

Fetal hemivertebra: associations and perinatal outcome

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ABSTRACT

Objectives To assess the accuracy of antenatal diagnosis of hemivertebra, to quantify the association with coexisting anomalies and to determine the perinatal outcome.

Method This was a retrospective observational study of all cases of suspected fetal or neonatal hemivertebra identified via the UK Southwest Congenital Anomaly Register (SWCAR) between 2002 and 2012.

Results From a total of 88 cases of hemivertebra identified during the study period, data were obtained for 67 of them: 45 (10 isolated and 35 with coexisting anomalies) cases were suspected antenatally and 22 (10 isolated and 12 with coexisting anomalies) were diagnosed postnatally. Of the cases detected postnatally, five (four with coexisting anomalies) were unsuspected and diagnosed at postmortem examination. The most commonly associated anomalies included additional skeletal abnormalities ($n=16$), genitourinary abnormalities ($n=10$), VATER/VACTERL association ($n=5$), cardiac abnormalities ($n=4$) and central nervous system abnormalities ($n=4$). In cases with coexisting anomalies there was a 48% fetal/neonatal loss, compared to 19% in cases with isolated hemivertebra.

Conclusions Although antenatal diagnosis of hemivertebra was accurate, a third of the cases were diagnosed only postnatally. These data suggest a difficulty in antenatal diagnosis of the condition. The majority of cases of hemivertebra had coexisting anomalies, and in these cases the rate of perinatal loss was high. These data should be useful in providing additional information for counseling when a diagnosis of hemivertebra is made. Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.

INTRODUCTION

With improvements in real-time ultrasound, increasing numbers of subtle fetal abnormalities are being identified antenatally, yet the significance of these findings is often uncertain. Hemivertebra is a congenital vertebral abnormality occurring in 1–10 per thousand births^{1–3}. The absence of one of the two chondrification centers results in the absence of half of the vertebral body and neural arch on one side⁴. This may affect single or multiple vertebrae and can result in scoliosis².

There is limited information in the literature to assist counseling in the context of prenatally diagnosed hemivertebra^{5–8}. The aim of this study was to review the cases that have been identified via the UK Southwest Congenital Anomaly Register (SWCAR).

METHODS

All fetuses and neonates diagnosed with hemivertebra between January 2002 and January 2012 in the Southwest of the UK were identified from the SWCAR. The register relies on hospitals in the southwest of England reporting abnormalities that are identified antenatally or postnatally.

All cases of hemivertebra were included and all other spine abnormalities including spina bifida were excluded. Data on maternal characteristics including parity, age and body mass index (BMI) (raised BMI defined as >30 kg/m²) were collected retrospectively. Fetal and neonatal data included gestational age (weeks) at antenatal diagnosis or age at postnatal diagnosis, location of hemivertebra on the spine (cervical, thoracic, lumbar or sacral), coexisting anomalies, karyotype if known, gestational age at delivery (preterm birth defined

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as delivery < 37 completed weeks of gestation) and birth weight (small-for-gestational age defined as < 10th centile). Outcome of pregnancy was categorized as termination of pregnancy, live birth, stillbirth (fetal loss after 24 completed weeks of gestation) or neonatal death (death within 28 days of birth). In the event of fetal or neonatal loss, data were collected from postmortem reports if performed. This project falls under the definition of 'service evaluation' by NRES standards and is therefore not subject to ethics approval (NRES 'Defining Research'; <http://www.hra.nhs.uk/documents/2013/09/defining-research.pdf>).

Data are described as absolute numbers and percentages. Medians and ranges were computed for non-normally distributed continuous variables. Logistic regression analysis was performed to identify associations between time of diagnosis, survival, presence of coexisting anomalies, involvement of single or multiple vertebrae and location of the hemivertebra. Odds ratios (OR) and associated *P*-values were determined for the variables. Statistical significance was declared in cases of *P* < 0.05. All statistical analysis was carried out using SPSS 20.0 (IBM Corporation, Armonk, NY, USA).

