J. Fetal Med. (March 2014) 1:33–39
DOI 10.1007/s40556-014-0010-2

ORIGINAL ARTICLE

At Least an Infantogram if not Perinatal Autopsy

Dipika Deka · Moumita Naha · Vatsla Dadhwal · Madhulika Kabra · Neerja Gupta

Received: 2 June 2014 / Accepted: 3 June 2014 / Published online: 19 July 2014

Abstract To study the feasibility and value of postmortem fetal infantogram (X-ray film) in pregnancies terminated for prenatally diagnosed fetal congenital malformations and stillborn fetuses with congenital anomalies. Forty-two fetuses were diagnosed antenatally by ultrasonography to have fetal congenital malformation, 36 couples opted for medical termination of pregnancy (MTP) and intrauterine death (IUD) occurred in six cases. Informed written consent for autopsy including infantogram was given by 41 couples, one couple permitted only radiographs. On infantogram, the antenatal ultrasound diagnoses were confirmed in all the cases of central nervous system anomalies, but were not useful for genitourinary anomalies or cardiac anomalies. In five cases of antenatally suspected skeletal anomalies, radiographs changed the diagnosis of thanatophoric dwarf to osteogenesis imperfecta type llC in one case and achondrogenesis type 1B in another case. Infantogram made the syndromic diagnosis in three cases—sirenomelia, Roberts syndrome and caudal regression syndrome. Congenital diaphragmatic hernia was diagnosed at infantogram in a case missed on ultrasound. In three cases of nonimmune hydrops, X-ray films correlated with ultrasound findings, but could not find the cause. If autopsy, the 'goal standard' test is refused or cannot be done, at least an infantogram should routinely be done in pregnancies terminated for prenatally diagnosed fetal congenital malformations and stillborn fetuses with congenital anomalies, as it is noninvasive, easily available and consent given. It may change the diagnosis and counseling for future pregnancies, hence very useful in perinatal medicine.

Keywords Congenital anomaly · Radiograph · Ultrasonography · Recurrence risk

D. Deka (✉) · M. Naha · V. Dadhwal
Department of Obstetrics and Gynecology, AIIMS, CI/17, AIIMS, Ansari Nagar, New Delhi 110029, India
e-mail: dpk.deka@gmail.com

M. Kabra · N. Gupta
Genetics Unit, Department of Pediatrics, AIIMS, New Delhi, India

Introduction

After an MTP or a stillbirth due to fetal congenital malformation diagnosed on prenatal ultrasound, most parents want to know whether the fetus was actually malformed or not, and what were the abnormalities. Often, they wish to remove the guilt feelings at terminating a wanted, planned pregnancy, besides being anxious to know whether it is a hereditary condition, the recurrence risk (RR), and the chances of good outcome in future pregnancies. Answers to these questions are often incomplete and inaccurate without valuable information gained from an autopsy which is the 'gold standard' and the 'final diagnosis.' 'Perinatal autopsy' is defined as the postmortem examination on the newborn fetus or baby performed to ascertain and confirm the cause of death. An infantogram or radiograph of the fetus/newborn is an essential component, and intriguing especially for suspected skeletal defects as it may confirm and correlate completely to the antenatally suspected malformation, or the defect may not be found, or additional malformations may sometimes be detected that could change the final diagnosis. This is very significant for genetic counseling of the couple about RR, and essential in targeting tests for periconceptional and antenatal care in subsequent pregnancies [1, 2].

