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# Editorial

# Evolution of Thoracic Surgery

It may not be inappropriate to state that "Pulmonary Tuberculosisis the History of Thoracic Surgery".

Tuberculosis has infected human population for thousands of years and existed even during the prehistoric period in the Paleolithic as well as Neolithic era.

As learnt from the available literatures, Open drainage of a Tubercular pleural empyema was the first thoracic surgical procedure ever practised.

During those days thoracic surgical operations were performed mostly for infective conditions and were considered as last resort only when no other therapy was available.

Moreover thoracic surgical options were very limited, confined only to drainage of empyema as well as various forms of collapse therapy such as Plombage, Induced Pneumothorax, Phrenic Nerve Crush,Thoracoplasty etc.

Gorgio, a Roman physician in 1696 observed dramatic improvement of a TB patient after a sword wound in his chest producinga pneumothorax.

Italian physician Forlanini in 1890 observed that lung collapse tended to have a favorable impact on the outcome of tuberculosis.

Thoracoscopy was introduced by Jacobeaus in 1910 for adhesiolysis in TB.

There is no denial that introduction of Endotracheal intubation and closed circuit anesthesia in 1910 to 1920 revolutionarised the practice of Thoracic surgery.

Graham in 1923 successfully carried out "Pulmonary lobectomy" in a case of lung cancer.

Earlier attempts at mass ligation of hilum were resulting in disastrous results.

Techniques of lung resection for TB and lung cancer perfected in 1930s.

Usefulness of Thoracoplasty was widely accepted and the operative procedure was perfected in various German and American clinics for treating TB cases in sanatoria.

In 1950, Price Thomas developed sleeve resection for central bronchial tumors.

Invention of drugs active against tuberculosis have been the most important weapon for saving the human race from tuberculosis.

With the introduction of effective and safe antitubercular drugs, tuberculosis Thioacetazone was identified as a potential antitubercular agent in 1940's by Domagk in Germany. This drug was extensively used in Germany before streptomycin was widely available.

After the advent of streptomycin, a number of antitubercular drugs were invented in rapid succession during the subsequent years.

In 1946, Para amino salicylic acid was found to be effective against Mycobacterium tuberculosis.

In 1951, Isoniazid was used for the first time having antitubercular property though it was synthesized in 1912 by Meyer and Malley in Prague.

In 1952, Ethionamide was synthesized by Lieberman and was used as a 2$^{nd}$ line drug due to its toxicity.

Introduction of successful anti-tubercular chemotherapy decreased the need of surgical interventions for majority of infective pleuro pulmonary diseases.

Interest in surgery for tubercular pleuro pulmonary diseases increased again with the appearance of MDR-TB in the clinical scenario.

Rapid development of Imaging Modalities including X Ray, USG, CT Scan, MRI, PET, Nuclear Medicine Scans etc. helped in further advancement of Thoracic Surgery.

Endoscopic procedures such as Flexible Bronchoscopy, Immuno-Fluorescent technology, Endo Bronchial Ultrasound etc. also contributed substantially in the advancement of Thoracic Surgery.

Recent advancements in technologies and their introduction in thoracic surgery have accelerated the growth of the specialty offering surgical therapy for almost all thoracic surgical disorders.

Video Assisted thoracic Surgery (VATS) and Robotic surgery have already been established as a comparable therapeutic option for a wide range of thoracic diseases .

Lung transplantation has also been accepted as a therapeutic modality with commendable outcome for end stage lung diseases.

It may be concluded that in addition to the advancements in thoracic surgery simultaneous development in the fields of diagnostic imaging, cell biology, tumor markers, drug therapy, genomic studies, endoscopic procedures etc. have become the game changers in the practice of Thoracic surgery.

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Prof. (Dr.) Bhabatosh Biswas, Principal, RKMSP, VIMS

Original Article

# Distinguishing Essential Tremor from Dystonic Tremor-Archimedean Spiral Drawing

Dr. Barun Kr. Sen[1], Dr. Koushik Pan[2], Dr. Angshuman Mukherjee[3]

**Abstract:**

Tremor may be one of the core manifestations of various Neurological diseases. Its pattern helps in distinguishing some diseases. Analysis of spiral hand drawing may be helpful in distinguishing Essential tremor (ET) from Dystonic tremor (DT). We analyzed hand drawn spiral axis of 108 patients among which 84 are ET cases and 24 are DT cases. We found 64.29% (54/84) single tremor orientation axis in ET cases and predominantly no clear axis seen in DT cases. Multiple tremor orientation axis in spiral drawing is seen more in ET cases.

**Introduction:**

The human tremor is a common neurological disorder.[1] Various types of tremor (rest, action –postural, intention) can be seen in different Neurological diseases like Essential tremor (ET), Parkinson's disease, Dystonic tremor (DT) etc. Details history, clinical examination, specific signs help in distinguishing different diseases with tremor. Pattern of tremor is different in various Neurological diseases. Drawing in patients with tremor reveals the presence of oscillatory errors that vary in frequency and amplitude. Tremor has been found to be consistently worse in unsupported spiral drawing that dependant on the severity of tremor and generally have a tremor orientation axis.[2] Hand-drawing patterns are commonly assessed by means of visual rating scales. In clinical settings, the differentiation of essential tremor and dystonic tremor may be very challenging. Archimedean spiral drawing may be a very useful screening tool to distinguish ET cases from DT cases.

**Key Words :**

DT vs ET, Archimedean Spiral Drawing

**Aims :**

The aim of this study was to analyze spiral drawing feature of patients with ET and DT.

**Materials & Methods :**

Data collected from patients proforma stored in the movement disorder clinic, BIN, IPGMER Kolkata. We analyzed hand-drawn Archimedean spirals of total 108 patients of DT and ET.

Each of the Archimedean spirals was assessed for the presence of an oscillation error; if present, then assessed for single identifiable clear tremor orientation axis, direction of axis, oscillation error without clear axis and multiple tremor orientation axis (figure-1 & 2) and analyzed the association between the tremor axis and the diagnosis.

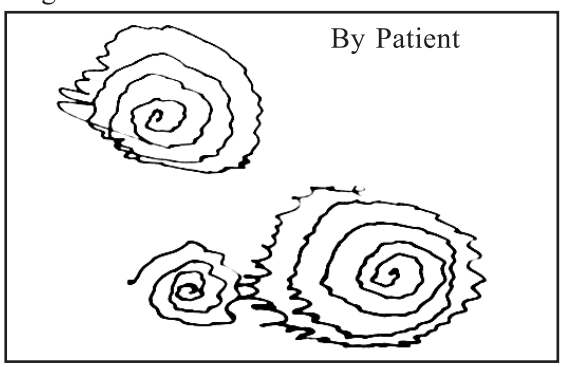


**Figure 1: Single axis**

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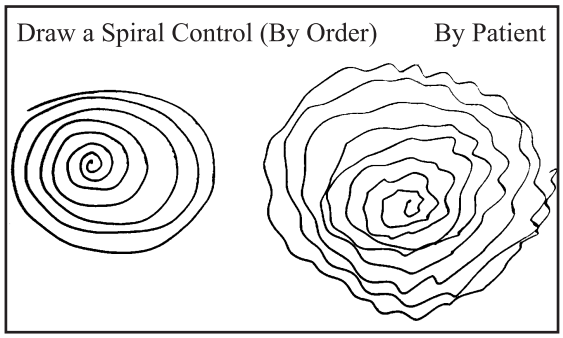


**Figure 2: Multiple axis**

**Results:**

There were 84 ET cases and 24 DT cases (cervical dystonia13, generalized dystonia 2, hand dystonia 6, multifocal dystonia 3). Identifiable tremor orientation axis (figure 3) seen in ET cases-single axis in 64.29% (54/84), multiple axis in 23.81% (20/84) and no clear axis in 11.90% (10/84) cases whereas in DT cases-single axis in 29.17% (7/24), multiple axis in 33.33% (8/24) and no clear axis in 37.5% (9/24) cases.

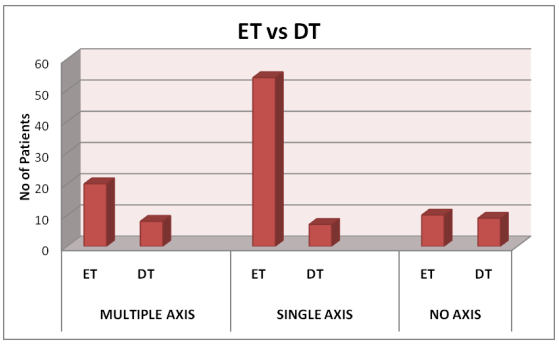


**Figure -3**

Single identifiable clear tremor orientation axis was seen more in ET cases than DT case and it is statistically significant (P= 0.0022). Multiple identifiable tremor orientation axis was seen more in DT cases but it is not statistically significant (P=0.3477). In DT cases mostly there was no clear tremor orientation axis.

**Discussion:**

In our study handwritten spirals appear to have a predominant single axis in ET than DT cases where as no clear axis seen mostly DT cases. Many patients having a diagnosis of "ET" actually have another neurological disorder. Studies show that in clinical practice settings 30 – 50% of ET cases are mis-diagnosed. One previous study on misdiagnosis of tremor disorders reported that of the 26 patients with false ET, 6 (23.1%) were diagnosed with dystonia. Another study of the over-diagnosis of ET demonstrated that 4 (40%) of 10 ET patients had dystonia. These studies reported that these false ET were actually Parkinson disease, dystonia where multiple tremor axis predominantly seen. The presence of a single tremor orientation axis would be one clinical feature that would make the ET diagnosis more likely.

**Conclusion :**

The evaluation of Archimedean spirals axis has moderate diagnostic validity as a screening tool to distinguish ET cases from those with DT. Spiral drawing is safe, inexpensive, fast, portable, non invasive and can be administered to a large cohort of patients without instruments. This screening tool is not meant to replace in-person evaluations, but rather, to serve as a screening method to save time and resources.

**Limitation :**

The study had limitations.

1. Spirals drawn on paper, a computerized spiral analysis is more precise.
2. Small number of cases.
3. Follow up study to exclude misdiagnosis not done.

**Acknowledgments :**

This work was supported by the team of Movement disorder clinic, BIN-IPGME&R

**References :**

1. Buijink AWG, Contarino MF, Koelman JHTM, Speelman JD, van Rootselaar AF. How to tackle tremor–systematic review of the literature and diagnostic work-up. Front Neurol. 2012;3:146.
2. Jain S, Lo SE, Louis ED. Common misdiagnosis of a common neurological disorder: how are we misdiagnosing essential tremor? Arch Neurol. 2006; 63(8):1100–4.
3. Schrag A, Munchau A, Bhatia KP, Quinn NP, Marsden CD. Essential tremor: an overdiagnosed condition? J Neurol. 2000;247:955–9.
4. Louis ED, Yu Q, Floyd AG, Moskowitz C, Pullman SL. Axis is a feature of handwritten spirals in essential tremor. Mov Disord. 2006;21(8):1294–5.
5. Louis ED, Hernandez N, Alcalay RN, Tirri DJ, Ottman R, Clark LN. Prevalence and features of unreported dystonia in a family study of "pure" essential tremor. Parkinsonism Relat Disord.2013;19(3):359–62.
6. Gironell A, Kulisevsky J. Diagnosis and Management of Essential Tremor and Dystonic Tremor. Ther Adv Neurol Disord. 2009;2(4):215–22.
7. Knoebel M, Bain PG. Spirography in essential tremor and parkinsonism. Mov. Disord. 2009;249 (24 Suppl. 1):S503.

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Original Article

# A Prospective Study of Fetal Outcome in Multigravid Singleton Women with Reduced Fetal Movements

Dr. Arunabha Das[1], Dr. Asif Ahmed[2], Prof. Krishnendu Gupta[3]

**Introduction :**

Reduced fetal movements (RFM) are a common presentation in general practice and hospital obstetrics. RFM is perceived as a state of fetal compromise by the mother and often poses a dilemma of management for the clinician. In order to reduce the perinatal mortality, formal counting of the fetal movements by pregnant women could identify a fetus which is at-risk of compromise, thus allowing for prompt and appropriate action. The recording of fetal activity serves as an indirect measure of the central nervous system integrity and function indicating that fetal movements are a reliable sign of fetalwell being. Maternal perception of reduced fetal movements causes concern to both pregnant women and obstetricians in late pregnancy. Maternal perception of gross fetal movements appears to be an accurate reflection of fetal activity. Active fetal movement patterns have been associated with good fetal outcome.From 18–20 weeks of gestation, most pregnant women become aware of fetal activity.[1] Using the Cardiff count to ten charts, Liston et al found that 60% of patients who reported decreased fetal activity did exhibit evidence of fetal compromise.[2] Using the Cardiff count to ten charts, Liston et al found that 60% of patients who reported decreased fetal activity did exhibit evidence of fetal compromise. In a study done by Sinha et al to review the outcome of women who presented primarily with reduced fetal movements and to compare with women of similar age and gestation who did not have reduced fetal movements (controls), he found that some 19% of intrauterine growth restricted babies were found in the study group, compared with none in the control group. In the study group, 32% of women needed intervention solely due to fetal compromise compared with 21% in the control group.[3] Fewer than ten movements in 12 hours maybe an early warning sign of problem.[4] Maternal monitoring of FM can aid opportune delivery of infant who are at increased risk of intrauterine death.[5,6] Many aspects of practice are not based on the available evidence.[7] Further investigation is required to determine an effective method of identifying patients with reduced fetal movements and to determine the best subsequent management.[8] 30 such movements are made each hour.[9] Hypoglycemia was associated with increased fetal movements.[10] Absence of fetal activity requires further assessment before one concludes that fetal compromise exist.[11] Maternal assessment of fetal activity depends on placental location, the length of fetal movements, the amniotic fluid volume, and fetal anomalies.[12] Anomalies of the CNS are most commonly associated with decreased activity.[13] Pregnancy induced hypertension was associated with fetal activity which significantly lower than controls at the beginning of third trimester and significantly higher at term.[14]

**AIM and Objective :**

To determine the fetal outcome among

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multigravid singleton pregnant women presenting with reduced fetal movements on or after 32 weeks of period of gestation.

**Study Design and Methodology :**

**Study Design :**

This was a hospital based prospective observational study.

**Study Site and Setting :**

This study was carried out in the Department of Obstetrics and Gynaecology at Ramakrishna Mission Seva Pratisthan, Vivekananda Institute of Medical Sciences (RKMSP, VIMS), 99 Sarat Bose Road, Kolkata-700026. RKMSP, VIMS is a tertiary 626-bedded multispeciality hospital which serves as a training facility for postgraduate students of the West Bengal University of Health Sciences (WBUHS). The hospital attends to referral patients and also acts as a primary hospital serving many inhabitants of West Bengal.

The department of Obstetrics and Gynaecology is staffed by faculty/consultants, registrars, post-graduate trainees (PGTs) and nurses as technical staff. Each year an average of 4500–5000 deliveries are conducted. The routine standard of care for a patient who presents with reduced fetal movements is history and physical examination, followed by depending on the gestational age, they are evaluated and managed appropriately by use of "fetal kick count" (FKC) chart, CTG monitoring, modified biophysical profile (MBPP) and Doppler velocimetric studies.

The care of patients in the labour ward is primarily done by registrars in consultation with faulty/consultants. Once a formulated care plan is decided upon, it is implemented by competent labour ward nursing staff. Ward rounds by the consutants is done both in the morning and evening, while the registrars and PGTs are available round the clock. Labour process is monitored by a partograph. The delivery room has five delivery beds and delivery is conducted by PGTs. Maternity theatre is on the 4th floor of that same building with two operating tables. Emergency and elective caesarean sections (CS) are performed there. A registrar is always available to perform emergency CS and elective CS is usually performed by the consultant on-call. Monitoring of these patients has been enhanced because the upgraded labour ward with three CTG machines and back up of a dedicated departmental USG machine.

This study concentrated on MBPP as method of fetal surveillance employed to evaluate pregnancies with reduced fetal movements. Printed documental evidence of CTG tracings were made available to all patients.