RESULTS

A total of 88 cases of hemivertebra were identified over a 10-year period; 21 were from out of area and data could not be obtained. Data were obtained for the remaining 67 cases. Among these, 45 (67.2%) cases were diagnosed antenatally (43 between 18 and 23 weeks' gestation, at the routine ultrasound assessment, and two in the third trimester); 35 (77.8%) of these cases had coexisting anomalies. Twenty two (32.8%) of the 67 cases were diagnosed postnatally; five diagnoses among these were made on postmortem examination and 11 (50%) cases had coexisting anomalies. All fetuses underwent antenatal anomaly screening between 18 and 23 weeks' gestation.

Parity was three or below in all but two women; 10 (15%) of these women were above 35 years of age. Twenty-one (31%) women had a raised BMI and none had a BMI < 18 kg/m². Of the women with a raised BMI, nine were among those with a postnatal diagnosis (median, 38 (range, 30–50) kg/m²) and 12 were among those with an antenatal diagnosis (median, 35 (range, 31–44) kg/m²).

Two women had a family history of hemivertebra requiring spinal surgery and one had a family history of neural tube defects. Forty-seven (70.1%) cases had coexisting anomalies as listed in Table 1 and the remaining 20 were isolated cases of hemivertebra.

Although there was a trend towards a higher neonatal survival rate in cases with single and lower involvement of the vertebrae, the survival rate was significantly greater only in the absence of coexisting anomalies (Figure 1). In comparison to isolated hemivertebra, coexisting anomalies increased the OR of antenatal diagnosis of hemivertebra by 1.6 (1.01–2.77) and that of fetal or neonatal loss by 4.1 (*P* = 0.042) (Table 2).

Table 1 Coexisting anomalies detected among 67 cases diagnosed with hemivertebra (*n* = 47)

System affected	n (%)	Coexisting anomaly	n (%)
Musculoskeletal	16 (34.0)	Additional spine anomalies (scoliosis/kyphosis)	12 (25.5)
		Dysplastic radii	2 (4.3)
		Cleft lip and palate	1 (2.1)
		Goldenhaer syndrome	1 (2.1)
		LUTO	4 (8.5)
Genitourinary	10 (21.3)	Anhydramnios	2 (4.3)
		Renal agenesis	2 (4.3)
		Bilateral dilated kidneys	1 (2.1)
		Large kidneys	1 (2.1)
		Holoprosencephaly	2 (4.3)
Central nervous	4 (8.5)	Ventriculomegaly	2 (4.3)
		Double outlet right ventricle	2 (4.3)
Cardiovascular	4 (8.5)	Transposition of great arteries	1 (2.1)
		Ventricular septal defect	1 (2.1)
		Echogenic bowel	1 (2.1)
Gastrointestinal	1 (2.1)	Trisomy 18	1 (2.1)
Chromosomal	1 (2.1)	VATER/VACTERL	5 (10.6)
Multiple	11 (23.5)	Other	6 (12.8)

LUTO, lower urinary tract obstruction; VATER/VACTERL syndrome, association of vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, and renal and limb abnormalities.

All 20 fetuses in pregnancies that were terminated had coexisting anomalies, of which 18 were diagnosed antenatally. Of the two cases in which hemivertebra was diagnosed on postmortem examination, one had a coexisting partial absence of the sacrum and the other had a lower urinary tract obstruction with oligohydramnios. Three fetuses were stillborn, two of which had an antenatal diagnosis of hemivertebra; one had coexisting renal agenesis and the other had no coexisting anomalies. The third fetus was diagnosed postnatally on postmortem examination and was found to have multiple bifid thoracic vertebrae. Two neonatal deaths occurred. One of the neonates had a normal anomaly scan and antenatal course but failed to breathe and attempts at intubation and tracheostomy failed; postmortem examination revealed absence of the trachea and presence of thoracic hemivertebra. The other neonatal death occurred at 4 days of age in one of the dichorionic twins who had been diagnosed antenatally with an absent stomach, large ventricular septal defect and overriding aorta. The cotwin had normal anatomy on ultrasound examination; his karyotype remained unknown since the parents declined karyotyping. Following delivery at 35 weeks' gestation, the affected twin died, secondary to coexisting anomalies. Postmortem examination confirmed tracheoesophageal fistula and cardiac abnormality and also revealed a single hemivertebra.

