

# Fetal Postmortom Imaging (Virtopsy): A Comparative Study with Conventional Autopsy

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## A B S T R A C T

**Introduction:** Fetal autopsies are done in dead babies born or aborted with congenital anomalies to know the anatomic details of the anomaly and the syndromic association to plan subsequent pregnancies. In patients who defer fetal autopsy due to cultural, religious, ethical and emotional reasons, virtopsy using CT and MR can be considered a safe alternative. Though many studies have proven that virtual autopsies are at par with conventional autopsies, limited data is available regarding the role of virtopsy in detecting fetal anomalies using CT and MRI. Study objectives were to evaluate the accuracy of Virtopsy in diagnosing congenital abnormalities in fetus by using CT and MRI and to compare virtopsy findings with conventional autopsy findings in fetuses.

**Material and Methods:** This was a prospective study conducted on 30 fetuses over two years period. Whole body CT and MRI of expelled fetus was performed using 1.5T MRI scanner and 64-slice MDCT. The sensitivities, specificities and predictive values of post mortem virtopsy, were assessed with conventional autopsy as gold standard.

**Results:** Findings were classified as neurological, renal, skeletal, cardiac, infective and miscellaneous subtypes, anatomical morphology was assessed and was compared with the conventional autopsy findings. This study showed 87.50% sensitivity, 50% specificity, 87.5% positive predictive value, 50% negative predictive value, positive likelihood ratio of 1.75 and negative likelihood ratio of 0.25. The diagnostic accuracy of this study is 80%. The chi squared test yielded p value of 0.03998. The chi-square statistics is 4.2188. The result is significant at  $p < 0.05$

**Conclusion:** Virtopsy can be used as diagnostic means in cases where the parents are unwilling to subject the fetus to autopsy for emotional, cultural, religious and ethical reasons. Virtopsy is particularly useful in detecting neurological and skeletal anomalies. Virtopsy cannot be used in assessing congenital complex cardiac anomalies

**Keywords:** Virtopsy, Fetal Post Mortom Imaging, Fetal CT Imaging, Fetal MR Imaging, Conventional Fetal Autopsy

## INTRODUCTION

The prevalence of congenital anomalies in foetuses is about 1.9% of which the few are incompatible with life account.<sup>1</sup> It is important to know the abnormalities in terms of anatomical, structural and syndromic subtypes, in order to know the risk for subsequent pregnancies in terms of recurrence. Hence these foetuses must undergo conventional autopsy which is Gold standards till today that can give additional information. But owing to cultural, ethical and emotional reasons, not all parents give consent to autopsy. Further the fetus has to be fixed for about 15 days which can lead to autolysis and change in composition leading to time lapse and difficult dissection. There are numerous studies regarding the role of post mortom imaging in adults by using MRI and fewer studies using CT.

The word autopsy is a greek word derived from words 'autous' and 'opsomei' which means to see by one's own eyes.

It is defined as the dissection of dead body to determine through observation the cause of death or the nature of disease. Inspired by rapid technological improvements, researchers in several countries have been exploring the possibility that medical imaging—in particular, MRI and CT scans—might substitute a “virtual autopsy” for the more traditional variety.

Virtopsy is a virtual alternative to traditional autopsy conducted with scanning and imaging technology. This name is a trademark registered to Prof. Richard Dirnhofer, the former Head of institute of Forensic Medicine of University of Bern, Switzerland. The term “VIRTUAL” has its Latin root *virtus* implies the qualities of capability, efficiency, effectiveness and objectivity. Virtual also has the sense of digital.

There is high precision, clean bloodless visualization, easy documentation and, storage of data that can be reproduced easily. Virtopsy basically consists of (a) body volume

documentation and analysis using CT, MR imaging, and microradiology; and (b) 3D body surface documentation using forensic photogrammetry and 3D optical scanning. The resulting data set contains high-resolution 3D color-encoded documentation of the body surface and 3D volume documentation of the interior of the body.<sup>2-4</sup>

During the last few years, modern cross-sectional imaging techniques have pioneered forensic medicine. Magnetic resonance imaging and especially multiline computed tomography are becoming increasingly implemented into post-mortem examinations. These non-invasive techniques can augment and even partially replace a traditional autopsy.<sup>4</sup>

The purpose of fetal autopsy is to know the anatomical and structural abnormalities, syndromic association and description of new pathogenic mechanisms and diseases to support prenatal counseling. It also helps in counselling about probabilities of recurrence in future pregnancies. In India, there is diversity in cultural and ethnical background, there are parents who defer autopsy due to cultural, religious beliefs and emotional reasons. There is limited data available regarding the role of fetal postmortem imaging. Few studies are available regarding virtopsy of adult patients.<sup>4-7</sup>

We are evaluating the accuracy of virtopsy using CT and MRI in comparison with that of conventional autopsy as a pilot study.