The department of Radiology in RKMSP is operational round the clock. Doppler studies are performed by a consultant radiologist and/or registrars of the department. Reporting is usually done by the registrar or the consultant who performed the procedure and results are usually available within one hour of the procedure. The neonatal intensive care unit (NICU) at RKMSP is well equipped with incubators and ventilators required in the management of newborn with respiratory problems. It also has several phototherapy machines. Patients admitted there are kept warm, put on oxygen, intravenous drugs and fluids as per needs. The registrar of the department of Paediatrics is always available at the time of delivery of a high-risk pregnancy in helabour ward and operation theatre to receive the baby, evaluate and provide effective management.

**Study Duration** :

One year (September 01, 2016 to August 31, 2017).

**Study Participants' Recruitment and Enrolment :**

The study participants were recruited in labour ward at the time of admission. At RKMSP, all women with reduced fetal movements are admitted through labour ward for initial assessment before being transferred to the antenatal ward. Pregnant women who presented with reduced fetal movements as a primary complaint and met the eligibility criteria were consented and routine standard care of management was followed.

**Study Population :**

This tertiary hospital renders services to patients coming from Kolkata and adjacent districts of West Bengal. Pregnant mothers who presented with reduced fetal movements to RKMSP at =32 weeks gestation as a primary complaint and met the eligibility criteria were consented, and they formed the study population.

**Inclusion Criteria :**

1) Singleton pregnancy
2) = 32 weeks of gestation
3) Multigravidae
4) Mothers willing to give consent.

**Exclusion Criteria :**

1) Primigravidae
2) Multiple pregnancy
3) Fetus with diagnosed congenital anomaly.

**Sample Size :**

A total of 200 women was selected as per inclusion and exclusion criteria.

**Outcome :**

**Table-1: Age distribution of the patients.**

The mean age (mean ± s.d) of the patients was 29.1±4.2 years with range 18-41 years and the median age was 28 years.

| Age group (years) | Numbers | % |
|---|---|---|
| 18-20 | 2 | 1 |
| 21-25 | 38 | 19 |
| 26-30 | 74 | 37 |
| 31-35 | 63 | 31.5 |
| 36-40 | 22 | 11 |
| >40 | 1 | 0.5 |
| **Total** | **200** | **100** |

**Table-2: Distribution of patients according to period of gestation.**

The mean period of gestation (mean ± s.d.) of the patients was 37.80 ± 1.74 weeks with range 33-41 weeks and the median was 38 weeks. Most of the patients (76.5%) were with period of gestation between 37-40 weeks.

| Period of gestation (in weeks ) | Numbers | % |
|---|---|---|
| 32 - <37 | 36 | 18 |
| 37-40 | 153 | 76.5 |
| >40 | 11 | 5.5 |
| **Total** | **200** | **100** |

**Table-3: Distribution of liquor color of the patients.**

| Liquor color | Numbers | % |
|---|---|---|
| Meconium stained | 29 | 14.5 |
| Clear | 171 | 85.5 |
| **Total** | **200** | **100** |

Most of the liquor color (85.5%) was clear. 14.5% of the liquor color was Meconium Stained.

**Table-4: Distribution of amount of liquor of the patients.**

| Liquor amount | Numbers | % |
|---|---|---|
| Increased | 168 | 84 |
| Decreased | 23 | 11.5 |
| Scanty | 9 | 4.5 |
| **Total** | **200** | **100** |

4.5% of patient had scanty liquor and 11.5% had decreased liquor.

**Table-5 : Distribution of birth weight of baby of the patients.**

| Birth weight of baby (in grams) | Numbers | % |
|---|---|---|
| <1000 | 0 | 0 |
| 1000 - <1500 | 0 | 0 |
| 1500 - <2500 | 22 | 11 |
| 2500 - 3500 | 172 | 86 |
| >3500 | 6 | 3 |
| **Total** | **200** | **100** |

The mean birth weight of babies (mean ± s.d.) of the patients was 2.86±0.34 kg with range 1.8 – 3.9 kg and the median was 2.8kg

**Table-6: Fetal Outcome**

| Outcome | Value | Numbers | % |
|---|---|---|---|
| APGAR score at 5min | <7 | 20 | **10** |
| | =7 | 180 | **90** |
| Resuscitation | yes | 21 | **10.5** |
| | no | 179 | **80.5** |
| Admission to NICU | yes | 18 | **9** |
| | no | 182 | **91** |
| Feasible congenital anomalies noted | yes | 3 | **1.5** |
| | no | 197 | **98.5** |
| Fresh still birth | yes | 2 | **1** |
| | no | 198 | **99** |
| Macerated still birth | yes | 1 | **0.5** |
| | no | 199 | **99.5** |

**Results :**

* The mean age (mean ± s.d) of the patients was 29.1±4.2 years with range 18-41 years and the median age was 28 years. (Table-1)
* The mean period of gestation (mean ± s.d.) of the patients was 37.80 ± 1.74 weeks with range 33-41 weeks and the median was 38 weeks. Most of the patients (76.5%) were with period of gestation between 37-40 weeks. (Table-2)
* Most of the liquor color (85.5%) was clear. 14.5% of the liquor color was Meconium Stained. (Table-3)
* 4.5% of patients had scanty liquor and 11.5% had decreased liquor. (Table-4)
* The mean birth weight of babies (mean ± s.d.) of the patients was 2.86±0.34 kg with range 1.8 – 3.9 kg and the median was 2.8 kg. (Table-5)
* Most newborn (90.0%) had good five minute APGAR score (=7) while 20(10.0%) had APGAR score <7 at 5 minutes. The newborns resuscitated were 21(10.5%) and 18(9.0%) were admitted to NICU. There were 2(1.0%) cases of fresh stillbirth and 1(0.5%) case of macerated still birth. Visible congenital anomalies noted in 3(1.5%) cases. (Table-6)

**Discussion :**

**Burden of Suffering :**

In our study, total of 200 women were selected randomly in the labor ward. The study participants were between 18 and 41 years with a mean age of 29.1 years and median of 28 years. This group is representative of the peak reproductive age group and not different from the general population. The drug use by the study participants was negligible thus removing a confounder in

the study as drugs are known to affect fetal movements, how it is perceived and the outcome of the pregnancy. This shows that drug use in our set-up by pregnant mothers is not a major cause of reduced fetal movements. In this study most mothers with reduced fetal movements were at term. It can be attributed to the fact that by this time most mothers will have attended antenatal clinic and emphasis on danger signs raise their awareness to reduced fetal movements. It can also be attributed to anxiety due to previous poor outcomes. Nelsdam S (1980) assessed the value of maternal monitoring of fetal movements in 2250 pregnant woman and demonstrated that maternal monitoring of fetal movements can identify infant with increased risk of intrauterine fetaldeath.Pregnant women should be emphasized to monitor their fetal kicks and a chart be availed to those with increased risk like hypertension and diabetes. Women information can be improved by development of brochure of information that aims to increase maternal awareness and vigilance to significance of decrease in fetal activity, and to aid health promoting behavior.

**Effectiveness of Early Detection :**

In our study, out of 200 cases with abnormal heart rate features either individually or in combination, we could detect 21 babies (10.5%) with poor APGAR score at 1 minute, of which 17 (8.5%) still had a poor APGAR score at 5 minutes. So, we were able to save these 21 babies from deteriorating further and landing up in cerebral palsy or intrapartum stillbirth or early neonatal death. But the main lacuna of our study was that we could not follow up the babies or mothers. It is true that we could detect early, but how effectively this early detection helped in the long term benefit of the baby could not be assessed in our study.

**Summary :**

This was a hospital based prospective observational study, conducted between September 01, 2016 to August 31, 2017. This study was carried out in the Department of Obstetrics and Gynaecology at Ramakrishna Mission Seva Pratisthan, Vivekananda Institute of Medical Sciences, Kolkata. The study was done to know the fetal outcomes among multigravidae with singleton pregnancy presenting with reduced fetalmovements on or after 32 weeks. A total of 200 pregnant patients beyond 32 weeks of gestation were selected randomly for the study, depending on the inclusion and exclusion criteria.

* The mean age (mean ± SD) of the patients was 29.1±4.2 years with range 18-41 years and the median age was 28 years, the mean period of gestation (mean ± SD) of the patients was 37.80 ± 1.74 weeks with range 33-41 weeks and the median was 38 weeks. Most of the patients (76.5%) were with period of gestation between 37-40 weeks.
* Most newborn (90.0%) had good five minute APGAR score (=7) while 20(10.0%) had APGAR score <7 at 5 minutes. The newborns resuscitated were 21(10.5%) and 18(9.0%) were admitted to NICU. There were 2(1.0%) cases of fresh stillbirth and 1(0.5%) case of macerated still birth. Visible congenital anomalies noted in 3(1.5%) cases.
* The study showed that there was significant association between APGAR score at 5 minutes, Newborn resuscitation, NICU admission and CTG at admission of the patient.

**Reference :**


1. Baskett TF, Liston RM. Fetal movement monitoring: clinical application. ClinPerinatol. 1989;16:613-25.
2. Liston R, Cohen A, Mennuti M et al. Antepartum fetal evaluation by maternal perception of fetal movement. Obstet Gynecol. 1982;60:424.
3. Sinha D, Sharma A, V. Nallaswam et al. Obstetric outcome in women complaining of reduced fetal movements. Obstet Gynaecol. 2007;27:41-3.
4. Froen Jr, Saastad E, Tveit JV et al. clinical practice variation in reduced fetal movements. Tidsskr Nor Laegeforen. 2005;125(19):2631-4.
5. Neldam S. Fetal movements as an indicator of fetal wellbeing. Lancet 1980;1(8180):1222-4.
6. Heazell AE, Froen JF. Methods of fetal movement counting and the detection of fetal compromise. J Obstet Gynecol. 2008;28(2):147-54.
7. Heazell AE. Midwives and obstetrician's knowledge and management of women presenting with decreased fetal movements. Acta Obstet Gynecol Scand. 2008;87(3):331-9.
8. Olesen AG and Svare JA. Decreased fetal movements: background, assessment, and clinical management. Acta Obstet Gynecol Scand. 2004; 83(9): 818-26.
9. Patrick J, Campbell K, Carmichael L et al. Patterns of gross fetal body movements over 24-hour observation intervals during the last 10 weeks of pregnancy. Am J Obstet Gynecol. 1982;142:363.
10. Holden K, Jovanovic L, Druzin M et al. Increased fetal activity with low maternal blood glucose levels in pregnancies complicated by diabetes. Am J Perinatol 1984;1:161.
11. Natale R, Clewlow F, Dawes G. Measurement of fetal forelimb movements in the lamb in utero. Am J Obstet Gynecol 1981;140:545.
12. Sorokin Y, Kierker L. Fetal movement. Clin Obstet Gynecol 1982; 25:719.
13. Rayburn W, Barr M. Activity patterns in malformed fetuses. Am J Obstet Gynecol 1982;142:1045.
14. Simon A, Ohel G, Mor et al. Fetal movement in hypertensive pregnancies. Aust NZ J Obstet Gynaecol. 1985;25(3):178-81.

Original Article

# Role of Arteriovenous Fistula as Vascular Access for Haemodialysis in Patients with End Stage Renal Disease

**Dr. Bhabatosh Biswas[1], Dr. Rajarshi Basu[2], Dr. Bhaskar Das[3], Dr. Rupak Bhattacharya[4], Dr. Kaushik Das[5], Dr. Gautam Majumdar[6], Dr. Jayanta Basu[7]**

**Introduction :**

It has been established that survival of patients with End Stage Renal Disease (ESRD) can be prolonged with renal transplant or lifelong haemodialysis.

Credit goes to Belding Hibbard Scribner, a U.S. physician and a pioneer in kidney dialysis, who described External radiocephalic shunt in the left arm (Scribner shunt) in 1960.

Construction of subcutaneous arteriovenous fistula (AVF) between the radial artery and an adjacent vein was described by Cimino and Brescia in 1966. These fistulae have been accepted as the best mode of vascular access for haemodialysis due to their good long-term patency as well as fewer complications.[1]

Radiocephalic fistula has been accepted as the most suitable vascular access followed by the brachiocephalic fistula. Arteriovenous grafts (saphenous/synthetic) are reserved for those cases where radiocephalic or brachiocephalic fistula could not be done or have failed.

There is always concern about maturation of fistula. Maturation has been defined as the ability of AV fistula to be needled and provide ongoing functional haemodialysis at the sixth week from the access procedure.[2, 3]

Failure-to-mature fistula is defined as a fistula that has never matured so as to be useful, is difficult to cannulate, or that fails to generate the necessary blood flow (600 mL/min) for a successful two-needle dialysis.[4]

Several variables were identified in relation to maturation of AV fistula viz., gender, diabetes, systolic Blood Pressure, Peripheral Vascular Disease, size and elasticity of vein, type of fistulae, coagulability etc.

This study has focused on various types of arteriovenous fistula created for hemodialysis with special reference to outcome and maturation.

**Materials and Methods :**

This study was conducted with 260 patients from September 2017 to August 2019 on patients of End stage renal disease (ESRD) who underwent AV fistula surgery at Calcutta Medical Research Institute, Kolkata.

All thepatients who had AV fistula surgery with native vessels (radial artery/ brachial artery and neighbouring superficial veins) during this period were included in this study.

Cases of AV fistula who needed autologous or synthetic grafts as well as redocases were excluded from the study.

All the patients had thorough clinical work-up. Arteries and peripheral veins of both the upper limbs were examined to identify the suitable site as well as most appropriate vessels for creation of AV fistula.

Viral serology (Anti HCV, HbsAg, HIV), Prothombin Time and INR were specially checked, in addition to other laboratory parameters.

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AV fistula surgeries were done on days other than the day of haemodialysis.

**Operative Technique :**

All the cases were operated under local anesthesia using 2% Xylocaine with loupe magnification. The suitable site (lower forearm/cubital fossa) for creation of AV fistula was identified in each patient on the basis of softness as well as proximal patency of the veins.

Fistulae were created at distal and mid forearm (with radial artery) or in the cubital fossa (with brachial artery) depending on identification of suitable vein.

After skin incision,veins and arteries were mobilized adequately and brought side by side without tension. At first Venotomy was done after applying clamps both proximally and distally. Proximal and distal patency of the veins was ascertained by injecting heparinized saline. Thereafter, arteriotomy was done.

Side to side anastomosis between vein and artery was performedwith continuous 7-0 polypropylene sutures.

Skin closure was done with 3-0 ethilon interrupted sutures. The wound was covered with noncompressive dressing. Thrill was felt and bruit was heard at the operation site on operation table.

In case of absence or doubtful thrill and bruit, AV fistula was created at another side in the same sitting.

Patients were given certain advices for avoiding low flow status for maintaining adequate blood flow in the vessels of the operated limbs.

Blood sample collection, blood pressure check-up, use of tight clothing or jewelleryetc were advised to be avoided in the operated limb.

Thrill and bruit over the fistula side was observed regularly.

Fistula maturation and its cannulation for use of haemodialysis was decided on the basis of visible dilated veins.

Maturation usually required 4-6 weeks after creation of AV fistula.

**Results :**

This study included 260 consecutive cases fulfilling the inclusion as well as exclusion criteria.

In this series 162 (62.30%) patients were males and remaining 98 (37.70%) patients were females.

212 (81.54%) of our patients were older than 45 years of age.

205 (78.84%) patients of the series had AV fistula with radial artery at distal and mid forearm whereas 55 (21.16%) patients had AV fistula with brachial artery in the cubital fossa.

There were 10 (3.84%) failures in the entire series of 260 cases undergoing AV fistula.

There were 8 (3.90%) failures out of 205 cases of AV fistula created with radial artery whereas 2 (3.63%) failures out of 55 cases of AV fistula created with brachial artery.

Out of 10 cases of failures, 1 case had infection and pseudoaneurysm formation at brachial artery fistula site.

Closure of fistula, debridement as well as repair of artery was undertaken in this case. The limb survived and the patient had to undergo AV fistula creation in the opposite upper limb.

Another case of the series presented with extensive aneurysmaldilatation of the fistula site vessels along with gross edema of the operated limb 20 months after creation of the fistula with

brachial artery at cubital fossa. The fistula was closed with reconstruction of the brachial artery along with ligation of the grossly dilated veins to salvage the limb.

Another 8 failed cases were related to radial artery fistula and had thrombotic occlusion at cannulation sites during haemodialysis.

Out of 260 cases 12 (4.61%) cases were identified as immature AV fistula. Most of the immature fistulae had diabetes, peripheral vascular disease, narrower native veins, unsatisfactory flow through the fistula or infection.