Twenty-two cases of hemivertebra were diagnosed postnatally, of which five were diagnosed on postmortem examination as described above. Of the remaining 17 cases, two had scoliosis and six had coexisting anomalies including a cardiac abnormality, ventriculomegaly, VACTERL, tracheoesophageal fistula, bilateral short radii

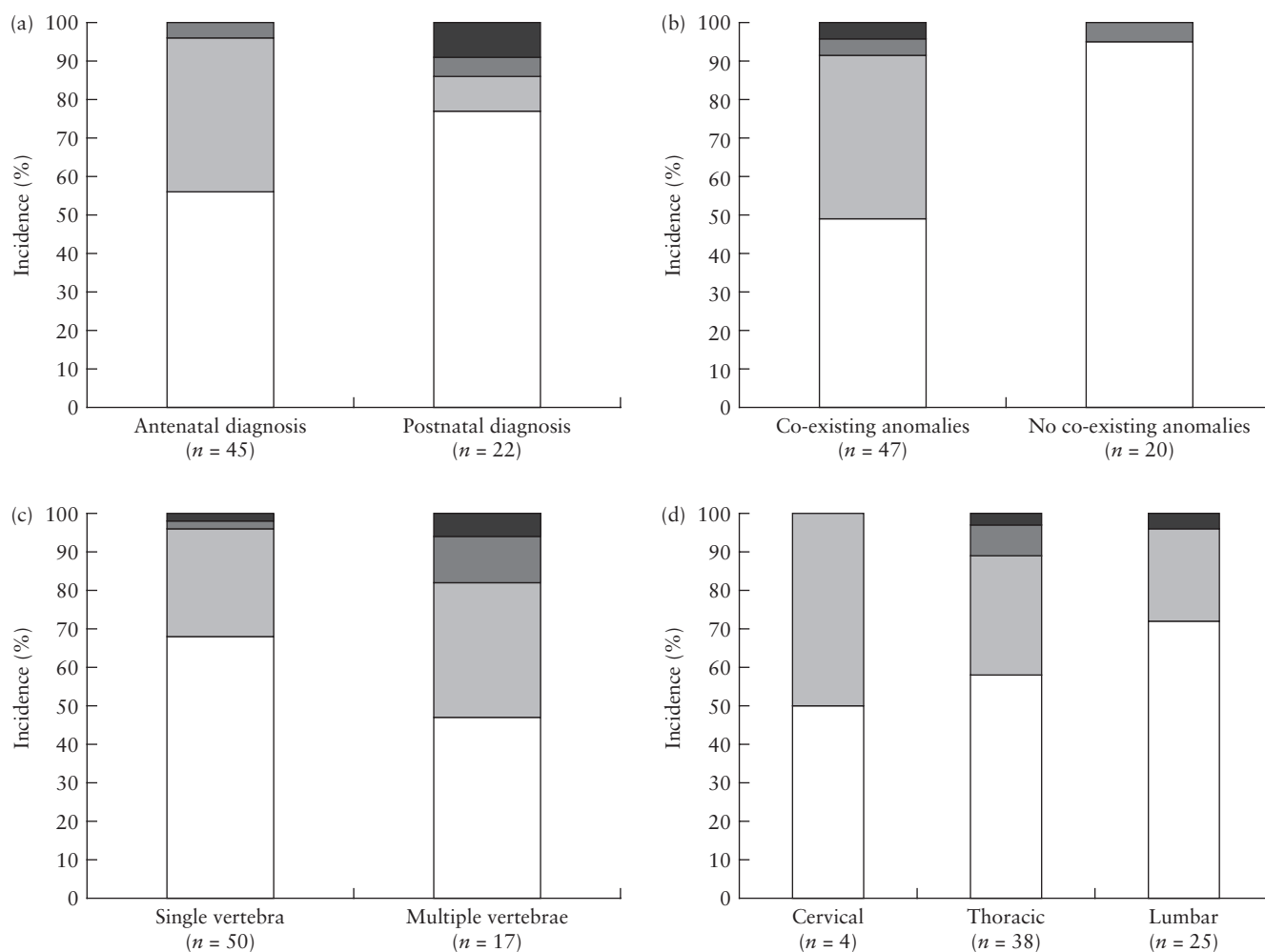


Figure 1 Outcome in neonates diagnosed with hemivertebra, with respect to: (a) time of diagnosis, (b) presence of coexisting anomalies, (c) vertebral involvement and (d) level of spinal involvement. ■, neonatal death; ▒, termination of pregnancy; ▓, stillbirth; □, neonatal survival.

Table 2 Significance of factors associated with pregnancy/neonatal loss determined by logistic regression analysis

Associated factor	Pregnancy loss		
	Rate (%)	OR	P
Antenatal diagnosis	44	2.2	0.135
Coexisting anomalies	48	4.1	0.042*
Multiple vertebral involvement	55	3.4	0.064

* $P < 0.05$. OR, odds ratio.

and sacral agenesis. There was no record of coexisting anomalies in the remaining nine cases. Karyotype analysis was performed in 15 of the cases that were diagnosed antenatally and in nine of those that were diagnosed postnatally, of which five were diagnosed during postmortem examination. All cases with an antenatal diagnosis of hemivertebra had a normal karyotype except one that was found to have trisomy 18.

DISCUSSION

The etiology of hemivertebra is unknown but it has been suggested that it may result from abnormal distribution

of the intersegmental arteries of the vertebral column⁹. Also, sclerotomal deficiency and poor nutritional intake have been hypothesized to be associated with failure of chondrification of the vertebral precursors¹⁰. Although chromosomal abnormalities are not commonly associated with hemivertebra, they may have syndromic associations such as Jarcho–Levin syndrome, Klippel–Feil syndrome and VATER or VACTERL¹¹. There was a wide range of coexisting anomalies across various systems that were identified in our study, for which no association with genetic or environmental factors was identified¹², the most common being musculoskeletal (34%), a finding that is consistent with previous studies^{2,13}.