At present, there are only a few institutions worldwide that have recognized the feasibility and possible impact of cross-sectional imaging in postmortem investigation and that have invested efforts in its implementation.<sup>4</sup>

- For example, the Office of the Armed Forces Medical Examiner (Washington, DC; Dover, Del),
- the Institute of Forensic Medicine (Copenhagen, Denmark), and the
- Victorian Institute of Pathology (Sydney, Australia)

The CT scanning times are short (whole-body documentation takes 5–10 minutes), depending on the section thickness and the volume to be covered. Postprocessing techniques such as multiplanar reformation, MIP, and 3DVR can provide strong visual evidence for use.

MR imaging clearly has a greater impact in demonstrating structural anomalies because of its high resolution, particularly CNS abnormalities.

Study aimed to evaluate the accuracy of Virtopsy in diagnosing congenital abnormalities in fetus by using CT and MRI and to compare virtopsy findings with conventional autopsy findings in fetuses.

## MATERIALS AND METHODS

The local scientific regulatory board and ethical committee approved the study, and all parents gave informed consent. This was a multi departmental prospective study, conducted

by the Departments of Radiology and pathology Units of the ESIC medical college and Postgraduate institute of medical research

All the fetuses that were terminated with suspected neurological, skeletal, structural, genitourinary, pulmonary abnormalities that were thought to be incompatible with life were included in this study between May 2015 to August 2017.

CT, MRI and conventional methods conducted both virtopsy and postmortem conventional autopsy on these fetuses. Virtopsy consisted of CT scan for abnormalities using bone and soft tissue windows and by MRI using T1W, T2W and STIR were performed and evaluated by radiologist blinded to antenatal USG findings.

An expert pathologist blinded to radiological information performed autopsy.

The gestational age was based on last menstrual period age and First trimester scan gestational age.

They were divided in to fetuses less than 24 weeks or greater than 24 weeks.

### Virtopsy protocol

Structural and anatomical evaluation was done using MRI and CT.

CT was done using Philips 64 slice MDCT machine. The Plain axial sections, coronal and sagittal reformations were done. 3-D Volume rendered images and surface shaded display were analyzed using workstation. Images were acquired in soft tissues and bone windows. Time taken was 3-5 minutes approximately. Following parameters were used - kvp of 80 and mas of 100. slice thickness was 3mm.

Whole body MRI was done using 1.5 T using Philips achieva with a combination of body and spinal coil. MRI protocol consisted of T2W, T1W and STIR images, axial, coronal and saggital sections.

T2W parameters were 25 slices adjusted to 25 slices on average adjusted to size of fetus, 3mm slice thickness, FOV 350x 350mm, Matrix 256x256. Axial,saggital and coronal sections were studied.

An axial T1-weighted Turbo FLASH sequence was performed using following parameters: 25 slices; slice thickness, 3 mm; intersection gap, 1.5mm; FOV, 250x250; matrix, 187x256; 464 TR/TE = 15 mms/4.58 mms; averages, 1; resulting voxel resolution, 1.7 × 1.5 × 6.0 mm<sup>3</sup>.

Axial FLAIR sequence was studied using parameters 20 slices, slice thickness – 2mm;intersection gap 1.5mm,fov 250x250; matrix 187x256;of 140 ms echo time and 11000 repetition time. The whole examination time ranged between 30 and 45 min.

Virtopsy and autopsy data were recorded and compared using predefined categorical variables, anatomical morphology, associated findings possible congenital disorder



Figure-1: CT Virtopsy showing absence of radius and ulna and hands bilaterally -Phocomelia

