these studies may not reflect the true prevalence in the general population.

In the present study, females exhibited a higher frequency of cervical costal anomalies in a statistically significant manner in consensus with most studies, barring a few (Tables 4 and 5). The deformity is observed in both genders, but the higher prevalence in females need further exploration.

A greater number of unilateral cases as compared to bilateral for cervical costal anomalies were observed in the

present research, though the difference was statistically insignificant. Several positive cases with asymmetrical bilateral anomaly (Figure 1D) i.e. CR on the right and ETP of C7 on the left side, were counted as individual unilateral anomalies of the respective sides. Perhaps this would have been responsible for the higher frequency of unilateral cases in the present study.

The occurrence of unilateral deformity of bilateral traits represents a proxy of developmental disturbances because of genetic or environmental stress [40]. In mice models, diminished coordination between the development of the right and left somites is observed most prominently around CTJ due to deficient retinoic acid signalling [41]. Unilateral costal anomalies of C7 were slightly higher on the right side in the present study, which resonates with the findings of most of the other studies (Tables 4 and 5).

During development, the CR forms and then regress to the C7 transverse process. Various stages in this evolution range from a complete C7 rib to rudimentary forms associated with a fibro cartilaginous band [3]. This concept is strengthened by the observation on a cadaver where 7 cm long CR was confirmed as cartilaginous in the skiagram [39]. The size of the costal element depends on the differentially expressed HOX genes [42]. Presence and size of cervical rib is proportionally associated with the severity of medical illness [43,44]. Higher prevalence of ETP of C7 in comparison CR can be very well correlated with this fact. Perhaps subjects with ETP might have fewer severe comorbid conditions as compared to CR, therefore, have a better chance to survive.

The current research reported a higher prevalence of anomalous cervical costal elements as compared to thoracic. In these thoracic anomalies, the prevalence of RFR was higher than compared to that of synostosis of first and second rib (Table 1). Davran et al. reported a 0.31% prevalence of RFR in the Anatolian population compared to 3.39% prevalence of CR in an MDCT study [25]. In a study on deceased fetuses and infants, Galis et al. reported 54.8% prevalence of CR in comparison to 2.1% of RFR [43]. These observations affirm that the anomalies of the first thoracic costal element are rare as compared to cervical. The potential mechanism for such a phenomenon is still unexplained. Osteological specimens showing synostosis between first and second ribs have been reported in the literature and have been termed as a bicapital rib [45,46]. In radiological studies, 0.008-0.77% prevalence of synostosis anomaly of the first rib has been noted [13,25,47,48].

Adverse effects of costal malformations at thoracic outlet depend upon their size and associated defects of fascio muscular components [49,37]. The presence of a prominent transverse process of C7 has been shown to have a 2.64 times greater risk for developing brachialgia [50]. Evidence suggests that the anomalies of the first rib are responsible for various symptoms of TOS [14,51-55]. Synostosis of rudimentary first rib with the second rib may present even with stroke [56].

The diagnosis of the bony anomalies at CTJ is usually done by X-rays. Sometimes, to confirm the diagnosis, CT scan is recommended. But the associated fascio-muscular anomalies which may additionally be the potential cause of symptoms may be missed by using these methodologies; therefore, MR examination should be done [57]. Apart from etiology for TOS, anomalous ribs at a thoracic outlet may indicate an underlying systemic disorder; hence a thorough evaluation of such individuals may further help in anticipating diseases in advance [58].

## Conclusion

A total prevalence of anomalous development of the costal element at CTJ was observed to be 13.02%. The present study reported a higher prevalence of cervical rib (1.49%) in the reference population. The elongated transverse process of the 7th cervical vertebrae was the commonest anomaly which was observed in 10.71% subjects. First rib anomalies were less common. For both cervical anomalies, females were affected significantly more. Unilateral cases were more frequent, but no statistically significant preference for laterality or sidedness was observed.

## Limitations

The study has certain limitations, apart from the small sample size, as radiographs were collected retrospectively of patients attending tertiary care hospital, co-morbidities of these patients were not known, hence the study cohort does not represent the prevalence of anomalies in a healthy population subset. However, results highlight the significance of careful observation of the costal element at CTJ for clinicians. This data may be utilized to evaluate any interim shift of these anomalies, which can help to establish any alteration in the genomic architecture over a period of time.

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