We found coexisting anomalies in 70.1% of our study group, similar to previous studies (59–73%)^{6,7}. The NHS Fetal Anomaly Screening Programme guideline recommends screening for spinal anomalies by assessing the vertebrae and skin in the transverse and sagittal views¹⁴. However, in the absence of a spine-curvature deformity, especially with single vertebral involvement, the rate of detection of isolated hemivertebra is likely to be low. Fewer than a third of the cases in our study had isolated hemivertebra. This may represent under

Table 3 Summary of published literature on the perinatal diagnosis of hemivertebra

Reference	Design	Anomalies (n (isolated, coexisting))	Coexisting anomalies	Findings/Conclusion
Zelop (1993) ⁸	Antenatal diagnosis	27 (11, 16)	Cardiac, intestinal, renal, intracranial and limb	Coexisting anomalies reduced survival by 50%; isolated hemivertebra was associated with normal karyotype
Goldstein (2005) ²	Antenatal diagnosis	26 (3, 23)	Cardiac, cranial, renal, intestinal and skeletal	Ultrasonographic screening of the fetus allows early prenatal diagnosis of hemivertebra
Weisz (2004) ⁷	Antenatal diagnosis	6 (2, 4)	VATER syndrome, gastroschisis and pyelectasis	Prenatal diagnosis is feasible; antenatal diagnosis and multidisciplinary approach may improve outcome
Forrester (2006) ³	Epidemiological study, antenatal, postnatal	42 (2, 40)	Cardiac, skeletal, cardiac cleft lip/palate, gastrointestinal and genitourinary	Hemivertebra rate of 1.33 per 10 000 live births; normal karyotype in 18 tested; 27% infant mortality, causes of death not known
Segata (2007) ²⁰	Antenatal diagnosis	17 (10, 7)	VACTER syndrome, Pfeiffer syndrome, exomphalos and talipes	Normal karyotype in all cases; isolated hemivertebra(e) might be associated with favorable postnatal outcome
Wax (2008) ⁶	Antenatal diagnosis	19 (5, 14)	Cardiac, genitourinary, skeletal, gastrointestinal and central nervous system	Normal karyotype in all cases; neonates with non-isolated hemivertebra have high mortality rates