Table 1 Correlation of infantogram with ultrasound and autopsy findings in single organ malformations

I	Musculoskeletal malformation on USG	Infantogram	Final diagnosis
1	Radial bone hypoplasia	Radial bone hypoplasia	Radial bone hypoplasia
2	B/L lower limbs symmetrically flexed	Fixed flexion deformity at hip, fixed extension deformity at knee. *Nonsyndromal arthrogryposis* (Fig. 1)	*Nonsyndromic arthrogryposis*
3	Arms flexed at wrist, legs hyperextended, B/L club foot	Fixed flexion at wrist, hip joints, fixed extension at knee joints. *Nonsyndromal arthrogryposis*	*Nonsyndromic arthrogryposis*
4	Thanatophoric dwarf	Depressed nasal bridge, extreme non-ossification of cranial vault, thin ribs contiguous separate fractures, multiple fractures of long bones. *Osteogenesis imperfecta type llC* (Fig. 2)	*Osteogenesis imperfecta type llC*
5	Short limb dwarf (thanatophoric dwarf)	Short limb bones, short ribs, cupped metaphysis, spurs in metaphysic of femur, poor ossification of spine. *Achondrogenesis type 1B* (Fig. 3)	*Achondrogenesis type 1B*

II	GIT malformation on USG	Infantogram	Final diagnosis
6	Hyperechoic bowel, gross ascites	*Speckled calcification in abdomen* (Fig. 4)	? Cystic fibrosis (lost to follow-up for molecular diagnosis)
7	Large omphalocele with liver inside	NAD	Omphalocele

III	CNS malformation on antenatal USG	Infantogram	Final diagnosis
8	Ventriculomegaly	Enlarged skull	Hydrocephalus
9	Anencephaly	Absent cranial vault	Anencephaly
10	Anencephaly	Absent vault	Anencephaly
11	Meningomyelocele	Defect in spine	Meningomyelocele
12	B/L ventriculomegaly	Enlarged skull	Hydrocephalus
13	Holoprosencephaly	NAD	Holoprosencephaly
14	Meningocele Chiari ll malformation	Defect in cervical spine	Meningocele Chiari ll malformation
15	Hydrocephalus	Enlarged skull	Hydrocephalus
16	Meningomyelocele	Defect in spine	Meningomyelocele

IV	GUT malformation on USG	Infantogram	Final diagnosis
17	B/L cystic enlarged kidneys	NAD	B/L MCDK
18	B/L cystic enlarged kidneys	NAD	B/L MCDK, USG guided biopsy inconclusive
19	B/L absent kidneys	NAD	B/L absent kidneys
20	B/L cystic enlarged kidneys	NAD	B/L MCDK
21	B/L kidneys hugely enlarged with multiple small cysts	NAD	PCKD
22	B/L cystic enlarged kidneys	NAD	B/L MCDK
23	Huge dilated bladder, key hole appearance of urethra	NAD	Posturethral valve with Lt. hydronephrosis
24	B/L enlarged kidneys with multiple cysts of variable sizes	NAD	Unilateral renal agenesis with MCDK

V	CVS malformation on antenatal USG	Infantogram	Final diagnosis
25	Single vessel arising from the base of heart, large VSD	NAD	Congenital heart disease
26	ASD + VSD, cerebellar hypoplasia	NAD	ASD,VSD, trisomy 21
27	Oligohydramnios	NAD	Large ASD, SUA trisomy 21

ASD atrial septal defect, *B/L* bilateral, *DWM* Dandy–Walker malformation, *MCKD* multicystic kidney disease, *NAD* no abnormality detected, *PCKD* polycystic kidney disease, *USG* ultrasonography, *VSD* ventricular septal defect

Currently in India, perinatal autopsy is rarely performed, primarily because of the general ignorance of its importance not only among the public but even among the obstetricians, the wrong notion about autopsy being of little practical use for future reproductive outcome, and the lack of basic facilities to perform an autopsy. In addition, for postmortem examination to be carried out on the fetus, an informed written consent of parents is required. Often, the recently bereaved, emotional couple considers the idea of dissection of their child gruesome and horrifying, and so