There was no operative morbidity in our series.

**Discussion :**

Proper haemodialysis at suitable intervals is essential for survival of patients suffering from ESRD.

Continuation of successful haemodialysisrequires creation and maintenance of adequate vascular access.

Construction of subcutaneous arteriovenous fistula (AVF) between the radial artery or the brachial artery with an adjacent vein, has been proved to be essential for successful haemodialysis. These fistulae have been established as the most suitable vascular access for haemodialysis due to their good long-term patency as well as fewer complications.

P. Sahasrabudhe et al, considered this operation to be the gold standard for vascular access for haemodialysis and it accounted for 180 (66.4%) of their operative procedures.[5]

Patients who receive dialysis with AV fistula have lower complication rates and longer duration of event-freepatency than patients with catheter access and arteriovenous grafts (AVGs).[6,7]

We preferred creation of AV fistula in all our patients suffering from ESRD as the first choice of vascular access.

In our study, age and sex had no significant relation with the outcome of AV fistula.

The most common operative procedure was the creation of the distal radio cephalic fistula, initially described by Brescia, et al. in 1966.[1]

However, 205 (78.84%) patients of the our series had AV fistula with radial artery at distal and mid forearm whereas 55 (21.16%) patients had AV fistula with brachial artery in the cubital fossa.

We had 8 (3.90%) failures out of 205 cases of AV fistula created with radial artery whereas 2 (3.63%) failures out of 55 cases of AV fistula created with brachial artery.

But most large-volume centers report 15-30% primary failure rates for distal radio cephalic AV fistula.[8, 9]

In our series, out of 260 cases 12 (4.61%) cases were identified as immature AV fistula. Most of the immature fistulae had diabetes, peripheral vascular disease, narrower native veins, unsatisfactory flow through the fistula or infection.

Muhammad A. Siddiqui et al reported a gender difference, with AVF maturation rates of 60% for men and 48% for women, respectively.[10]

**Conclusion :**

Patients suffering from ESRD require haemodialysis at regular intervals for survival.

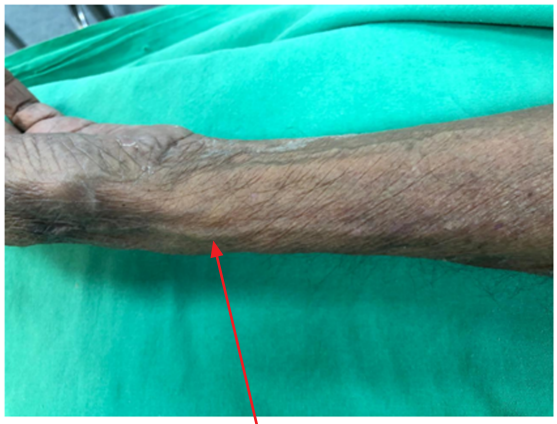
Creation and maintenance of adequate vascular access has been established as essential for continuation of successful haemodialysis.

Construction of arteriovenous fistula (AVF) preferably with a peripheral upper limb artery

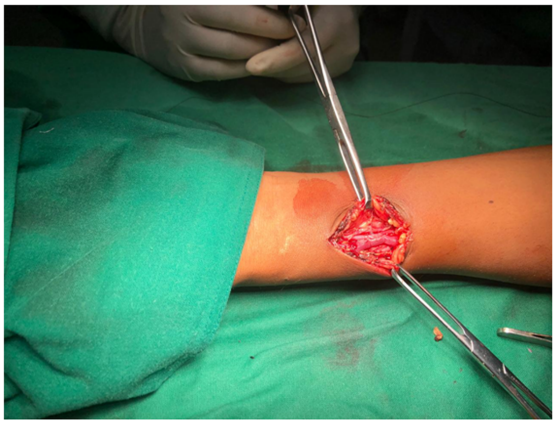
and an adjacent vein, has been accepted as gold standard for successful haemodialysis.

Failure rates of AV fistula have become very low.

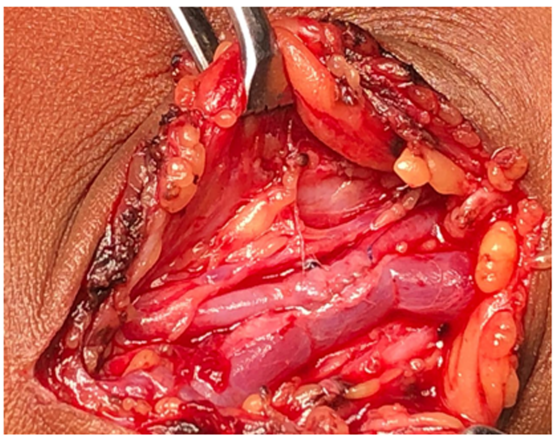
Dreaded complications like pseudoaneurysm or extensive aneurysmal dilatation of the fistula site vessels along with gross edema of the operated limb occur very infrequently.



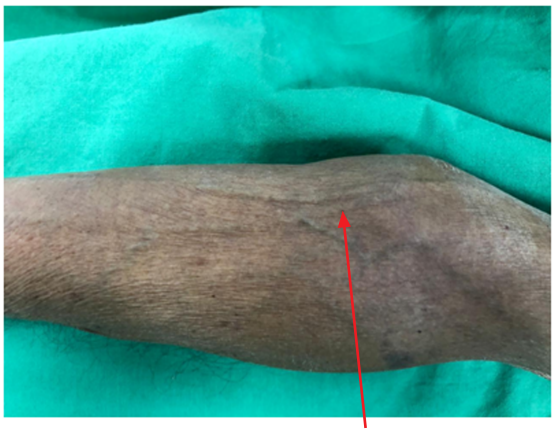
**Cephalic Vein in lower forearm**



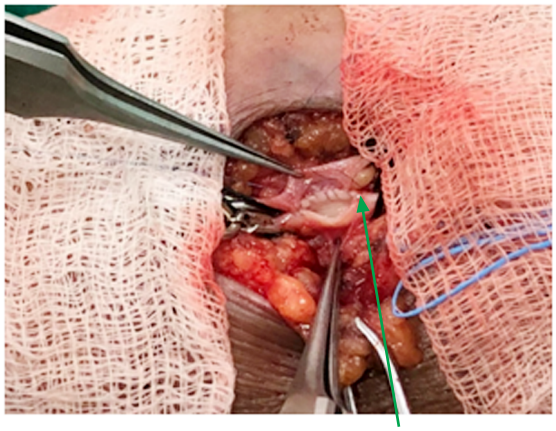
**AV fistula with Radial Artery at lower forearm – anastomosis completed**



**AV fistula with Radial artery at lower forearm – anastomosis completed (Magnified view)**

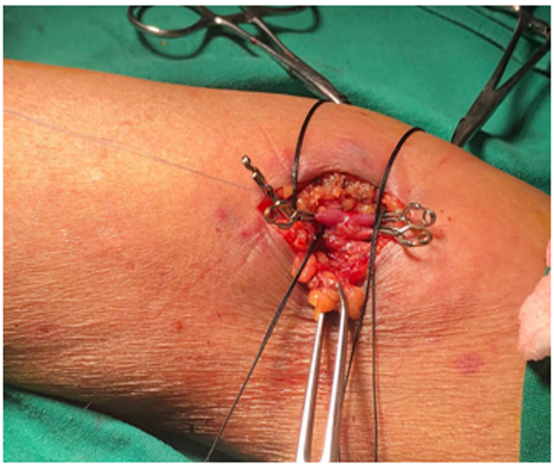


**Basilic Vein in Cubital fossa**

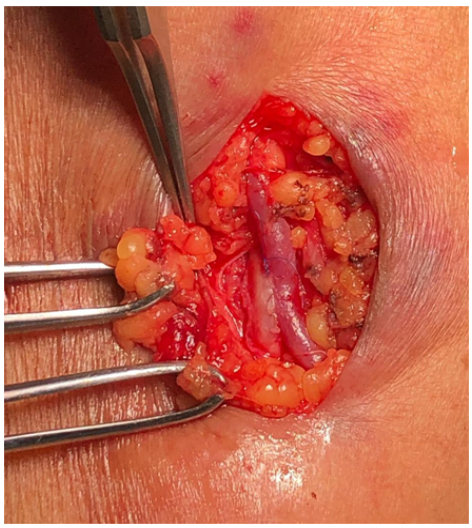


**Side to side anastomosis Posterior wall completed**

**Brachial artery AV fistula**



**Brachial artery AV fistula – completed**



**Brachial artery AV fistula – completed (Magnified view)**

**Reference :**


1. Brescia MJ, Cimino JE, Appel K, Hurwich BJ. Chronic hemodialysis using venipuncture and a surgically created arteriovenous fistula. N Engl J Med 1966; 275: 1089-92.
2. National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations 2006 updates: hemodialysis adequacy, peritoneal dialysis adequacy, vascular access. Am J Kidney Dis 48:S1-S322, 2006.
3. Patel ST, Hughes J, Mills JL Sr. Failure of arteriovenous fistula maturation: an unintended consequence of exceeding dialysis outcome quality initiative guidelines for hemodialysis access. J VascSurg 38:439-445; discussion 445, 2003.
4. Dhoul N, de Lusignan S, Dmitrieva O, Stevens P, O'Donoghue D. Quality achievement and disease prevalence in primary care predicts regional variation in renal replacement therapy (RRT) incidence: an ecological study. Nephrol Dial Transplant 27:739-746, 2012.
5. P Sahasrabudhe, T Dighe, N Panse, S Patil1. Retrospective analysis of 271 arteriovenous fistulas as vascular access for hemodialysis. Indian Journal of Nephrology 2013; 23 (3)m: 191-195.
6. Young EW, Dykstra DM, Goodkin DA, Mapes DL, Wolfe RA, Held PJ. Hemodialysis vascular access preferences and outcomes in the Dialysis Outcomes and Practice Patterns Study (DOPPS). Kidney Int 2002; 61:2266-71.
7. Roy-Chaudhury P, Kelly BS, Melhem M, Zhang J, Li J, Desai P, *et al*. Vascular access in hemodialysis: Issues, management, and emerging concepts. CardiolClin 2005;23:249-73.
8. Haimov M, Baez A, Neff M, Slifkin R. Complications of arteriovenous fistulas for hemodialysis. Arch Surg 1975;110:708-12.
9. Al Shohaib S, Al Sayyari A, Abdelkarin Waness A. Hemodialysis angioaccess choice and survival in a tertiary care Saudi Arabian center from 1993 to 2004. Nephro-Urology Monthly 2011;3:69-73.
10. Muhammad A. Siddiqui, Suhel Ashraff, Derek Santos et al. Predictive parameters of arteriovenous fistula maturation in patients with end-stage renal disease. Kidney Res ClinPract 37:277-286, 2018.

Original Article

# A Clinico Serological Study of Severe Dengue Cases Admitted in A Tertiary Care Hospital of Eastern India

**Dr. Dipika Menon Mukherjee[1], Dr. Dibyendu Banerjee[2], Dr. Salil Pal[3], Dr. Rajyshri Guha Thakurta[4], Dr. Bhabatosh Biswas[5]**

**Abstract :**

Dengue fever along with its different forms, including Dengue Haemorrhagic Fever, Dengue Shock Syndrome and Expanded Dengue Syndrome, are major health concerns. Since there is no specific treatment for the diseases, only appropriate medical care can save the lives of patients with serious complications.

Dengue may present with atypical features (EDS) complicating the diagnosis further. Certain studies have shown that gastrointestinal symptoms along with fever may be a presenting symptom in dengue patients. Our study, conducted in our tertiary care hospital, involving 100 patients, for a duration of three months, further corroborates this, with 52% of these dengue patients suffering from gastrointestinal symptoms.

**Key words :**

Dengue fever, atypical features, NS1 titre, severe dengue

**Introduction :**

Dengue is one of the most important emerging viral diseases of humans in the world afflicting humanity in terms of morbidity and mortality. Dengue fever (DF) and its severe forms — dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) — have become a major international public health concern. Over the past three decades, there has been a global increase in the frequency of dengue fever DF, DHF and DSS and their epidemics. This is particularly observed in tropical and subtropical areas, especially in urban and semi urban areas. According to the data provided by the WHO, an estimated 50 million dengue infections occur worldwide annually while an estimated 500000 people with DHF require hospitalization each year.

A very large proportion (approximately 90%) of them are children aged less than five years, and about 2.5% of those affected die.

Dengue and DHF is endemic in more than 100 countries in the WHO regions of Africa, the Americas, the Eastern Mediterranean, South-East Asia and the Western Pacific. The South-East Asia and Western Pacific regions are the most seriously affected.

The disease is caused by a virus belonging to the family *Flaviviradae* that is spread by *Aedes* (*Stegomyia*) mosquitoes. There is no specific treatment for dengue, but appropriate medical care frequently saves the lives of patients with the more serious dengue hemorrhagic fever. The most effective way to prevent dengue virus transmission is to combat the disease-carrying mosquitoes.

According to the *World Health Report 1996,*1 the "re-emergence of infectious diseases is a warning that progress achieved so far towards global security in health and prosperity may be waste."

Hence the magnitude of the problem cannot be underestimated. Added to this problem, is the appearance of dengue with a typical symptoms.

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This has necessitated the need of introduction of the term Expanded Dengue Syndrome (EDS) by WHO (2012) which includes the atypical symptoms of dengue.

Realizing the importance of this, we carried out a retrospective study, in our tertiary care hospital, Calcutta National Medical College and Hospital. Our study involved 100 patients, during the period September 2017 to December 2017, who had fever for 5 days and were NS 1 reactive. History regarding gastrointestinal symptoms as well as record of laboratory and radiological reports were noted. It was seen that 52% of the patients suffered from gastrointestinal symptoms.

**Material and Methods :**

The present work was a hospital based retrospective study carried in Calcutta National Medical College Hospital during the period September 2017 to December 2017.

The study population were patients (fever less than 5 days) admitted in the medicine ward of the hospital who were NS1 reactive. No control was required since it was a descriptive study.

Number of patients considered was 100. The blood of these patients admitted with features of dengue was sent to the microbiology laboratory of the hospital. Serum was separated from the sample received and it was refrigerated, in case the test was not carried out the same day.

ELISA technique using Panbios kits was used to determine the NS1 reactivity as well as the titre value. (The NS1 gene product is a glycoprotein produced by all flavivirus and is essential for the replication and viability of the virus. The protein is secreted by mammalian cells and not by insect cells. NS1 antigen appears as early as Day 1 after the onset of fever and declines by 5-6 days. Hence, tests based on this antigen can be used for early diagnosis)

The ward in which these NS1 reactive patients were admitted was visited and their history was noted in detail, particularly those relevant to the gastrointestinal tract.

Laboratory investigations, if done was noted, with special reference to liver function.

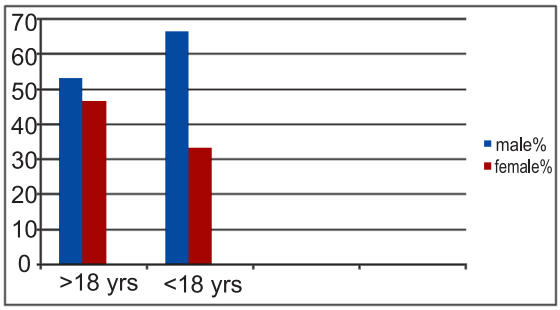
Radiological imaging, if done, was also noted. Data correlating gastrointestinal symptoms with NS1 reactive patients was analyzed.