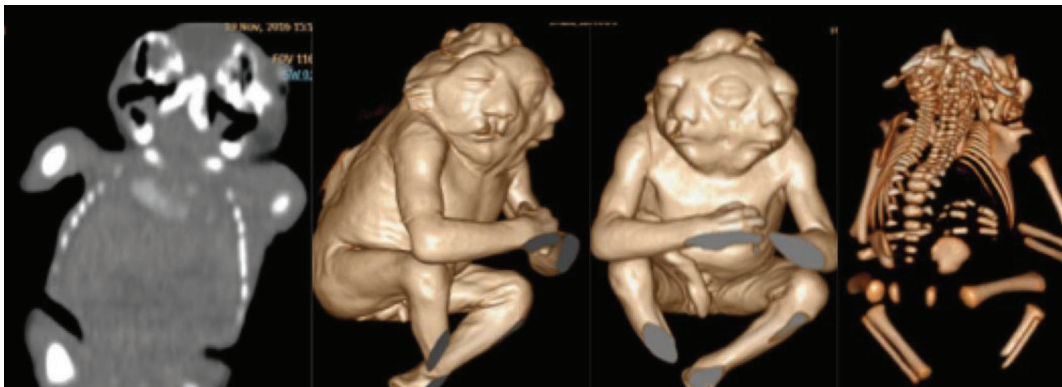


Figure-2: CT Virtopsy showing fusion of twins in the cephalic aspect with fusion of mid face and eyes with cleft palate and lip - Craniophagus with cyclops and cleft lip

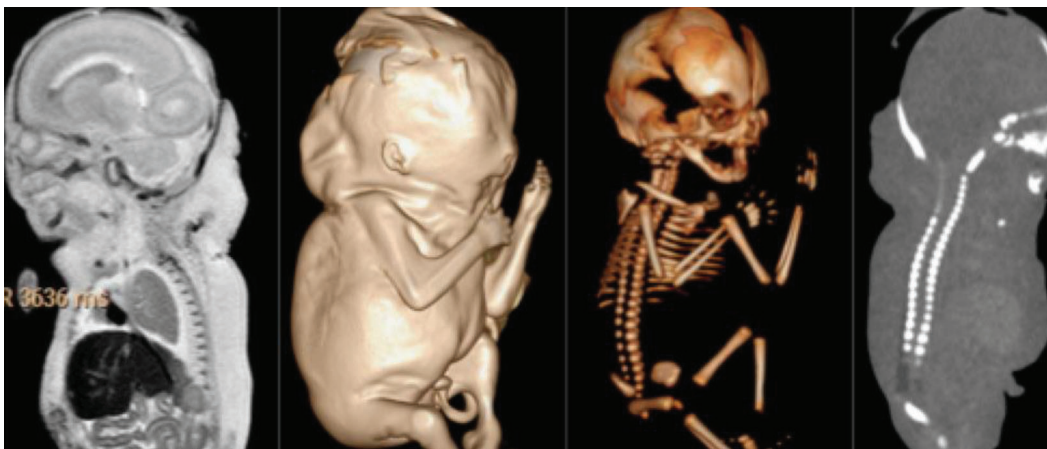


Figure-3: MR and CT Virtopsy showing subcutaneous swelling suggestive of Cystic Hygroma in a turner baby



Figure-4: CT VIRTopsy Showing fusion of perineal region – Conjoint Twin with no other congenital anomalies

## STATISTICAL ANALYSIS

Analysis was carried out using the statistical software package SPSS, version 22.0 A  $P$ -value  $< 0.05$  was considered statistically significant.

This study showed 87.50% sensitivity, 50% specificity, 87.5% positive predictive value, 50% negative predictive value, positive likelihood ratio of 1.75 and negative likelihood ratio of 0.25. The diagnostic accuracy of this study is 80%. The chi squared test yielded  $p$  value of 0.03998. The chi-square statistics is 4.2188. The result is significant at  $p < 0.05$ .

## RESULTS

This was prospective study conducted in tertiary referral hospital in 30 fetuses that were terminated due to congenital abnormality after obtaining consent from parents. The fetuses were divided in to two groups—fetus expelled before 24 weeks and fetus expelled after 24 weeks. There were 26 singletons, 2 pairs of twins encountered in this study. There was consanguineous marriage encountered in 8 cases. Two mothers were diagnosed with antenatal infection one with HIV and another with fever of unknown origin.

Findings were classified as neurological, renal, skeletal, cardiac, infective and miscellaneous subtypes and also anatomical morphology was assessed.

These fetuses were subjected to conventional autopsy and findings were noted. Both radiologist and pathologist were blinded to data. The observations were compared with each other and findings were statistically analyzed. There was good concordance between virtopsy and conventional autopsy in about 23 cases. Neurological abnormalities and renal abnormalities showed excellent correlation. Skeletal abnormalities were diagnosed better on Virtopsy that was not picked up on conventional autopsy. Cardiac anomalies could not be diagnosed on Virtopsy.