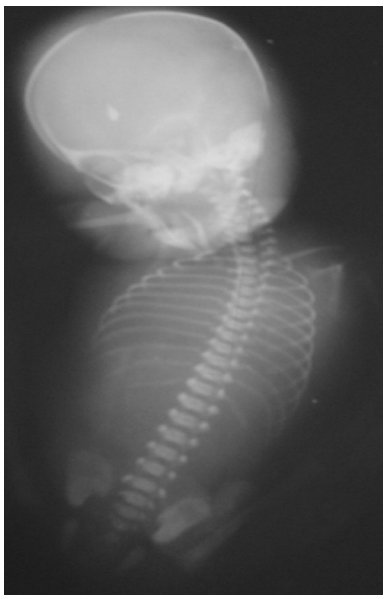

Fig. 1 Infantogram showing arthrogryposis (nonsyndromal)

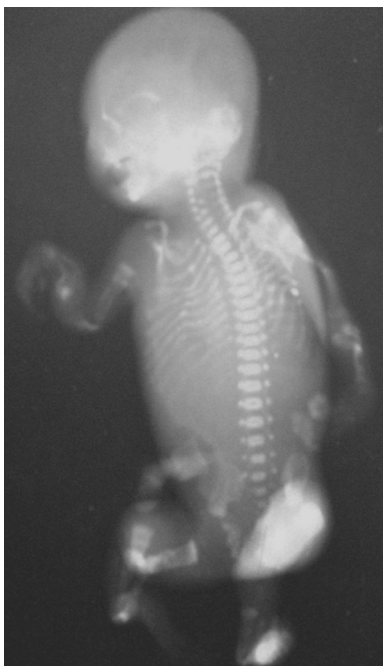

Fig. 2 Infantogram showing OI type llC

the consent is refused. Autopsy is often refused for religious reasons also.

Under these circumstances, if a complete autopsy is refused, the health professional could encourage the performance of at least a partial or external autopsy—radiographs and photographs [3]. An obstetrician or a physician in a primary, secondary or tertiary set up can easily get a radiograph of the abortus with congenital malformation or the stillborn baby, which could often be very useful for genetic counseling.

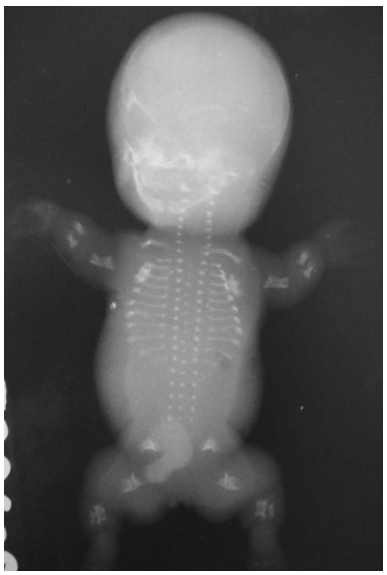

Fig. 3 Infantogram showing achondrogenesis type 1B

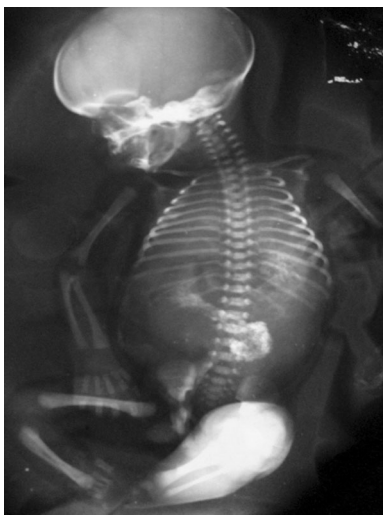

Fig. 4 Infantogram showing speckled calcification in the abdomen, hyperechoic bowel

Materials and Methods

The prospective observational study was carried out in the Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, in 2 years. Of the 42 fetuses diagnosed antenatally by ultrasonography (USG) to have fetal congenital malformation, 36 couples opted for MTP, while IUD occurred in six cases. Informed written consent was asked from the parents for autopsy. While 41 couples gave their consent, one couple refused full autopsy but permitted a radiograph.