**Results :**

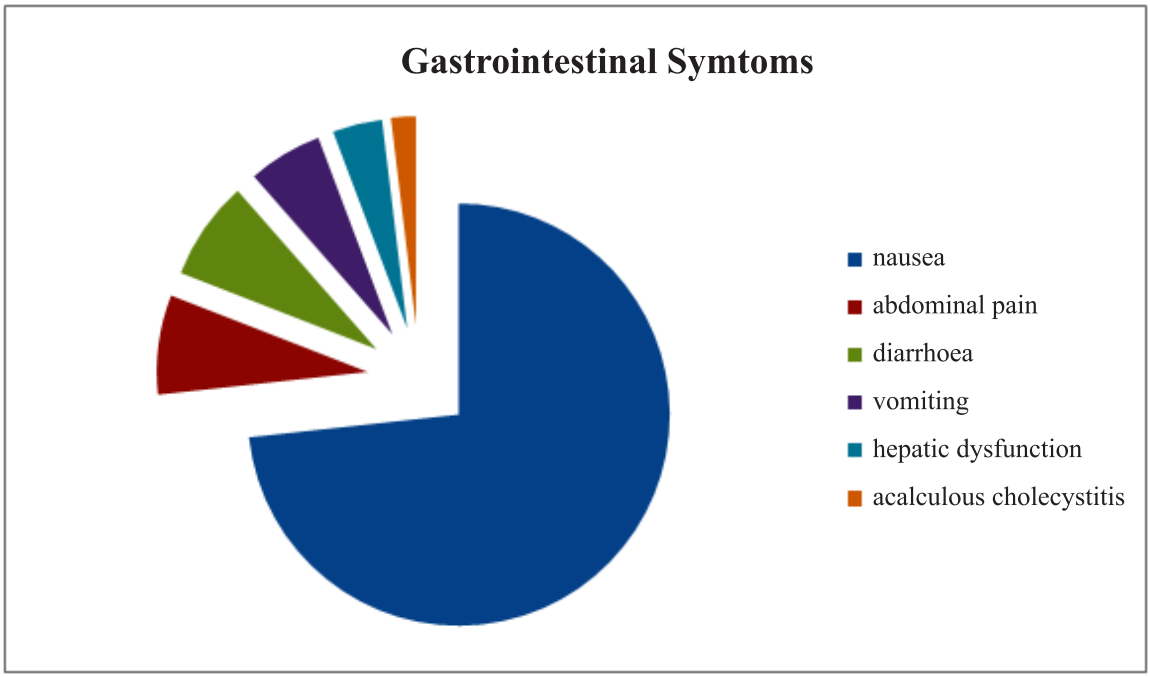
Of the 100 patients 52 had gastrointestinal symptoms. Of these 52, 30 were above the age of 18, 16 being males. The rest, ie 12 patients, were below the age of 18. Among these 12, 8 were males.

**Age and Sex distribution of spatients with symptoms :**

| Age years | Number (n= 52) | Number of males | % of males | Number of females | % of females |
|---|---|---|---|---|---|
| >18 | 30 | 16 | 53,.3 | 14 | 46.6 |
| <18 | 12 | 8 | 66.6 | 4 | 33.3 |




Of the 52 dengue patients with gastrointestinal symptoms, 38 had symptoms of nausea (73%), while 4 had abdominal pain (7.6%) and 4 had diarrhea (7.6%), 3 suffered from vomiting (5.7%) and 2 suffered from hepatic dysfunction (3.8%). Only 1 suffered from acalculous cholecystitis (1.92%).




(None of the patients suffered from DHS or DSS or suffered from mortality)

Few individuals had overlapping symptoms. The commonest overlap being between acute abdomen and nausea. 3 out of 4 patients (75%) suffering from abdominal pain also suffered from nausea.

**Discussion :**

Dengue virus is one of the most common arboviruses found in India. It has 4 serotypes (DEN-1to DEN-4). A fifth serotype DEN-5 was discovered in 2013. Dengue virus belongs to the family of Flaviviridae. The principal vector is Aedes aegypti, followed by Aedes albopictus.

According to traditional WHO classification (1997) dengue can be classified into three clinical stages, dengue fever, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

The latter two, are severe syndromes, more common in children who have passively acquired antibodies from the mother or individuals who have heterologous antibody caused by previous infection by a different serotype. These antibodies are non neutralizing and cause immunological catastrophe. The key pathological feature in DHF is increased vascular permeability with plasma leakage into interstitial spaces associated with increased vasoactive cytokines. This may lead to life threatening shock in some patients.[1]

The more recent classification of dengue by WHO in 2009, grades it into two stages based on severity of disease. Dengue with or without warning signs and severe dengue.

In 2012, WHO introduced a term Expanded Dengue Syndrome (EDS). The various atypical and unusual presentations of dengue was brought under this. These included symptoms involving the gastrointestinal, respiratory, cardiovascular, nervous, musculoskeletal system etc.

Going by the traditional classification, which is most commonly followed, the features of DF include sharp rise in temperature, flushed face, headache, retro orbital pain, arthralgia, bone pain, rash, skin hemorrhage may be present. However hemorrhagic complication is rare.

In DHF the above symptoms are present and the patient may also complain of epigastric discomfort, tenderness at the right costal margin, generalized abdominal pain. Hemorrhagic manifestations in the form of petechiae, ecchymoses, purpura or bleeding from mucosa, gastrointestinal tract, injection sites etc. The critical stage marked by plasma leakage is characterized by symptoms like pleural effusion, ascites, or hypoproteinaemia / albuminaemia or rising hematocrit value more than 20% from baseline.[2,3]

In severe cases there is persistent vomiting, abdominal pain, refusal of oral intake, lethargy or restlessness oliguria, postural hypotension signs of circulatory failure and finally shock. The patient may die unless suitable treatment is given on time.

Other than the typical symptoms mentioned above, dengue may present with atypical symptoms as well. This had necessitated the inclusion of the term EDS in 2012.

Of all the atypical symptoms the common one is involving the gastrointestinal tract. Previously features of gastrointestinal symptoms were considered when the patient was suffering from DHF or going by 2009 WHO classification, abdominal pain, vomiting were considered warning symptoms in dengue. While raised liver enzyme were considered in the criteria for severe dengue reflecting organ involvement.[4]

Retrospective analysis of abdominal and gastrointestinal symptoms in dengue fever was carried out by Ramos – De La Medina A et al. In a cohort of 8559 patients in 2006, abdominal and gastrointestinal symptoms were present in 67% of patients. The most frequent symptom being nausea 52%, followed by abdominal pain 36% diarrhea 17% hepatomegaly 2% gastrointestinal bleeding 0.3% and ascites 0.1%.[5]

Lovekesh Kumar et al. put forward a case report on 'Unusual Presentation of Dengue Fever Leading to Unnecessary Appendectomy'.[6,7]

Khor et al. reviewed 328 patients with DHF/DSS, only 14 had acute abdomen. Cause of acute abdomen being acute cholecystitis in 10 patients, nonspecific peritonitis 3 and acute appendicitis in one.[8]

Premaratna et al. reported 12 cases of dengue fever mimicking appendicitis.[9]

The above citations further reflects how dengue fever may present with acute abdomen leading to diagnostic dilemma.

Our study below carried out in our tertiary care hospital further corroborates the results. The laboratory tests available for diagnosis of dengue include analysis of hematological parameters, viral isolation, viral nucleic acid test-polymerase chain reaction (RT PCR, Nested RT PCR, Real time RT PCR, isothermal amplification method) and viral antigen detection-detection of NS1 antigen by ELISA and dot blot assay.

Immunological response test and serological tests includes hemagglutination test (HI), complement fixation (CF), neutralization test (NT) Ig M capture enzyme linked immunosorbent assay and indirect Ig G ELISA.[10,11]

MAC – ELISA and Ig G ELISA are the common tests used. However these tests might not provide early diagnosis, thus in our study NS 1 reactive

cases were taken. Detection of NS1 antigen has moderately high sensitivity and very high specificity to dengue. Commercial kits available do not differentiate between serotypes, however apart from providing an early diagnostic marker for clinical management it may also facilitate the improvement of epidemiological surveys of dengue infection.

**Conclusion :**

From the above study we corroborate the fact that patients with dengue fever may present with gastrointestinal features.

The study would have further substantiated information if it was carried out for a longer period, covering a larger area and involving patients who were Ig M positive as well.

Hence in the differential diagnosis of fever with gastrointestinal symptoms, dengue fever must be kept in mind. Particularly in cases of fever with acute abdomen, differential diagnosis of dengue may eliminate the chances of unnecessary operations.

**References :**


1. Gupta, N, Srivastava, S, Jain, A, Chaturvedi, U.C. Dengue in India. IJMR. 2012;136(3): 373-390.
2. Guzman, M. G, Halstead, S. B, Artsob. Dengue : a continuing global threat. Nat Rev Microbiol. 2010;8(12): 7-16.
3. Gubler, D. J, Manasa, G. Dengue and dengue haemorrhagic fever. Clin Microbiol Rev. 1998;11(3): 480-496.
4. Randall, M, Packard. Break bone disease in Philadelphia, 1780: Reflections on History of Disease. Bulletin of Medicine. 2016;90(2): 193-221.
5. Prasanth, V. N, Manasa, G. Study of gastrointestinal manifestations in dengue fever. IJAM. 2019;6(5): 11-14.
6. Kumar, L, Singh, M, Saxena, A, Kolhe, Y, Karande, S. K. Unusual Presentation of Dengue Fever Leading to Unnecessary Appendectomy. Case Reports in Infectious Diseases. 2015;2015 (May): 3-6.
7. Wiwanitkit, V. Dengue hemorrhagic fever presenting as acute abdomen. SQUMJ. 2012;12(1): 129-130.
8. Khor, B. S, Liu, J. W, Lee, I. K, Yang, K. D. Dengue hemorrhagic fever patients with acute abdomen: clinical experience of the 14 cases. The American Journal of Tropical Medicine and Hygiene,. 2006;74(5): 909-914.
9. Premratna, R, Bailey, M. S, Ratnasena, B. G. N, De-silva, H. J. Dengue fever mimicking acute appendicitis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2007;101(7): 683-68
10. Trofa, A. F, De-fraites, R.F, Smoak, B. L, Kanesa-thanesa, N, King, A.D. Dengue fever in US military personnel in Haiti. JAMA. 1997; 277 (April): 1546-1548.
11. Thisyakorn, U, Thisyakorn, C, Limpitikul, W, Nisalak, A, King, A. D. Dengue infection with central nervous system manifestations. Southeast Asian J Trop Med Public Health. 1999;30: 504-506.

Original Article

# Outcome of Surgery of Hydatid Cysts of Lungs

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**Abstract :**

Hydatid cysts are characterised by cystic space occupying lesions in the lungs, the liver and rarely in other parts of the body.

Surgical removal is the treatment of choice for lung hydatids.

A retrospective study was conducted in the department of CTVS, R G Kar from February 2006 to August 2017.

The clinical records of 286 consecutive cases of Hydatid cysts of lungs, operated during this period were analysed.

It was concluded from the study that surgery was the safe therapeutic option and could be practiced in all most all the cases of hydatid cysts with minimal mortality and very low morbidity.

**Introduction :**

Hydatid disease is prevalent and wide spread in most sheep-rearing countries in Asia, Australia, South America and Southern Europe.

Human is affected by the larval stage of Echinococcus.

The genus Echinococcus include following four species :

*Echinococcus Granulosus,*

*Echinococcus Multilocularis,*

*Echinococcus Oligarthus and*

*Echinococcus Vogeli.*

Out of all these species, Echinococcus Granulosus is the commonest organism for affecting human being and producing hydatid cysts of lungs, liver and other organs.

These cysts are produced in human by the larval stage of Echinococcus.

*Echinococcus Granulosus is the commonest species infesting human beings.*

***Echinococcus Granulosus (Adult Worm)***

**Hydatid Cyst consists of the following structures -**

Wall of Hydatid Cyst Consist of Three layers:

1. *Endocyst (Germinal Layer)* – This layer is 25 µm thick, secreting 'Hydatid fluid' and producing 'Brood Capsules as well as Scolices'.
2. *Ectocyst* - This layer is 1 mm thick, tough, elastic and looking like hardboiled egg white. This is derived from the parasite and composed of Mucopolysaccharide material.
3. *Pericyst* - This layer is produced by cellular reaction of the host. This may become calcified and the parasite within the cyst may die or Degenerate in due course.

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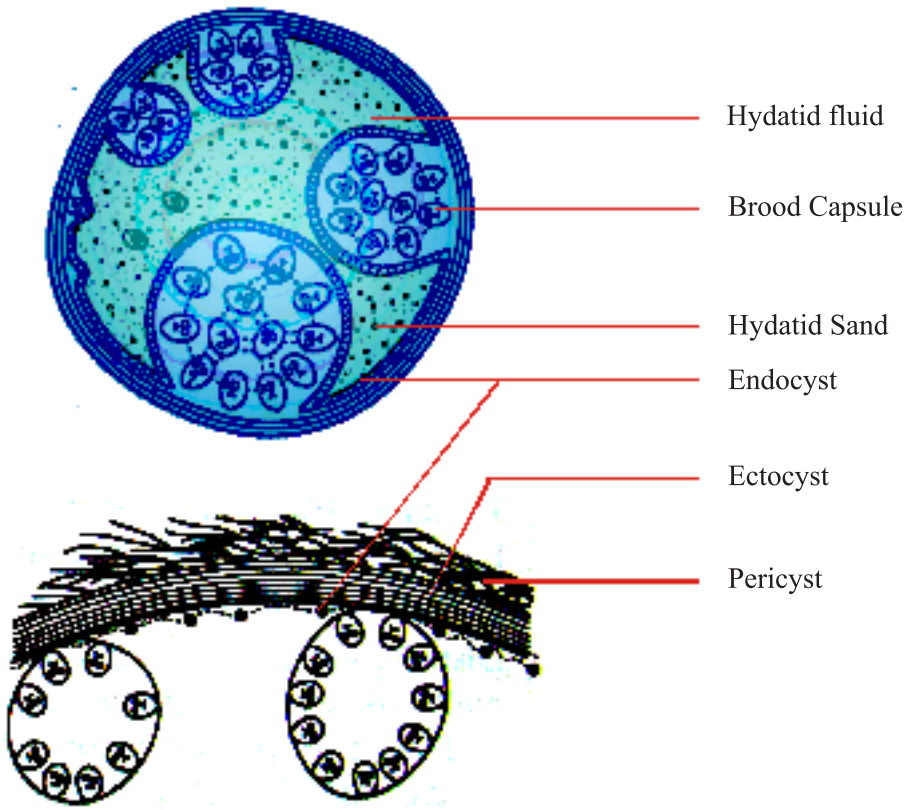


**Structure of Hydatid Cyst**

The cysts gradually enlarge within the lungs or other affected organs compressing the tissues harbouring the cysts. The cysts may get infected and finally may damage the organ irreversibly. Hydatid Cysts may be multiple affecting one or both the lungs, liver as well as many other organs of human body.

Therapeutic options include drug therapy with Albendazole, PAIR therapy as well as Surgery.

Ultrasound staging (CL, CE1, CE2, CE3, CE4 & CE5) is currently recommended for planning therapy. The following salient points of each USG stage of Hydatid cysts are useful for guiding therapy.

CL = Cystic lesion with no visible cyst wall.

CE1 = Cystic lesion with visible cyst wall and snowflake sign.

CE2 = Cystic lesion with visible cyst wall with internal septation.

CE3 = Transitional cyst.

CE4 = Inactive cyst with a non-homogenous mass.

CE5 = Inactive cyst with a Thick calcified wall.

Medical Therapy with 'Albendazole', 15 mg/kg of body wt. daily in two divided doses is usually recommended. Albendazole therapy alone for 3

to 6 months results in cure in 30% and improvement in another 50% cases of Hydatid cysts.

'Albendazole' therapy is started several days before surgery and is continued for several weeks after surgery.

PAIR Therapy (Percutaneous aspiration, infusion of scolicidal agents and re aspiration) is indicated for uncomplicated CE1, and some CE2 and CE3 lesions.

For PAIR therapy, Albendazole is usually started 4 days prior to PAIR and continued for atleast 4 weeks afterwards.

Praziquantel Therapy is reserved for selected cases and is recommended as scolicidal agent in the dose of 50 mg/Kg of body wt. daily for 2 weeks.

Surgical removal is the treatment of choice for all most all the cases of lung hydatids.

Surgery is the safe therapeutic option for lung hydatids.

Removal of the Hydatid Cyst should be done under cover of 'Albendazole'. Conservative surgery is successful for majority of the cases.

Lung Resection may be required in selected cases only with irreversible damage of the affected lung.

Currently 'Minimally Invasive Surgery' (VATS) has also very limited role in the surgical management of Hydatid cysts and it is reserved for selected cases only.

**Materials and methods :**

A retrospective study was conducted in the department of CTVS, R G Kar from February 2006 to August 2017. All the patients admitted in the department were studied.

The clinical records of 286 consecutive cases of Hydatid cysts of lungs, operated during this period were analysed.

Detailed clinico pathological parameters of all the patients were noted.

Medical Therapy was started with 'Albendazole' in the dose of 15 mg/kg of body wt. daily in two divided doses in all the patients preoperatively.