In neurological subtype, anencephaly, occipital encephalocele, inencephaly, spina bifida with Arnold chiari malformation, caudal regression, corpus callosal agenesis syndrome and myelomeningocele were found.

In facial anomalies, cleft palate with lips and proboscis case were studied.

In skeletal abnormalities, phocomelia, thanatophoric dysplasia and achondroplasia were seen.

There were three cases of complex cardiac anomalies, which were not picked up on virtopsy. This is because of collapsed cardiac chambers.

Amongst GIT spectrum, there were cases of gastroschisis, oesophageal atresia and duodenal atresia, which was picked up by both virtopsy and autopsy.

In GUT spectrum there was a case of renal agenesis and ambiguous genitalia.

In structural disorders there were craniophagus, ischiophagus, caudal regression syndrome and meckel

gruber syndrome

## DISCUSSION

In this study we compared diagnostic accuracy of conventional autopsy with virtopsy in 30 cases by the pathologist and radiologist blinded to clinical data. The study showed that parents were comfortable and preferred virtopsy procedure. virtopsy was highly reliable with good diagnostic accuracy in comparison with conventional autopsy for detection of congenital abnormality.

Within individual organ systems, Virtopsy was most accurate for detection of cerebral, spinal, structural, and renal abnormalities, however cardiac anomalies were not detected as the cardia was collapsed and hence could not be evaluated.

Skeletal abnormalities were better diagnosed on virtopsy, which was poorly diagnosed on conventional autopsy. CT virtopsy was difficult in fetuses less than 20 weeks however in combination with MRI yielded excellent results.

Amongst the imaging methods, CT virtopsy showed good diagnostic accuracy in skeletal, renal, structural anomalies and MRI autopsy showed better accuracy in CNS and pulmonary anomalies. The diagnostic accuracy improved by including both modalities.

For the conventional autopsy the specimen must be fixed for about 15 days or more days that can cause distortion and autolysis. This may disrupt pathological diagnosis. However virtopsy needs no tissue fixation hence the procedure can be done immediately and help in saving time.

The time taken for virtopsy is much lesser as it 3 to 5 minutes for CT Virtopsy and 20 to minutes for MRI virtopsy on comparison for Conventional autopsy that takes ~ 15- 20 days.

There was limited resource pertaining to this study as the other studies were done in fetuses and pediatric populations and were confined to MR Virtopsy. One other similar study included MR virtopsy and CT virtopsy in few cases, which showed similar results, but fairly good correlation was also obtained in cardiac cases. The results obtained in our study were similar to other studies.<sup>5-7</sup>

Use of Volume rendered techniques, Surface shaded display, in CT, thinner slices 3D MRI, high- resolution, isotropic images, helped in achieving good diagnostic yield.

Our study yielded greater results with excellent correlation in CNS, Skeletal, Renal abnormalities and structural abnormalities. However there was poor diagnostic yield in cardiac lesions.<sup>6,7</sup> Both CT and MRI could not detect cardiac abnormalities. in our study.

Our study had few limitations Smaller study sample size, but with diverse abnormalities. However the prevalence of fetal anomalies is low in the current trend.

Cardiac abnormalities showed very poor concordance as cardia was collapsed. This can be overcome by saline

with iodinated contrast infusion in to cardia, which will delineate cardiac abnormalities.

There is limited resource available regarding fetal virtopsy and no similar studies are available for reference, hence this study is done on a pilot basis. The available literature had studies done on neonatal and fetal population using postmortem MRI.

Thirdly we did not consider the economic aspects of this study. As ours is tertiary referral government hospital and all studies did not incur any cost to the parents of fetuses studied.

Rare pathological syndromes were not part of the spectrum studied hence diagnostic accuracy in them is not known.

This study has important implications in future and further research can be taken up based on results.

Virtopsy can yield excellent diagnostic accuracy in fetuses where conventional autopsy cannot be performed due to ethical reasons, cultural reasons or due to technical issues. In future separate studies can be done to assess cardia by injecting saline induced contrast

## CONCLUSION

Virtopsy can be used as a diagnostic means in situations where parents are unwilling to subject fetus to autopsy for emotional, cultural, religious and ethical reasons. Virtopsy is particularly useful in detecting CNS and skeletal pathologies. It can aid in diagnosis of associated congenital syndromes. Virtopsy without contrast cannot be used in assessing congenital complex cardiac anomalies. Virtopsy is safe and quick procedure with excellent diagnostic accuracy.

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