Whole body X-ray film (infantogram)—both AP and lateral views, of all fetuses were taken. The findings of the

Table 2 Organs involved in fetuses with MCA

Sr. no.	CNS	CVS	GUT	GIT	Musculoskeletal
1			+		+
2	+			+	+
3			+	+	+
4			+	+	+
5	+		+		
6	+				+
7	+				+
8	+			+	+
9			+	+	+
10	+				+
11	+				+
12				+	+

CNS central nervous system, *CVS* cardiovascular system, *GIT* gastrointestinaltract, *GUT* genitourinary tract

infantogram were correlated with the antenatal USG findings and fetal autopsy final diagnosis.

Results

There were 20 male fetuses, 19 female fetuses, and 3 fetuses had ambiguous genitalia. Twelve fetuses had multiple organ malformations, 27 had isolated organ malformation, three cases had nonimmune hydrops (NIH).

Of single organ malformations (Table 1), central nervous system (CNS) anomalies were the most common—nine cases, followed by gastrointestinal tract (GIT) malformations—eight cases. There were three cases of NIH. On infantogram, the antenatal USG diagnosis was confirmed in all the cases of CNS anomalies except one, but was not useful for genitourinary or cardiac anomalies. X-ray picture identified extensive intra-abdominal calcification in a case of hyperechoic bowel. The autopsy of the fetus showed peripancreatic fat necrosis and cystic fibrosis was to be ruled out, but the patient did not report back.

In five cases of antenatally ultrasound suspected skeletal anomalies, infantogram X-ray film demonstrated new findings to establish the final diagnosis in four cases: nonsyndromal arthrogryposis in two cases, osteogenesis imperfecta (OI) type llC in one case and achondrogenesis type 1B in one case. Infantogram changed the antenatal diagnosis of two cases of thanatophoric dwarf (RR-50 %) to OI type llC (RR-25 %) in one case and achondrogenesis type 1B (25 % RR) in another case.

In three cases of nonimmune fetal hydrops, radiograph demonstrated the fluid accumulation seen on ultrasound in all, but no other diagnostic feature to establish the cause of NIH.

There were 12 cases of multiple congenital anomalies (MCA) in the present study. Autopsy and infantogram (Tables 2, 3) showed that skeletal malformations were most consistently present (11/12 = 91.66 %) in combination with CNS (6), genitourinary (5) and GIT (6) malformations. Infantogram established the final diagnosis in eight cases: sirenomelia, Roberts syndrome (Fig. 5), caudal regression syndrome, iniencephaly (two cases), VACTREL, limb body wall complex, frontonasal dysplasia.

Discussion

Infantogram is a part of an autopsy, and we have tried to find out how much additional information can be obtained from a postnatal radiograph alone to come closer to the correct, final diagnosis of the congenital malformation. Fetal ossification starts at 16–18 weeks of gestation, and by 20 weeks the fetal bones are easily visualized on radiograph. Infantogram like an adult's radiograph also visualizes soft tissue structures like fetal lungs, heart, gut, heart, etc.

Studies have regularly documented the important value of autopsy, but it is still not regularly done. A large retrospective study of 206 fetuses, 138 terminated after detecting an anomaly in ultrasonogram and 68 spontaneous fetal losses, wherein fetal autopsy complemented by radiography was carried out in all cases, autopsy was able to provide a definite final diagnosis in 59 % (122/206) cases, and confirmed the ultrasound findings in all cases but 2. Moreover, the autopsy provided additional findings in 77 cases and of these, 24 cases had a significant change of RR. New information changed the predicted probability of recurrence in 18 % cases. Even though the prenatal ultrasonogram reasonably predicted the malformations, fetal autopsy gave significant additional malformations in one-third of the cases and was essential for genetic counseling [1]. Laussell-Riera [4] in a similar study found that the autopsy examination changed the prenatal 'hypothesis' in 20 %, provided extensive additional information in 41 % and confirmed the prenatal hypothesis in 30 %.