'Albendazole' therapy was started several days before surgery in OPD and was continued for several weeks after surgery.

Surgery was done with Thoracotomy, bi-lateral Thoracotomy or Sternotomy depending on number and sites of hydatid cysts.

Patients were operated with Double Lumen Endotracheal Tube (DLET) with ipsilateral lung collapse.

Postero-lateral Thoracotomy was practiced in the majority of the cases.

The area around the cysts with lung was packed with normal saline soaked mops.

Barret's technique was followed in the uncomplicated cases. Bronchial openings after removal of the cysts were closed with interrupted 3-0 vicryl sutures.

The Chest cavity was thoroughly washed with normal saline.

In infected cases, Barret's technique was not useful.

In the cases with gross lung damage, conservative lung resection done.

The chest was closed with two intercostal chest drains as a routine practice.

Chest drains were removed on variable days depending on the clinical progress.

The drains were removed when the underlying lung was found to be fully expanded both clinically and radiologically with minimal collection and without any air leak atleast for 48 hours.

Post-operative complications were recorded.

Patients were followed up in OPD clinic periodically.

**Results and analysis :**

This study, included 286 consecutive cases of Hydatid cysts of lungs fulfilling the inclusion as well as exclusion criteria.

In this series, 166 (58.04%) were males and remaining 120 (41.96%) patients were females.

In this study, maximum number of cases were between 20 years to 45 years age.

Our series comprised of 254 (88.81%) cases of Pulmonary hydatids of one lung (Right/Left ).

Remaining 32 (11.19%) cases had bilateral hydatid cysts. 8 of these bilateral cases also had liver hydatid cysts. 13 (5.37%) cases of hydatid cyst of right lung had associated hydatid cysts of liver also.

Out of 254 cases of Pulmonary hydatids of one lung (Right/Left ), 242 (95.28%) were managed with Single sided Thoracotomy (Right/Left) and the remaining 12 (4.72%) cases were managed with VATS.

13 (5.37%) cases of hydatid cyst of right lung had associated hydatid cysts of liver also. These cases were managed with Right Thoracotomy and Phrenotomy.

Out of 286 cases, 32 (11.19%) cases having bilateral hydatid cysts were managed with bilateral thoracotomy either in single sitting or as staged procedure.

8 of these bilateral cases also had liver hydatid cysts. These cases were managed with thoracotomy and phrenotomy.

Phrenotomy and Thoracotomy was required in 21 (7.34%) cases having liver hydatids along with pulmonary hydatids in the entire series.

In our series of 286 cases, 45 (15.73%) were infected, 28 (9.79%) cases were ruptured and the remaining 213 (74.84%) had uncomplicated cysts.

122 cases (42.66%) underwent cyst excision by Barrett's technique and 16 cases had conservative lung resection in the form of Wedge Resection, Segmentectomy or Lobectomy.

Post-operative recovery was uneventful in most of the cases. However, air leak continued for almost 3 weeks in 25 patients. There was no mortality in this series.

**Discussion :**

Hydatid cysts are the cystic space occupying lesions in the lungs, the liver or infrequently in any other parts of the body.

In our study, 213 out of 286 cases of Hydatid Cysts were uncomplicated.

Mitrofan C. et al observed in their study that 134 out of 247 patients had uncomplicated cysts[1].

Our series comprised of 254 (88.81%) cases of one lung (Right/Left ) Pulmonary hydatids and 32 (11.19%) cases of bilateral hydatid cysts.

Ulkü R et al found Isolated pulmonary hydatid cysts in 61 out of 83 patients (92.4 %) in their series[2].

Mitrofan C. et al observed that the cysts were located in the right lung in 115 cases (46.5%), in the left lung in 98 cases (39.5%) and bilaterally in 34 cases (14%)[1].

Phrenotomy along with Thoracotomy was required in 21 (7.34%) cases having hydatid cysts of liver along with lung.

However in the series of Mitrofan C. et al, liver cysts were associated with lung hydatids in 28 cases (11.3%) out of 247 cases[1].

In the study of et al, 87 cases of 422 had cysts in the liver along with lung hydatids[3].

In our series of 286 cases, 16 (5.59%) had conservative lung resection in the form of Wedge Resection, Segmentectomy or Lobectomy.

In the series of 247 cases reported by Mitrofan C. et al, Pulmonary resection was used in 46 cases (18.5%), including 16 wedge resections, 27 lobectomies and 3 pneumonectomies[1].

Post-operative recovery was uneventful in most of the cases. However, air leak continued for almost 3 weeks in 25 (8.74%) patients of our series of 286 patients.

Prolonged air leak was observed in 8 (7.48%) cases out of 107 patients of hydatids in the series reported by et al[4].

We had no mortality in our series of hydatids. Death of 3 (1.8%) patients were reported by et al in a series of 169 patients of hydatids[5].

**Conclusion :**

Surgical removal is the treatment of choice for all most all the cases of lung hydatids and have been established as the safe therapeutic option for lung hydatids.

Safe surgical removal of hydatid cysts have also been reported for bilateral lung hydatids as well as for lung and liver hydatid cysts.

Though staged surgery for bilateral hydatids are commonly practiced, simultaneous bilateral thoracotomy for bilateral lung hydatids have also been reported.

Removal of the Hydatid Cyst should be done under cover of 'Albendazole'. Conservative surgery is successful for majority of the cases.

Lung Resection may be required in selected cases only with irreversible damage of the affected lung.

**References :**


1. Mitrofan C, Aldea A, Mitrofan E, Bosanceanu M, Farmatu L, Jitaru I, Moldoveanu C, losep G., Surgical treatment of lung hydatid cysts, Langenbecks Arch Surg. 2009 Jan; 394(1):199-204.
2. Ulkü R, Onen A, Onat S; Surgical treatment of pulmonary hydatid cysts in children: report of 66 cases; Eur J Pediatr Surg. 2004 Aug;14(4):255-9.
3. Dakak M, Genç O, Gürkök S, Gözübüyük A, Balkanli K; Surgical treatment for pulmonary hydatidosis (a review of 422 cases); J Royal College Surg Edinb. 2002 Oct;47(5):689-92.
4. Hasdiraz L, Oguzkaya F, Bilgin M; Is lobectomy necessary in the treatment of pulmonary hydatid cysts?; ANZ Journal of Surgery, 01 Jun 2006, 76(6):488-490.
5. Ulkü R, Yilmaz HG, Onat S, Ozçelik C.; Surgical treatment of pulmonary hydatid cysts: report of 139 cases; Int Surg. 2006 Mar-Apr;91(2):77-81.

Case Report

# Mediastinal Hemangioendothelioma Presenting as A Surgical Emergency — A Rare Case Report And Review of Literature

Dr. Eshpuniyani Prriya[1], Dr. Deshpande Ramakant[2], Dr. Kulkarni Ulhas[3], Dr. Doshi Kumar[4], Dr. Pathan Sameer[5]

**Abstract :**

Epithelioid hemangioendothelioma (EHE) of soft tissues is a rare low-grade vascular tumour, with variable malignancy. Mediastinal localization is exceptional.

We report a case in which a 43 year old patient with no comorbidities presented to us in emergency with severe breathlessness and severe orthopnoea. Computed tomography of patient done elsewhere showed a large anterior mediastinal mass more on the left hemithorax with mild left pleural effusion.

An emergency surgery was done with median sternotomy wherein an awake intubation was imperative. 20cm. anterior mediastinal mass was excised in toto and sent for histopathology. Final histopathology showed it to be Anterior Mediastinal Hemangioendothelioma (MHE) which was confirmed by Immunohistochemistry.

Patient underwent the surgery uneventfully and was extubated after 24 hours of elective ventilation. His Intercostal drains were removed on 6th and 8th day and he was discharged on postoperative day 9. He was stable on first follow up after 15 days. EHE should be considered in the differential diagnosis of mediastinal masses in adult patients. After radical removal prognosis is generally favourable, but strict follow-up must be performed because aggressive forms have been described.

**Introduction :**

Epithelioid hemangioendothelioma (EHE) is a rare type of endothelial tumor that demonstrates an intermediate behavior between benign hemangioma and malignant angiosarcoma.[1,2,3] It was first described by Weiss and Enzinger in 1982(7) Soft tissues EHE occurs in the extremities (65%), head and neck (12%), trunk (8%), mediastinum (8%), genitals (4%) and retroperitoneum (2%).[4,2] EHEs have also been reported in the lung (so-called intravascular bronchiolar tumours) and liver.[4] Mediastinal EHEs usually originate from medium-sized or large veins: EHEs arising from superior vena cava (SVC) and left brachiocephalic vein have been reported.[4] Surgery is the treatment of choice. Adjuvant radiation therapy is considered in the case of high-risk features or when complete removal is not feasible.[1] We report a case of a large mediastinal hemangioendothelioma originating from a branch of internal mammary artery causing severe respiratory distress in a 43 year old gentleman.

To the best of our knowledge there has been no report of mediastinal hemangioendothelioma arising from internal mammary artery and our case is the first such in the literature.

**Case Report :**

43 year old gentleman presented to our department with severe breathlessness and orthopnea. A Contrast enhanced computed tomography (CECT) done elsewhere revealed a large mediastinal prevascular partially necrotic lesion comprising the arch of aorta suggestive

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of necrotic lymph node most probably neoplastic in etiology.

CT guided biopsy showed delicate vascular channels in spindly hyalinised myxoid stroma. He was given 1 cycle of Chemotherapy (Etoposide + cisplatin) empirically with working diagnosis of teratoma.

At time of presenting to our department, he was severely breathless and orthopneic. In view of his general condition an emergency surgery wit awake intubation was performed via median sternotomy. Intraoperative findings showed a large encapsulated firm lobulated mass in anterior mediastinum more on the left side adherent to a branch of left internal mammary artery. The mass was excised in toto. Both lungs expanded well on table. Patient was electively ventilated for 24 hours and was extubated uneventfully thereafter. He had a stable postoperative period. The intercostal drains were removed on postoperative day (POD) 6 and 8. He was discharged on POD10.

Final Histopathology gross showed a lobulated nodular and smooth mass covered with fatty tissue weighs 1638.1gm and measures 20.0 x 10.0 x 9.0 cm. Serial cut slices reveal a tan soft to firm surface with scattered small and large cystic area containing hemorrhages to necrotic debris along with large geographic areas of necrosis. Microscopy revealed hemangio-endothelioma, anterior mediastinum. Maximum tumor size is 20.0 cm. Post-chemotherapeutic changes are evident as areas of necrosis with intact overlying capsule. Perineural invasion not seen. Immunohistochemistry showed positivity for CD31, CD 34,Vimentin, D2-40, ERG, focal positivity for CD 99 and cytokeratin (AE1/AE3) and Mib-1 had moderately high index.

He was doing well at first follow up after 15 days. However at the end of 3 months his imaging showed recurrence of the lesion. He was started on chemotherapy including bevacizumab by the medical oncology team however he progressed rapidly and expired at the end of 8 months postoperatively.

**Discussion :**

Epithelioid haemangioendothelioma (EHE) is a rare neoplasm of vascular origin, defined by the 2002 WHO classification as a lowgrade locally aggressive angiosarcoma with metastatic potential.[5] Haemangioendothelioma demonstrates an intermediate behavior between benign hemangioma and malignant angiosarcoma.[1,2,3] Epithelioid hemangio-endothelioma (EHE) is probably the most aggressive histological subtype.[1] It usually occurs in adults of both sexes.[4,1,6,7,3] but may rarely also affect children.[1]

The common sites of involvement include bone (especially involved the long tubular bones in lower extremity), soft tissue, liver and lung. Occasionally, it can occur in mediastinum.[7] Most patients of mediastinal hemangio-endothelioma are asymptomatic[4,1,2,3] however when mediastinal vessels are involved, SVC syndrome or symptoms of compression of surrounding structures may be present.[4] Other symptoms of mediastinal hemangioendothelioma may be nonspecific, mainly due to the local compression and stimulation of the adjacent organs, such as chest pain, cough, dyspnea, hoarseness in voice.[2] EHEs are generally located in the anterior mediastinal compartment[2] although cases originating in the posterior compartment have been reported.[4]

Our patient was a 43 year old gentleman who presented to us with severe orthopnea. On

imaging he had a large anterior mediastinal mass with compression on arch of aorta. However there was no SVC obstruction.

Computed tomography (CT) shows a soft-tissue mass with a welldefined margin[2,4] Calcification is observed in approximately 40% of MEHE cases, which could be attributed to metaplastic bone formation, osteoclast-like giant cells, or phleboliths[2] 18F-FDG-PET/CT can be useful to evaluate metabolic activity of EHEs and search for metastases.[4,1]

CT scan of our patient revealed a well circumscribed anterior mediastinal mass with compression of arch of aorta. (Fig1)

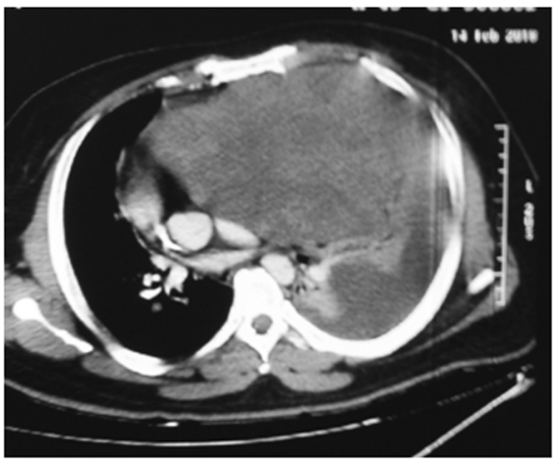

**Fig 1: CECT shows a large mediastinal (Predominantly left) prevascular lesion comprising the arch of aorta and mild left pleural effusion**

Intraoperatively mediastinal hemangio-endothelioma is usually observed to originate from blood vessels, especially from veins, such as brachiocephalic vein, superior vena cava, azygos vein, etc.[6,2]

Our patient had a tumour arising from Internal mammary artery. To the best of our knowledge there has been no other reported literature of internal mammary artery as origin.

Complete surgical resection is the treatment of choice.[4,1,3] Most of the MHEs are encapsulated[2] or well circumscribed[4] intraoperatively.

Angiogenesis inhibition with bevacizumab and paclitaxel stopped disease progression in a case of aggressive metastatic disease.[5,1]

We performed a R0 resection of the tumour arising from the internal mammary artery. It was a well circumscribed mass with no infiltration to surrounding structures. (Fig2).

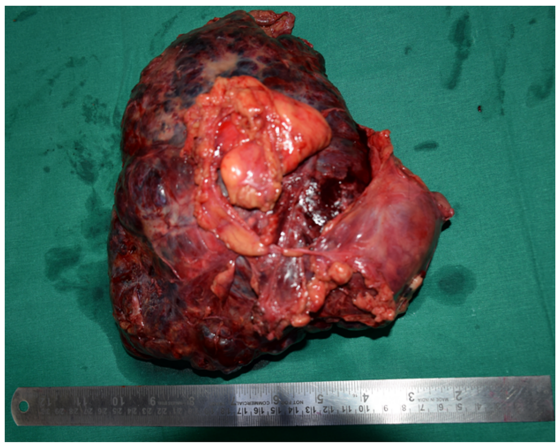

**Fig 2: Well circumscribed, encapsulated, lobulated (20X10cm) anterior mediastinal mass**

Diagnosis is confirmed by Immuno-histochemistry with samples staining positive for CD31, CD34, F8 and Fli-1. While CD34 is non-specific, CD31 is both specific and sensitive, being positive in 90% of cases.[5]

Immunohistochemistry showed in most studies positive testing for Factor VIII-related antigen and CD34.[6,5,2] Our IHC showed positivity for CD 31 and CD 34 among others to confirm the diagnosis.

He was started on paclitaxel and bevacizumab

on recurrence however he progressed rapidly. The mean survival period of patients with EHE is 4.6 years (range, 6 months to 24 years).[2] Studies have reported that 10% and 20% of MEHE cases showed local recurrence and metastases, respectively.[2,4]

Our patient had disease free period of 3 months only inspite of R0 resection with no metastases at diagnosis and progressed rapidly. He expired at the end of 8 months post surgery.