Only the first author of each study is given. VATER/VACTER syndrome, association of defects including vertebral, anal, (cardiac), tracheal, esophageal and renal.

diagnosis rather than true incidence and there may be an over-representation of coexisting anomalies in these cases.

We found that the presence of coexisting anomalies is associated with an increased risk of pregnancy loss (OR = 4.1) and with termination of pregnancy. It is interesting to note that in a postnatal series of children requiring surgical excision of hemivertebra due to increasing spine curvature, 45% had coexisting abnormalities¹⁵. Among these, 24% had genitourinary abnormalities and 8% had cardiac abnormalities. This is similar to the incidence of genitourinary abnormalities (21.3%) and of cardiac abnormalities (8.5%) in the group of cases with coexisting abnormalities in our series.

Hemivertebra is the most common cause of congenital scoliosis¹⁶. The diagnosis may not be obvious until the spine deformity becomes evident with increasing curvature, often observed later in childhood¹⁷. Progression of hemivertebra is variable; 25% of cases show no progression into scoliosis, 50% progress slowly and the remaining 25% progress rapidly¹². Optimal timing of intervention is crucial in achieving a straight spine at skeletal maturity and in preventing deterioration of scoliosis. This can be achieved by early diagnosis, thorough assessment and regular follow-up to increase the ability to anticipate progression to scoliosis^{7,13}. Antenatal diagnosis of hemivertebra, being early, allows for planning of postnatal follow-up to achieve a good outcome.

A study of spine anomalies identified in the first trimester of pregnancy showed that early diagnosis of hemivertebra during the antenatal period is associated with higher likelihood of severe spine abnormality, high incidence of coexisting abnormalities and poor

outcome¹⁸. Most of the diagnoses in our series were made between 18 and 23 weeks' gestation when there is a higher likelihood of identifying subtle abnormalities than in the first trimester; therefore, outcomes were different and relatively better. We found a trend towards worse prognosis with an antenatal diagnosis in comparison to postnatal diagnosis, but this difference was not statistically significant.

Prognosis has also been linked to the site and number of vertebrae involved in the hemivertebra¹². Although data that support the relationship of the site to the outcome are inconsistent^{12,16}, we found a trend towards a decreased fetal/neonatal survival rate with multiple, as compared to single, vertebral involvement and according to location higher along the spine, e.g. cervical as compared to lumbar vertebrae (Figure 1). These differences, however, were not statistically significant.

Our study is limited by its retrospective methodology. Furthermore, the data are unlikely to represent true incidence in the population since more subtle anomalies are likely to be missed at ultrasound assessment of fetal anatomy. Changes in ultrasound technology and resolution, and changes to guidelines for assessment of fetal anatomy, would have influenced the cases identified over the duration of the study.

Use of three-dimensional (3D) ultrasound and magnetic resonance imaging (MRI) in fetal imaging has increased over the last decade and has improved antenatal diagnosis. There has been conflicting evidence of an added advantage of using 3D imaging over two-dimensional assessment in the prenatal diagnosis of fetal hemivertebra^{19,20}. This is particularly true with newer ultrasound machines that

provide high-resolution images. However, 3D imaging can be useful as an adjunct in difficult cases and MRI can be particularly useful in evaluation of the spinal cord²¹.

This is the largest series of perinatally diagnosed hemivertebra published to date (Table 3). We confirm that the presence of coexisting anomalies increases the rate of pregnancy loss significantly. These data should inform patients regarding associations with fetal hemivertebra and their outcomes and should allow involvement of a multidisciplinary team to ensure postnatal follow-up and timely assessment.

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