Noninvasive components of fetal autopsy—external examination, examination of placenta, cord, cytogenetic and metabolic laboratory investigations and imaging (radiographs, photography), MRI, CT are some of the options available for investigating perinatal deaths when the family declines to give consent for standard autopsy [5, 6]. In a developing country like India, the use of MRI routinely in postmortem fetal examination is not possible because of lack of resources and high cost and also because of lack of specialists. So in this study, postmortem radiography was done, which is cheap, available and no couple refused to give consent. Radiography of stillborn fetuses and infants dying at birth had been reported wherein 18 % developmental

Table 3 Correlation of infantogram with prenatal ultrasound and final diagnosis in multiple organ malformations

Sr. no.	Antenatal USG	Infantogram	Final diagnosis
1	20 weeks, anhydramnios, malformations could not be delineated properly	Single femur, absent sacrum, only upper third of single tibia, *sirenomelia*	*Sirenomelia*. B/L absent kidneys and ureters, single femur, absent sacrum karyotype-46 normal
2	Hydrocephalus, Dandy–Walker malformation large exomphalos, flexed limbs, other intra-abdominal organs not seen properly	Flexion deformity of all four limbs, severe extension of vertebral column, occiput lying in close contact with pelvic girdle	Iniencephaly with exomphalos
3	Gross oligohydramnios, large exomphalos with liver inside sac	Narrow thorax, B/L club foot, scoliosis, malrotated left lower limb	Limb body wall complex
4	Hydrocephalus, holoprosensephaly, cleft lip and palate depressed nose, severe IUGR trisomy 13	Hydrocephalus, Rt. talipes equinovarus, severe IUGR *(trisomy 13), missed cleft lip/palate*	*Pseudotrisomy 13.* Internal organs normal, HPE normal, Two vessels in umbilical cord karyotype-46 normal
5	DWM, CDH, cleft lip, frontonasal dysplasia	Bifid mandible	*Frontonasal dysplasia.* DWM, CDH with liver, stomach inside chest, B/L hypoplastic lung, bifid mandible, single umbilical artery, karyotype no metaphase
6	B/L enlarged cystic kidneys, no craniovertebral angle	Fused cervical spine	*VACTERL syndrome*. TEF, single Rt. ectopic kidney with cystic changes (HPE MCKD), Rt. ureter opening in common cloaca with bowel, absent anus Karyotype- normal
7	B/L ventriculomegaly, partial corpus callosal agenesis, scoliosis, bell shaped thorax, limbs are small, B/L hypoplastic lung, absent movement	Narrow thoracic cage, flexed lower limbs, all four limbs short, upper > lower, absent digits in upper arms Roberts syndrome (Fig. 5)	*Roberts syndrome*. Hypertelorism, depressed nose, deformed ear, cleft lip and palate, micrognathia, malar hypoplasia, quadrophenia (upper > lower), absent digits in upper limbs, flexed lower limbs, enlarged clitoris, syndactyly
8	DWM, hyperextended cervical spine	Hyperextended cervical spine, B/L talipes	Iniencephaly
9	Hypertelorism, cleft lip and palate, micrognathia, B/L talipes	No apparent skeletal malformation seen except B/L talipes	No syndromic diagnosis made
10	Gross oligohydramnios, B/L kidneys not seen	Absent sacrum, single lower limb with talipes, B/L absent thumbs, broad metacarpals caudal regression syndrome	*Caudal regression syndrome*. B/L absent kidneys, ureter, large colovesical fistula, absent sacrum. Single umbilical artery Karyotype normal
11	Gross IUGR, oligohydramnios, microcephaly, micromelia, B/L ventriculomegaly	Short proximal limb bones	No syndromic diagnosis made
12	Choroid plexus cyst in Rt. ventricle, gross hydronephrosis of Lt. kidney	NAD	No syndromic diagnosis made

B/L bilateral, *CDH* congenital diaphragmatic hernia, *DWM* Dandy–Walker malformation, *HPE* histopathological examination, *IUGR* intrauterine growth restriction, *MCKD* multicystic kidney disease, *NAD* no abnormality detected, *TEF* tracheoesophageal fistula

anomalies were detected, and in selected cases when structural abnormalities were evident on external inspection, the abnormality rate was 75 % [7]. The depicted abnormalities were frequently both severe and diagnostically useful, and in many cases, were helpful in family counseling. Specific radiographic techniques were suggested.