Mediastinal hemangioendothelioma is a rare occurrence. To the best of our knowledge a MHE arising from internal mammary artery has not been reported in the literature. However the behavior is very unpredictable inspite of the benign looking , well circumscribed, encapsulated tumour. It can recur or metastasize very rapidly or patient may survive for more than 20 years disease free.

**References :**


1) Maria Paola Ciliberti, Raffaella Caponio, Antonio Pascali, Gabriele Matichecchia et al. A rare case of intravascular epithelioid hemangioendothelioma of the cephalic vein treated with surgery and postoperative radiation therapy: a case report and review of the literature. Journal of Medical Case Reports 9:91; 2015.

2) Wan et al. Epithelioid hemangioendothelioma of right innominate vein mimics a teratoma A case report. Medicine (2017) 96:9.

3) Blanco M, et al. Hemangioendotelioma epitelioide mediastínico simulando un teratoma. Arch Bronconeumol. 2011;47:376–7.

4) Angela De Palma, Vincenzo Pagliarulo, Nicoletta Ardò and Domenico Loizzi. Surgical treatment of a rare case of epithelioid hemangioendothelioma of the azygos vein. Interactive CardioVascular and Thoracic Surgery 14 (2012) 91–93.

5) D. Patrini et al. Mediastinal hemangioendothelioma: Case report and review of the Literature. Respiratory Medicine Case Reports 22 (2017) 19e23 23.

6) Ziad Mansoura, Agne`s Neuvilleb, Gilbert Massarda, Mediastinal epithelioid haemangioendothelioma: a rare mediastinal tumour. Interactive CardioVascular and Thoracic Surgery 10 (2010) 122–124

Yang Liu, Yue-Feng Jiang, Ye-Lin Wang, Hong-Yi Cao et al. Epithelioid hemangioendothelioma of the anterior mediastinum: a case report. Int J Clin Exp Pathol 2016;9(5):5746-5752.

Case Report

# A Case of Primary Alamyloidosis Treated Previously as Chronic Liver Disease

**Dr. Pradeep Chakraborty[1], Dr. Sujata Mazumder[2], Dr. Barun Ghorui[3], Dr. Honey Maity[4], Dr. Shyamashree Mondal[5]**

**Abstract :**

Amyloid light chain (AL) results from the deposition of immunoglobulin light chain fragments, and can affect multiple organs/systems. Our patient was diagnosed as chronic liver disease because of ascites with splenomegaly with coarse liver echo texture, but the treatment was not effective and patient was not responding well. We did extensive laboratory examinations including serum/urine protein electrophoresis, bone marrow aspiration and biopsy along with liver biopsy and kidney biopsy.

**Conclusion :**

A diagnosis of primary AL amyloidosis was established.

**Abbreviations :** al = amyloid light chain, mg = monoclonal gammopathy, mgus = monoclonal gammopathy of undetermined significance, mm = multiple myeloma,

**Keywords :** amyloidosis, myeloma

**Introduction :**

Amyloidosis is a group of rare diseases caused by extracellular deposition of amyloid.[1] It may affect multiple organs with protean manifestations, thus often causing delayed or incorrect diagnoses. While nephrotic syndrome, cardiomyopathy and peripheral neuropathy are common in amyloidosis, it is relatively rare for a patient with the major presentation as chronic liver disease. Here, we report a caseof a middle-aged man whowas hospitalized because of the abdominal swelling.

**Case Report :**

66yr old male patient from Hooghly came to OPD with c/o gradual abdominal distension for last 1month with bipedal swelling for last 15 days.He also used to have mild irregular fever for last 15 days. He also felt that he was havingright upper quadrant abdominal pain for same duration. Patient is a known hypertensive on telmisartan.

He hadno history of haematemesis, melena, alcohol intake, blood transfusion, exposure, facial puffiness, paroxysmal nocturnal dyspnea, recent sore throat/skin infection and low back pain in the past. He was previously admitted in govt. hospital for ascites and he was diagnosed to have chronic liver disease because of splenomegaly with high SAAG ascites with coarse hepatic echotexture. But his symptom did not improve with diuretics and he was deteriorating day by day. Then he was admitted in our institute for detailed evaluation. After admission on examination of the patient, we found that patient was conscious, alert, co-operative with thin built, height 5.8 ft, weight 55 Kg. blood pressure 150/90 mmHg. Other vitals were within normal limit. On general survey, Pallor was present with bilateral pedal edema and inguinal lymph node > 2cm in size on both side.

On systemic examination, he had huge hepatomegaly withirregular surface and margin, splenomegaly and ascites. He was also found to have scrotal edema. Other systems were within normal limit.

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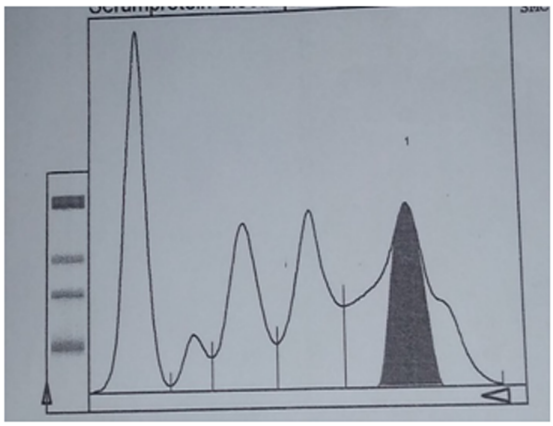
Investigations were started to find out cause of hepatomegaly because his liver was large instead of shrunken as found in majority of chronic liver disease.

- CBC Hb 10 gm/dl, TLC 7000/cmm, N65L28M3E4, Platelet 1.3 lakh/cmm.
- Sodium 136, potassium 4.5, urea 45, creatinine 1.1.
- Urine R/E albumin ++
- LFT: total bilirubin 0.2, total protein 5.1, albumin 1.8, globulin 3.3, ALP 335.
- SGOT and SGPT werenormal.
- Chest x-ray PA view was normal.
- Echocardiography was Normal.
- 24 hour urinary protein was 2.8gm/day.
- Ascitic fluid study showed high SAAG ascites with 250 cells/ml with all lymphocyte along with ADA 8.5 and malignant cell negative.
- USG whole abdomen : heterogeneous liver with hepatomegaly with mild splenomegaly with ascites.
- Splenoportal Doppler: normal.
- Upper GIEndoscopy: normal.

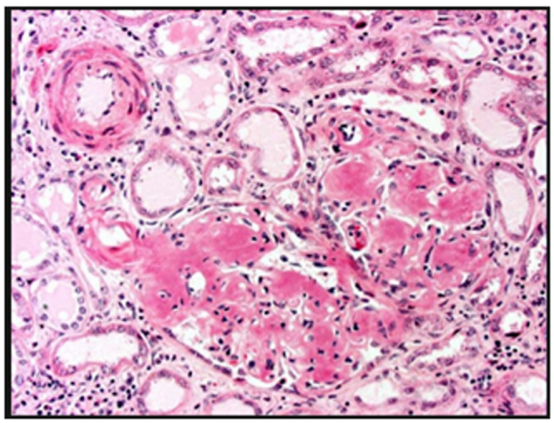
After analyzing the initial reports,patient was planned for further investigation to find out the cause.

- For further investigation planned for
- FNAC from inguinal lymph node
- kidney biopsy(for proteinuria)
- liver biopsy(heterogeneous liver with raised ALP)
- Serum protein electrophoresis was sent in view of altered A:G ratio
- CECT whole abdomen and chest was done.

Reports of serum protein electrophoresis and kidney biopsy are as follows :



**A. Serum protein electrophoresis showing sharp M Band.**



**B. Kidney biopsy showing renal amyloidosis (with al amyloid deposition in immunofluroscence)**

Bone marrow examination was done.It showed 12% plasma cells in bone marrow. Liver biopsy also showed amyloidosis.

Patient consulted with haematologist and Patient was put on treatment

- BORTEZOMIB
- DEXAMETHASONE

- CYCLOPHOSPHAMIDE
- CO-TRIMOXAZOLE
- FLUCONAZOLE

Patient improved with treatment and was discharged in stable condition. Patient improved significantly on follow up visit.

**Discussion :**

- This was a case of multiple myeloma with AL amyloidosis.
- Multiple myeloma can present with AL amyloidosis in 15% cases.
- Amyloidosis results in amyloid nephropathy which may lead to nephrotic syndrome/ subnephrotic proteinuria.
- Liver enlargement was due to amyloidosis
- According to diagnostic criteria of symptomatic multiple myeloma
  1. M band present in serum.
  2. Bone marrow plasma cell >12%
  3. Myeloma related organ impairment.

In a case report in Indian journal of nephrology 2016, Dr. A. Hazra and Dr. D. Bandyapadhya has mentioned that multiple myeloma can present with AL Amyloidosis of kidney with upto 10gm. proteinuria per day.

In another case report in journal of hepatology, 2003 from Spain also has mentioned that AL Amyloidosis can occur in liver in multiple myeloma. This type of cases associated with hepatic amyloidosis are usually associated with poor outcome.

AL amyloidosis results from the deposition of fibrillar protein consisting of the light chain of immunoglobulin with the lambda type accounting for 75% of all cases.[3] While this clonal B-cell disorder may be associated with multiple myeloma (MM) and lymphoma, it can also be idiopathic.[4] Clinical and laboratory data, shows plasmacytosis (12%) from bone marrow assay, indicate that the original disease is (MM). Amyloidosis occurs in about 15% of MM patients.[5] Protean manifestations often lead to delayed and incorrect diagnosis. Biopsy specimens with positive Congo red staining is critical for its diagnosis. Identification of the type of immunoglobulin light chains helps unveil the underlying diseases.[6] Although cumbersome, mass spectrometry of amyloid material remains the gold standard foritsfinal diagnosis.

**References :**


1. Wechalekar AD, Gillmore JD, Hawkins PN. Systemic amyloidosis. Lancet 2015;387:2641–54.
2. Lipsker D. Monoclonal gammopathy of cutaneous significance: review of a relevant concept. J EurAcad Dermatol Venereol 2017;31:45–52.
3. Merlini G, Stone MJ. Dangerous small B-cell clones. Blood 2006;108: 2520–30.
4. Kumar S, Sengupta RS, Kakkar N, et al. Skin involvement in primary systemic amyloidosis. Mediterr J Hematol Infect Dis 2013;5:e2013005.
5. Sipe J, Cohen A. Amyloidosis. In: Kasper D, Braunwald E, Hauser S, et al. eds. Harrison's Principles of Internal Medicine. 16th ed. New York: McGraw-Hill; 2005:2024.
6. Ohashi T, Kikuchi N, Yamamoto T. Unusual milia amyloidosis as initial signs of multiple myeloma-associated systemic amyloidosis. Int J Dermatol 2013;52:981–2.

7. Vrana JA, Gamez JD, Madden BJ, et al. Classification of amyloidosis by lasermicrodissection and mass spectrometry-based proteomic analysis in clinical biopsy specimens. Blood 2009;114:4957–9.

8. Sethi S, Theis JD, Leung N, et al. Mass spectrometry-based proteomic diagnosis of renal immunoglobulin heavy chain amyloidosis. Clin J Am SocNephrol 2010;5:2180–7.

9. Klein CJ, Vrana JA, Theis JD, et al. Mass spectrometric-based proteomic analysis of amyloid neuropathy type in nerve tissue. Arch Neurol 2011; 68:195–9.

10. Brambilla F, Lavatelli F, Di Silvestre D, et al. Reliable typing of systemic amyloidoses through proteomic analysis of subcutaneous adipose tissue. Blood 2012;119:1844–7.

11. Schreml S, Szeimies RM, Vogt T, et al. Cutaneous amyloidoses and systemic amyloidoses with cutaneous involvement. Eur J Dermatol 2010; 20:152–60.

Case Report

# A Rare Case of Juvenile Adrenal Pheochromocytoma

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**Abstract :**

Pheochromocytomas are rare tumours originating in chromaffin cells, representing 0.1–1% of all secondary hypertension (HT) cases. The majority are benign and unilateral, characterised by the production of catecholamines and other neuropeptides. Mainly located in the adrenal gland, they are more frequent between the 3rd and 5th decades of life; however, 10–25% can be associated with genetic familial syndromes (MEN 2, type 1 NF and VHL disease) in younger ages. We present a case of secondary HT and paroxysmal symptoms due to a Pheochromocytoma in a 15-year-old patient, whose metanephrine assay confirmed the diagnosis, and abdominal ultrasound and CT localised the tumour in the Left adrenal gland. HT was controlled with α and β blockers & laparoscopic left adrenelectomy was done with resolution of HT.

**Introduction :**

Pheochromocytoma is a rare tumor during childhood, originating from the chromaffintissue approximately 1/100 000[1]. Among patients with incidental adrenal masses approx 5% turns to be Pheochromocytoma. It produces catecholamines and other neuropeptides, originating in the adrenal gland medulla. The majority of cases are sporadic, but 10–25% can be associated with genetic syndromes such as Von Hippel-Landau (VHL) disease, type 1 neurofibromatosis (NF1) and multiple endocrine neoplasia type 2 (MEN 2), implying genetic testing in selected cases[2]. Approximately 1 to 25% of this tumor arise outside adrenal gland called as Paragangliomas, can arise in head, neck, thorax, abdomen and pelvis (including bladder)[3].

Sustained or paroxysmal hypertension is the most frequent sign, possibly associated with the classic triad: episodic headaches, profuse sweating and tachycardia[4]. Cardiovascular complications due to adrenergic stimulation can potentially be fatal, emphasising the importance of timely diagnosis and an effective therapeutic strategy[5].

**Case Report :**

Sagnik Sarkar, a 15 years old child admitted through emergency department of our hospital with the complaints of paroxysmal attacks of palpitation, dizziness, blurring of vision, convulsions and headache for last 2 months. On examination, patient had no abnormal physical findings except Blood Pressure (BP) is high during paroxysmal attack (Systolic BP varies from 140 to 210 mmHg and diastolic BP varies from 100 to 140 mmHg). Patient has no relevant personal, family and drug history.

**Investigations :**

Complete Blood Count, Random Blood Sugar, Blood urea and serum creatinine, LFT, Serum electrolytes, PTH, Thyroid function test, Chest X-rays, 2D ECHO and ECG reports were within normal limit.

[1,2,3,4,5,6,7,8]RKMSP, VIMS

Abdominal USG shows left sided suprarenal SOL likely adrenal in origin.

CECT(KUB)(Fig1) shows an ovoid mixed density lesion of size 38.7*34.3*30.8 mm in left adrenal region, with peripheral enhancement of +100 HU & central hypodense non enhancing area of +20 HU.

I -131 MIBG Scan (Fig2) findings are consistent with a Left supra renal SOL favouring Pheochromocytoma.

| | VALUE | REF |
|---|---|---|
| 1. Fasting Glucose (mg/dl) | 97 | 74-106 |
| 2. PTHi (pg/ml) | 32 | 15-65 |
| 3. Calcium (mg/dl) | 10.0 | 8.5-10.2 |
| 4. Calcitonin (pg/ml) | <2 | <5 |
| 5. Serum Cortisol (mcg/100ml) | 11.8 | 3.7-19.4 |
| 6. ACTH (pg/ml) | 57.6 | 7.2-63.3 |
| 7. Aldosterone (ng/dl) | 3.8 | 2-22 |
| 8. PRA, Plasma Renin Activity | >24 | 0.15-6 |
| 9. Urinary Metanephrine (ug/24hr) | 146.02 | <90 |

CECT (KUB) :

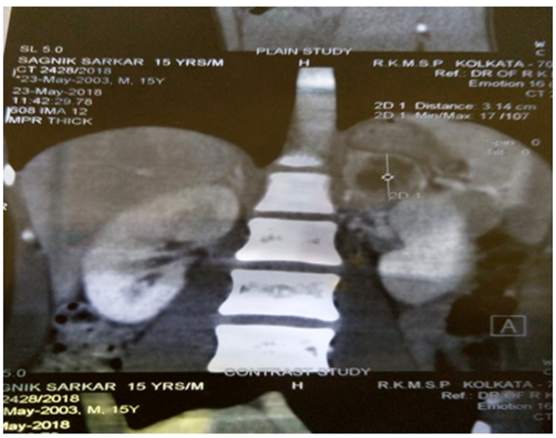


**Fig 1:CT scan revels left adrenal SOLI-131 (Metaiodobenzylguanidine)**

MIBG SCAN

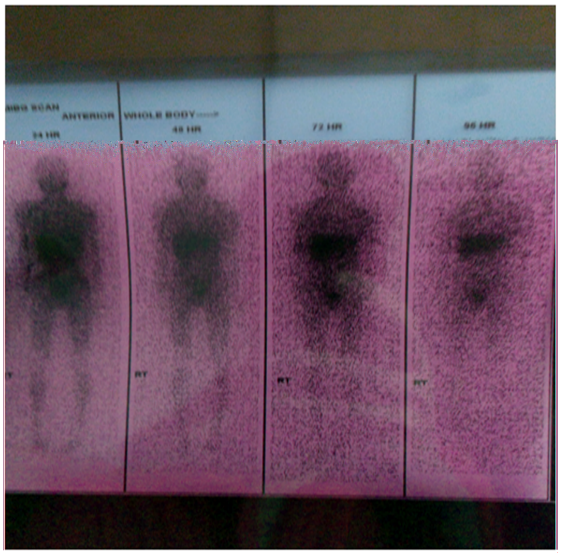

**Fig2 : L suprarenal SOL favouring Pheochromocytoma (increased concentration on left side)**

**Treatment :**

We planned for surgical removal of left adrenal gland (Laparoscopic Left Adrenalectomy). Patient was prepared for surgery with collaboration with Cardiologist, Endocrinologist and Anesthesiologist. Patient was given alpha blocker for 1 week preoperatively, Patient was also given beta blocker starting from 8th day of preoperative preparation for 5 days. Operation was done on 12th day of preoperative preparation and last dose of drugs were given on the morning of the day of surgery.