The proportion of cases with radiological abnormalities in perinatal postmortem radiography varies considerably in different studies. A study of 514 perinatally dead infants showed that pathologic radiologic findings were seen in 30 %. Ninety-nine cases had congenital defects, while the rest showed other skeletal or soft tissue abnormalities. Of those with congenital defects, there were six osteochondrodysplasias, 16 chromosomal malformation syndromes, 13 autosomal recessive inherited malformation syndromes and 18 multiple malformation syndromes of unknown etiology. There were also 18 cases with malformation sequences and 10 single malformations with abnormal radiologic findings. It was therefore very informative with special reference to the skeletal system [8]. Another study showed that the percentage of additional minor anomalies detected by radiographs and autopsies was 20 % [9]. Three

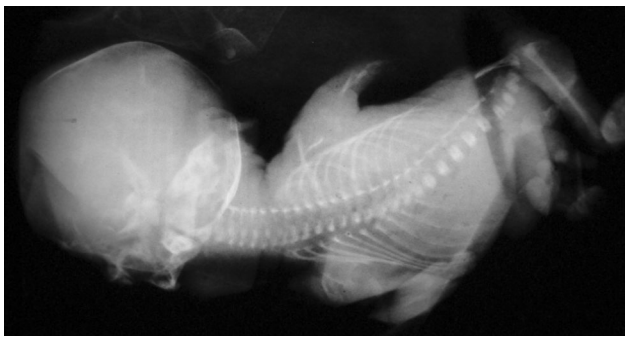

Fig. 5 Infantogram showing Roberts syndrome

percent of the minor anomalies detected by prenatal USG were not confirmed at autopsy.

Infantogram was very useful in the present study. Among five cases of antenally suspected skeletal system anomalies, it demonstrated new findings over ultrasound to establish the final diagnosis and RR in four cases: non-syndromal arthrogryposis (3 % RR) in two cases, OI type llC in one case (RR-25 %) and achondrogenesis type 1B (25 % RR) in one case (Table 1). Infantogram changed the antenatal diagnosis of two cases diagnosed antenatally as thanatophoric dwarf (RR-50 %) to OI type llC (RR-25 %) in one case, and to achondrogenesis type 1B (25 % RR) in the other case. Thus, genetic counseling for future pregnancies changes, as well as the method of prenatal diagnosis, e.g. DNA diagnosis for OI can now be made as early as 10 weeks of gestation.

In one of the cases where consent was not given for open body autopsy and final diagnosis was in doubt, infantogram clinched the diagnosis of Roberts syndrome (RR 25 %). In the group with multiple anomalies including skeletal malformations detected on antenatal USG, infantogram allowed clinching the syndromic diagnosis in five cases (sirenomelia, Roberts syndrome, and caudal regression syndrome and two cases of iniencephaly), and correlated with ultrasound and autopsy in two cases. Thus, specifically for suspected cases of skeletal malformations, postnatal radiograph (part of autopsy) is mandatory [1, 10–12].

There was one case of congenital diaphragmatic hernia (CDH) detected on antenatal USG, confirmed by radiograph. In another case, no GIT malformation was detected on antenatal USG (at 24 weeks) because of gross oligohydramnios; CDH was suspected at infantogram and later confirmed in autopsy. In both the cases, bilateral hypoplastic lungs with stomach and gut shadows in the chest, were the findings in the X-ray film. In three cases of NIH, radiograph correlated with USG findings, but could not find the cause. However, it was an important component of the workup.

Studies with postmortem infantograms show that they may identify several anomalies fitting into a syndromic pattern. Therapeutic preterm delivery was reported to have been conducted in one woman at 28 (+6) weeks gestational age due to oligohydramnios detected by antenatal USG. On infantogram, all toe-bones were stubby and rudimentary. The middle and terminal phalanges of 2nd, 3rd and 5th fingers and the terminal phalange of 4th finger on the right hand were absent. The middle and terminal phalanges of 2nd and 5th fingers and terminal phalange of 3rd finger were defected on the left hand; all abnormalities were consistent with the features of Adams–Oliver syndrome [2].

In conclusion, the conventional autopsy which includes radiograph of the abortus or stillborn baby still remains the desired 'goal standard' for final diagnosis. However, if consent for autopsy is denied, at least an infantogram should routinely be done when fetal congenital malformations especially skeletal malformations are suspected on antenatal USG, and couples opt for MTP or there is a stillbirth. It may establish or change the final correct diagnosis and RR for future pregnancies. X-ray infantogram is noninvasive, easily available and very useful in perinatal medicine for genetic counseling. Radiographs can also be sent to another location for analysis, can be used in courtrooms with no need for immediate presence of a pathologist, and the documents can be preserved.

References

1. Sankar VH, Phadke SR. Clinical utility of fetal autopsy and comparison with prenatal ultrasound findings. J Perinatol. 2006;26:224–9.
2. Jun SY, Khang SK, Park SH. An autopsy case of Adams–Oliver syndrome. J Korean Med Sci. 2000;15:482–4.
3. Gagnon A, Wilson RD, Allen VM, Audibert F, Blight C, Brock JA, et al. Evaluation of prenatally diagnosed structural congenital anomalies. Society of Obstetricians and Gynaecologists of Canada. J Obstet Gynaecol Can. 2009;31(9):875–81.
4. Laussel-Riera A, Devisme L, Manouvrier-Hanu S, Puech F, Robert Y, Gosselin B. Value of fetopathological examination in medical abortions: comparison of prenatal diagnosis and autopsy results of 300 fetuses. Ann Pathol. 2000;20(6):549–57.
5. Wright C, Lee RE. Investigating perinatal death: a review of the options when autopsy consent is refused. Arch Dis Child Fetal Neonatal Ed. 2004;89(4):F285–8.
6. O'Donoghue K, O'Regan KN, Sheridan CP, O'Connor OJ, Benson J, McWilliams S, et al. Investigation of the role of computed tomography as an adjunct to autopsy in the evaluation of stillbirth. Eur J Radiol. 2012;81(7):1667–75.
7. Griscom NT, Driscoll SG. Radiography of stillborn fetuses and infants dying at birth. AJR Am J Roentgenol. 1980;134(3):485–9.
8. Seppänen U. Perinatal postmortem radiography. Acta Radiol Diagn (Stockh). 1986;27(5):481–94.
9. Akgun H, Basbug M, Ozgun MT, Canoz O, Tokat F, Murat N, et al. Correlation between prenatal ultrasound and fetal autopsy findings in fetal anomalies terminated in the second trimester. Prenat Diagn. 2007;27(5):457–62.

10. Seppänen U. The value of perinatal post-mortem radiography. Experience of 514 cases. Ann Clin Res. 1985;17(44):1–59.
11. Lowry RB, Sibbald B, Bedard T, Hall JG. Prevalence of multiple congenital contractures including arthrogryposis multiplex congenita in Alberta, Canada, and a strategy for classification and coding. Birth Defects Res A Clin Mol Teratol. 2010;88(12): 1057–61.
12. Navti OB, Kinning E, Vasudevan P, Barrow M, Porter H, Howarth E, et al. Review of perinatal management of arthrogryposis at a large UK teaching hospital serving a multiethnic population. Prenat Diagn. 2010;30(1):49–56.