Elective laparoscopic left adrenalectomy done under general anasthesia plus epidural anasthesia, right IJV central venous catheterization done. A single episode of intraoperative hypertension occurred which was managed by infusion of Glyceryltrinitrate (GTN).

**Operative Specimen :**

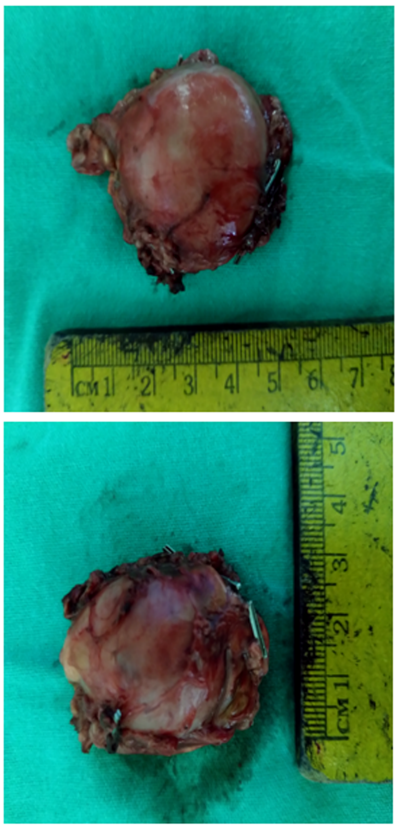

**Fig 3 : Left adrenal SOL specimen of size 3.2cm*3.5cm**

**Post Operative :**

Postoperative recovery was uneventful. Blood pressure becomes normal (Systolic 110 to 90 mmHg and diastolic 80 to 60 mmHg) from 1st POD without any drug.

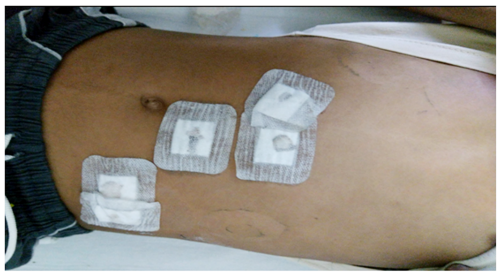

**Fig4: Post operative picture after lap left adrenelectomy**

**Immunohistochemestry Report**:

The lesional cells are positive for Synaptophysin and Chromogranin.S100 marks the subtentacular cells at periphery of the nests

**Impression: Pheochromocytoma, Left Adrenal.**

**Follow up:**

At 3 month and 6 month of follow-up, the patient remained asymptomatic and without headaches or visual problems; he was normotensive, with normal serum metanephrine assays.

**Conclusion :**

Pheochromocytoma can be considered as one of the cause for secondary hypertension. Although it is the causative factor of hypertension in about 0.1% to 0.6% of the hypertensive population, detection is mandatory, not only for the potential cure of the hypertension but also to avoid the potentially lethal effects of the unrecognized tumor.

**References :**


1. Vuguin P, Coppes M, et al. Pediatricpheochromocytoma treatment & management. http://emedicine.medscape.com/article/988683-overview.
2. Pereira MA, Souza BF, Freire DS et al. Pheochromocytoma.Arq Bras Endocrinol Metabol 2004;48:751–75;
3. Reisch N, Peczkowska M, Januszewicz A et al. Pheochromocytoma: presentation diagnosis and treatment. J Hypertens 2006;24:2331–9
4. Gardner DG, Shoback D Chapter:11 - Adrenal medulla and paraganglia. Greenspan's Basic & Clinical Endocrinology, 10e, 2007;
5. Eisenhofer G, Bornstein SR, Brouwers FM et al. Malignant Pheochromocytoma : current status and a initiatives for future progress. Endocr Relat Cancer 2004;11:423–36

Review Article

# Pregnancy Specific Biological Substances And Its Use/Potentialities in Regenerative Medicine : A Brief Update From A Recent Book on The Field

**Dr. Niranjan Bhattacharjee**

**Introduction :**

Some school of thoughts includes pregnancy under a chemical inflammation mediated by hormones and still some others believe pregnancy to be similar to neoplasm. One of the most important stages of embryo development in stem cell science is the inner cell mass stage of the blastocyst as this stage contains the three important germ layers namely, the ectoderm, mesoderm and endoderm along with the extra-embryonic part which gives rise to the placenta, amniotic sac, and the umbilical cord. The amniotic sac is a rich source of amniotic fluid which acts as a cushion for protecting the baby from bumps, injury, infection and helps in maintaining a constant temperature of the fetus. The amniotic membrane consisting of the chorion and the amnion. The placenta is the most important organ where it connects the fetus with the mother helping in the supply of oxygen, blood circulation, deliver essential growth factors and hormones for the development of the baby and by the end of pregnancy it passes antibodies so as to confer immunity to the fetus. other important functions include return of carbon dioxide, and other fetal waste products to the umbilical cord which are released in the mother's bloodstream.[1]

Placentophagy or eating of placenta is a well phenomenon observed among the animal kingdom and even in the case of herbivores like the cow. In traditional Chinese medicine, the placenta is often considered to be a very powerful healing medicine and is used in the form of dried version for medicinal purposes. Use of placenta has been documented over a century in Chinese system of medicine. The placenta is also used to ward off postpartum haemorrhage or post labor bleeding. Placental medicine can help in shortening the post bleeding time, restore the hormonal cycle, boost the immune system and increase lactation.In, 1910 for the first time Davis et al., used placenta membranes for skin transplantation followed by Sabella in 1913, where amniotic membrane was used for dressing and covering the burnt and ulcerated skin surfaces.The patients showed a marked improvement and since then, a new era in the field of dressing wounds started. In 1940, De Rotth first used placental membrane as a wound dressing model for ophthalmology in treating conjunctival epithelial defects. This paved the way for further use of placental membrane dressing in case of other ophthalmology defects.[2]

**Mythology :**

Various stories of mythologies like the liver regeneration of Prometheus, Durga, and Raktabeez is actually now a reality with regenerative medicine and cellular therapy strategies. Regenerative Medicine is that new branch of modern medicine which deals with the regeneration of degenerated organs, tissues and cells. Normally the classic natural example of regeneration in the biological world is pregnancy. Human curiosities regarding how pregnancy is mediated and how it survives in

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the hostile mother's environment for 9 months is still a mystery and an active area of research pursuit among transplantation and developmental biologists.[3]

**Details of the book :**

The book titled "Pregnancy Specific Biological substances" brings in about more than 70 distinguished and eminent professors working in the field of stem cell and regenerative medicine. Both Prof. Elaine Gluckman and the president of the Royal College of Physician, UK, Prof. Arul Kumaran has highlighted the important aspects and areas of research and treatment with pregnancy-specific biological substances. Dr. Ornella Parolini, an eminent stem cell scientist has further indicated the clinical significance and utility of these pregnancy-associated biological materials and a rich source for stem cells. Dr. Lin Huang and Prof. Andrew Burd of CUHK have indicated the massive global wastage of pregnancy specific biological substances and how it can be clinically utilized. In one of the chapters, Dr. Bon and Prof. Raudrant investigate the genetic factors associated with controlling the fetal growth, maternal nutrition factors, circulatory and hormonal placental factors. Prof. Pranke and Prof. Onsten discuss the utilization of cord blood transfusion, its strategies, immunology and its biochemistry. Prof. Robert Chow has discussed the utility of Hematopoietic stem cells from cord blood and its clinical use. Accounts of Dr. T. Brune and H. Garristen on the problems of autologous transfusion of placental/fetal blood to premature neonates have also been discussed at breadth. Dr. Shigeharu Hosono from Nihon University School of Medicine, Japan has also stated that the human cord blood transfusion can prevent the risk of transfusion-transmitted infections and suppress allogeneic reactions. Strategies of resuscitation can be also formulated by autologous transfusion of cord blood.[4] Prof. Ende further outlines the efficiency of cord blood in case of disasters and wars. Other important chapters include finding a true substitute for adult blood transfusion by legendary Professor E. Moore from the University of Colorado, USA, who have further concluded that only blood can substitute blood. Use of Human Umbilical cord blood cells for treating stroke patients and their enormous potentialities in regenerative medicine have been mentioned in one of the chapters by Prof. Sanberg. Further, the editor of the book, Prof. Dr. Niranjan Bhattacharya and Dr. Abhijet Chaudhuri has reviewed the use of placental umbilical cord blood in the ischemic brain, a high concentration of fetal hemoglobin or HbF and its higher oxygen concentration compared to adult hemoglobin. Use of cord blood in Ophthalmology has been detailed in this book by Dr. Kyung-Chul Yoon, a pioneer in the field of Ophthalmology. An account of the use of placental umbilical cord in cardiovascular surgery has been mentioned by Yale School of Medicine professors Dr. Alan Dardik and Prof. Herbert Dardik.[5] Prof. Robert Henning of The University of Florida, further discusses that the use of Human Umbilical cord blood cells can be used in case of myocardial infarction without the need for immune-suppressants as HUCBC has shown to significantly downregulate the inflammatory cytokines, neutrophils, CD3 and CD4 T-lymphocytes in heart with myocardial infarctions along with reduction in the myocardial infarct size. Clinically use of stem cells since, 2001 and its important effect in treating approaches have been highlighted by eminent stem cell scientist Prof. Amit Patel of The University of Pittsburg, Centre for Cardiac Cell Therapy and Mc Gowan

Institute for Regenerative Medicine, USA. Dr. Jose Miguell of TCA Cellular Therapy, LLC, LA, a world known expert on mesenchymal stem cells has shared views on the ontogeny of multipotent hematopoietic stem cells and hemopoiesis.[6]

The use and need of Human Umbilical Cord Blood derived hematopoietic stem cells and its superiority in terms of allogeneic bone marrow transplantation and its future and potential uses for curing auto-immune and bone marrow failures has been discussed by Jian-Xian Gao and Quansheng Zhou, Department of pathology and Comprehensive Cancer Centre, Ohio State University along with Cyrus Tang of Soochow University and Department of Molecular Biology at the Scripps Institute, La Jolla, CA.[7]

The chairman of Medistem Laboratories, Inc., California Dr Neil H. Riordan has mentioned that cord blood T cells produce significantly lower IFN-gamma, higher IL-10 upon activation with mature dendritic cells as against adult CD4 positive T cells. Further hyporesponsiveness was observed with respect to mitogen along with reduced level of LI-2 production and response to T cells. How stem cells survive and the importance of niche has also been noted by Prof. Ian MC Niece in this book.[8]

Dr. Suzanne Watt, NBS, NHS, UK has cited their works pertaining to cord blood banking and storage on similar grounds to the New York Cord Blood Bank in the 1990's and how these were established. Dr. Sabeen Askari has focused on total nucleated count or TNC an important parameter for cell dose and an important factor for HLA in donor choice. A threshold cell dose of >4 × 107 NC/kg at a collection and 3 × 107 NC/kg at infusion is recommended along with the correlation of CD34 positive cell count with engraftment where a dose of >2 × 105 CD34+ cells/kg is considered optimal. Due to the presence of inter-laboratory variability, there is a lack of standardization of counting method/protocol which has also been discussed in this book by Barker JN.[9]

Problems pertaining to the collection of cord blood have been detailed by Dr. Pilar Solves and Dr. Vincete Mirabet of the Tissue Engineering Bank in Valencia. According to them, the quality of UCB is basically defined by three important parameters which are total nucleated count or TNC which is an important tool for cell dose evaluation, CD34 positive cells, and colony forming units or CFU's meant for in vitro functionality assays of hematopoietic progenitors.[10]

The World-renowned stem cell scientist Prof. Anthony Atala has also contributed in this book where he emphasized on the current potentialities and isolation of stem cells from amniotic fluid and amniotic membrane. Details of more than 100 clinical case studies by Prof. Dr. Niranjan Bhattacharya with patients suffering from diabetic foot ulcers and other nonhealing ulcers due to burn, HIV, gangrene and other background diseases and their effective wound dressing model with freshly collected properly screened amniotic membrane has been also detailed in this book. Further Peter Hollands, the architect of UK cord blood banks has detailed his opinion on endothelial progenitor cells or EPC derived from Human cord blood and their role in neovascularization in rat ischemic models. The expert idea on EPC's by Italian scientist Dr. Maurizio Pesce from Milan has been further substantiated in this book. Dr. Shunichio Miyoshi of Keio University Medical School, Tokyo has shared that cardiomyocytes are terminal cells

incapable of undergoing further division after birth and therefore in cases of ischemia these cardiomyocytes fail to undergo any cell division and can be restored only by exogenous stem cells. They have shown in the book that murine marrow-derived mesenchymal stem cells can convert into cardiomyocytes for the first time but fail to do so in case of humans which can be due to the fact that the human nucleus is much more protected than the murine ones from spontaneous mutations and tumor formation.[11]

Other notable authors include Prof. David T Harris who has outlined the availability of multipotent stem cells in large numbers from cord blood and can be an alternative to hematopoietic and other sources of stem cells, Prof. Colin Mc. Guckin, Prof. Zygmunt Pojda, Dr. Thomas Ichim who all have shared their views on the use of pregnancy specific biological substances and their utilities and basic science in stem cell medicine.[12]

The book has received an immense positive review from Doody's Book review, a medical library and medical books, papers and journals review and evaluation website by Bruce A. Fenderson on January 2012 where it is mentioned that the book is a fascinating snapshot of current research pertaining to pregnancy-specific biological medicine and stem cells meant for clinicians and basic science researchers. The book has also received 5 citations in high indexed stem cell and regenerative medicine journals and books published by Springer Verlag-London.[13,14]

**Objective :**

The book is mainly meant for biomedical, medical students who want to update their knowledge in the field of regenerative medicine and the use of pregnancy specific biological substances in the field of stem cell therapies. Most of the true potentialities of these pregnancies specific biological substances have been ignored for some time. This book details the know-how, technology, and methods by which different stem cells can be utilized for treating diseases that are currently untreatable. The book encompasses areas of stem cell immunology, stem cell basics, animal and in vitro testing, quantification and validation and clinical cases. The book covers most of the diseases including their treatments with pregnancy-specific stem cells and is contributed by more than 50 renowned stem cell specialists and scientists. This book gives an overview of stem cell clinical and pre-clinical research that can benefit students and professionals who want to have a recent, updated and current view of stem cell and regenerative medicine.[15]

**References :**


1. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp. 11–23.ISBN 978-1-84882-718-9.
2. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp.VII.
3. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp.V.
4. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). Introduction, London: Springer-Verlag London. Page nos.VIII.
5. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific

Biological Substances (1 ed.). London: Springer-Verlag London. pp.VIII-X.

6. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp. XII.
7. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp.XIII.
8. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. Pp.XIV.
9. Barker JN, Davies SM, DeFor T, Ramsey NK, Weisdorf DJ, Wagner JE. Survival after transplantation of unrelated donor umbilical cord blood is comparable to that of human leukocyte antigen-matched unrelated donor bone marrow: results of a matched pair analysis. Blood. 2001;97:2957–2961. Full Text via CrossRef | View Record inScopus | Cited By in Scopus (167).
10. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp.XV.
11. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. Introduction.
12. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. pp. 11–23.ISBN 978-1-84882-718-9.
13. http//www.bookmetrix.com/detail/book/3ee28106-86c#-4787-a761-20acfdf2b6c5#reviews
14. http//www.amazon.in/Regenerative-Medicine-Pregnancy-Specific-Biological-Substances/dp/1848827172
15. Bhattacharya, Niranjan; Stubblefield, Phillip (2011). Regenerative Medicine Using Pregnancy-Specific Biological Substances (1 ed.). London: Springer-Verlag London. Foreword.

Review Article

# Exosomes : A Non-invasive Theranostic Tool for Disease Detection And Treatment

Dr. Anuran Bhattacharya[1], Dr. Bhabatosh Biswas[2], Dr. Urmi Chatterji[3]

## Introduction :

Communication between cells is extremely important to impart information to different parts of the body regarding status of nutrient and O2 supplies or warn against an invading pathogen. It is well established that certain chemicals are secreted by the cells into the blood or their surroundings which carry significant information to surrounding cells. However, recently it was discovered that cells could package their information and release them in very small nano-sized vesicles which are known as exosomes (Rak, 2013). As the mailman delivers the mail to designated addresses, exosomes carry information from donor cells and deliver them to the recipient cells. The size of exosomes ranges from 20-100 nano meter (Cocucci et al, 2009), which means they are much smaller than a bacterium, and are now particles of immense interest since they reflect the condition of a cell in their content and are easily accessible (Braicu et al., 2015).

Exosomal content depends upon their cell of origin. Basically, any cellular content present in the cytosol or nucleus of a particular cell type can be packaged and released in the form of exosome by a complex mechanism. The cargo (the content within the vesicle) of an exosome can be protein (Mathivanan et al., 2012), lipids, nucleic acids, such as various types of RNA (Huang et al., 2013), double stranded DNA (Lazaro-Ibanez et al., 2014), etc. With the help of these cargos, exosomes influence the recipient cells to a large extent. For the last few years, scientists have been focusing on the biogenesis of exosomes and analyses of their content as reflectors of the conditions of a cell. Detailed investigations have progressed on how the vesicles are made (Figure 1a), how they package their information, how they are finally released (Figure 1b) and how these exosomes are taken up by the recipient cells (Figure 1c), as well as their role in normal physiology as well as in the pathological processes of many disease states, like cancer.

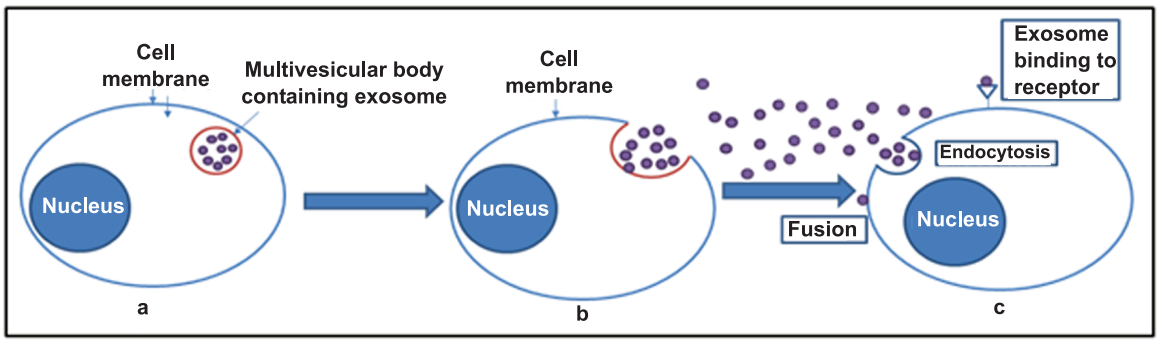


**Fig 1 : a) Biogenesis of exosomes within a cell, b) Release of exosomes from the cell, c) Uptake of exosomes by recipient cell**

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**Role of Exosomes in Cancer :**

Cancer is considered to be one of the most dreadful diseases worldwide and in India, more than 1300 people die every day due to cancer (according to Cancer Registry Programme of the India; Indian Council of Medical Research). The human body is made up of different types of cells and in the normal adult, these cells grow and divide under very tight and programmed regulations which make sure that the number of cells in every tissue does not exceed its maximum capacity. However, cells start dividing rapidly and their growth goes out of control, leading to formation of tumors, when the factors regulating the cell cycle undergo gain-of-function mutations. Although few tumors are benign and not fatal, tumors which turn malignant, are capable of invading surrounding tissues and are thus are able to spread themselves to other parts of the body ("metastasis"), where they can cause serious and, eventually, fatal damage.

Like normal cells, cancer cells also release exosomes and to the surprise of the researchers, the amount of circulating exosomes is nearly doubled in cancer patients compared to a normal adult. Further, it is also established that the cargo of exosomes released from cancer cells have prominent roles in tumor progression and metastasis (Figure 2). Exosomes therefore play a very important role in the communication process as they have the capability to prepare a suitable condition for tumor growth, maintenance and spread (Costa-Silva et al., 2015).

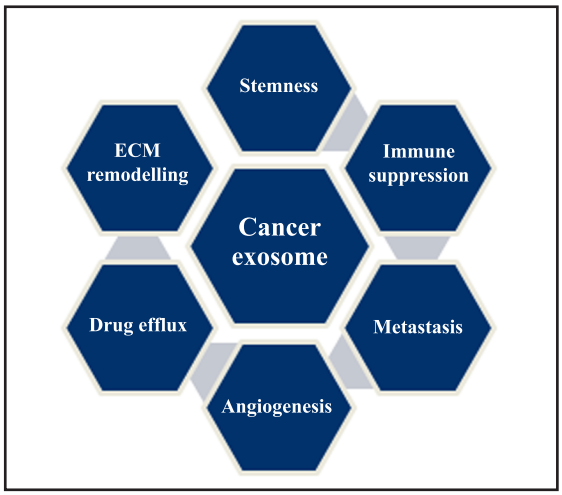



**Fig 2: Multi-faceted roles of exosomes secreted from cancer cells in cancer progression**

Tumor exosomes are known to contribute to epithelial-to-mesenchymal transition (EMT), a unique feature of tumor progression and metastasis, where epithelial cells lose their epithelial-like properties and gain migratory and invasive properties (Vella 2014). The cells eventually lodge onto distant organs and start growing there via a process called mesenchymal-to- epithelial transition (MET). The exosomal cargo possibly facilitates some aspects of cell differentiation which ultimately leads to both EMT and MET (Greening et al., 2015), and culminating in bad patient prognosis. Cancer exosomes are clearly powerful mediators which can influence and alter the behavior of neighboring cells. This becomes even more evident with their ability to promote the formation of the pre-metastatic niche, which further helps the cells coming from a primary tumor to colonize

properly for metastasis to occur (Costa-Silva et al., 2015).

The immune system of the human body attempts to stop cancer cells from growing and specific immune cells, like natural killer cells (NK cells) or cytotoxic T cells, are known to destroy the cancer cells. However, many-a-times the cancer cells escape immune suppression and this process has been seen to be facilitated by the cancer exosomes in various ways, like (i) apoptosis or death of the cytotoxic T cells can be induced by cancer exosomes through the death receptor pathway (Peng et al., 2011); (ii) cancer exosomes can lead to further T cell deregulation (Miller and Grunewald, 2015); and (iii) cancer exosomes can negate the cytotoxic functions of natural killer cells (Szczepanski et al., 2011). Such smart manipulations are often seen for lung cancers. Tumor exosomes also contribute to the drug resistance property of cancer cells. Cancer cells remove chemotherapeutic drugs like cisplatin and trastuzamab with the help of exosomes, which proves that cancer exosomes also have a drug-scavenging role (Peng et al., 2011).

**Exosomes in the detection of cancer**

Tumor-derived exosomes can exchange information between neighboring cancer cells and also can communicate with distantly located normal cells. Thus, tumor-derived exosome are considered as attractive tool nowadays, through which cancer biomarkers can be identified. Biomarker is a naturally occurring molecule by which a particular pathological or physiological process, disease (e.g. cancer), etc. can be identified. A huge importance is given to exosomes as cancer biomarker because cancer diagnosis through exosome would basically be a non-invasive technology, where tissue collection from patient would not be required, cutting down both cost and time of detection; diagnosis in this case can directly be done from biological fluids like blood/plasma or urine.

In an experimental set up, exosomes can be easily isolated to examine diagnostic features of a cancer cell, by profiling exosomal proteins or nucleic acids; therefore, exosomes have a high potential to be a non-invasive liquid biopsy tool for detection of cancer. As exosomes have selective cargo loading and the cargo carried by an exosome closely resemble their cell of origin, scientists are focusing on exosomes for discovering changes within a cell and such altered biomolecules may be developed as cancer biomarkers, opening avenues for personalized cancer detection, diagnosis, and prognosis. Tables 1 enlists protein biomarkers carried by exosomes which can be used not only in detection of different types of cancer but also other diseases which may lead to cancer (Lin et al., 2015). This can in future become an important tool for identifying and predicting the risk of cancer development in patients with apparently harmless diseases much before the disease progresses to a point of no return.

**Table 1 : Summary of Exosomal Proteins for Clinical Diagnostic Applications**

| Biofluid | Disease | Associated proteins |
|---|---|---|
| Plasma | Chronic hepatitis C | CD 81 |
| | Melanoma | CD 63, caveoline-1, TYRP2, VLA-4, HSP-70, HSP-90 |
| | Glioblastoma | Epidermal growth factor receptor VIII |
| | Prostate cancer | Survivin |
| | Plasma cell dyscrasias | c-src |
| Urine | Acute kidney injury | Fetuin-A, ATF-3 |
| | Liver injury | CD26, CD81,Slc3A1, CD10 |
| | Bartter syndrome type 1 | NKCC2 |
| | Bladdar cancer | EGF, α suunnit of $G_s$, resisitinn, Retinoic acid-induced protein-3, and so forth |
| | Prostate cancer | PSA, PCA-3 |
| Plasma, cell culture medium and ascites | Huma ovarian cancer | LICAM, CD24, ADAM10, EMMPRI, claudin |

Very recently, scientists have identified the cell surface proteoglycan, glypican-1, which is specifically enriched on cancer exosomes. Healthy subjects and patients with pancreatic cancer from early/late stage can be distinguished specifically by monitoring the glypican-1 on circulating exosomes (Melo et al., 2015). It also provides an example that exosomes is an efficient non-invasive screening tool for cancer.

**Exosomes in anticancer therapy :**

As tumor exosomes are a repository of tumorigenic information which promotes carcinogenic activity, they can be targeted or exploited for anti-cancer therapy. Researchers have identified certain molecules and techniques through which they can either block the biogenesis and release of the cancer exosomes (Christianson et al., 2013), or can inhibit the uptake of exosomes by recipient cells (Stephens et al., 2002). Thus, communication between the cancer cells within the tumor microenvironment can be disrupted, which in turn, can arrest tumor growth. In addition, exosomes can be used to manipulate crosstalk between cancer cells. In this case the exosomes are first isolated from the body fluid of a patient and then loaded with specific anti-cancer drugs. These drug-loaded exosomes are then injected into the circulation, where they are preferentially taken up by cancer cells, thus ensuring a targeted drug delivery (Kim et al, 2016).

**Advantage of exosomes in disease identification and treatment :**

Since the discovery of exosomes and their ability to mediate cell-to-cell communication, studies have focused on different approaches to manipulate this natural carrier of information into a specific and effective therapy delivery system. Exosomes are naturally present in all body fluids and are biocompatible and biodegradable. Consequently, exosomes are less toxic and less immunogenic when compared with other nanocarriers (Ha et al., 2016). In addition, exosomes could represent a novel approach in the treatment of brain malignancies, due to their capacity to cross the blood-brain barrier (Kawikova and Askenase, 2015, Li et al., 2017). Recently, exosomes are being considered as a potential repository of new biomarkers for cancer. A perfect cancer biomarker can reveal the existence of tumor mass and its molecular features in the early stages, which is otherwise almost impossible to detect unless specific signs become apparent, which often happens at later stages. Thus, exosomes have special properties which make them an ideal tool for early detection of cancer (Kalluri, 2016). Future research will improve the methods for isolation of pure exosomes necessary to distinguish them from other types of microvesicles and to understand the mechanism in which they are involved. These achievements will help booster the early diagnosis, control, prevention and therapy. Increasing knowledge of exosome biology and further insight into the uptake of exosomes and cell targeting behavior, will elucidate novel theranostic strategies, based on inhibition of exosome-mediated intercellular communication in cancer and novel diagnostic approaches.

**References :**


- Braicu C, Tomuleasa C, Monroi P, Cucuianu A, Berindan-Neagoe I, Calin GA. (2015) Exosomes as divine messengers: Are they the Hermes of modern molecular oncology? *Cell Death Differ*. 22: 34–45.
- Greening DW, Gopal SK, Mathias RA, Liu L, Sheng J, Zhu HJ, Simpson RJ. (2015) Emerging roles of exosomes during epithelial-mesenchymal transition and cancer progression. *Semin. Cell Dev. Boil*. 40: 60–71.
- Ha D, Yang N, Nadithe V. (2016) Exosomes as therapeutic drug carriers and delivery vehicles across biological membranes: current perspectives and future challenges. *Acta Pharmaceutica Sinica B.* 6(4): 287-296.
- Kawikova I, Askenase PW. (2015) Diagnostic and therapeutic potentials of exosomes in CNS diseases. *Brain Res*. 1617: 63-71.
- Li X, Tsibouklis J, Weng T, Zheng B, Yin G, Feng G, Cui Y, Savina IN, Mikhalovska LI, Sandeman SR, Howel CA, Mikhalovsky SV. (2017) Nano carriers for drug transport across the blood-brain barrier. (2017) *J. Drug Target.* 25(1): 17-28.
- Miller IV, Grunewald TG. (2015) Tumour-derived exosomes: Tiny envelopes for big stories. *Biol. Cell.* 107(9): 287-305.
- Peng P, Yan Y, Keng S. (2011) Exosomes in the ascites of ovarian cancer patients: origin and effects on anti-tumor immunity. *Oncol. Rep*. 25: 749–762.
- Szczepanski MJ, Szajnik M, Welsh A, Whiteside TL, Boyiadzis M. (2011) Blast -derived microvesicles in sera from patients with acute myeloid leukemia suppress natural killer cell function via membrane-associated transforming growth factor -beta1. *Haematologica.* 96: 1302–1309.
- Vella LJ. (2014) The emerging role of exosomes in epithelial-mesenchymal-transition in cancer. *Front. Oncol*. 4: 361.
- Webber J, Steadman R, Mason MD, Tabi Z, Clayton A. (2014) Cancer exosomes trigger fibroblast to myofibroblast differentiation. *Cancer Res*. 70: 9621–9630.
- Costa-Silva B, Aiello NM, Ocean AJ, Singh S, Zhang H, Thakur BK, Becker A, Hoshino A, Mark MT, Molina H. (2015) Pancreatic cancer exosomes initiate pre-metastatic niche formation in the liver. *Nat. Cell Boil. 17*: 816–826.
- Kalluri R. (2016) The biology and function of exosomes in cancer. *J Clin. Invest*. 126(4): 1208-15.
- Li Y, Zheng Q, Bao C, Li S, Guo W, Zhao J, Chen D, Gu J, He X, Huang S. (2015) Circular RNA is enriched and stable in exosomes: A promising biomarker for cancer diagnosis. *Cell Res. 25*: 981–984.
- Lin J, Li j, Huang B, Liu j, Chen X, Chen XM, Xu YM, Huang LF, Wang XZ. (2015) Exosomes: Novel Biomarkers for Clinical Diagnosis. *The Scientific World Journal*. 657086(8): 4-5.
- Cocucci E, Racchetti G, Meldolesi J. (2009) Shedding microvesicles: artefacts no more. *Trends Cell Biol.* 19: 43-51.
- Rak J. (2013) Extracellular vesicles-biomarkers and effectors of the cellular interactome in cancer. *Front. Pharmacol*. 4: 21.
- Mathivanan S, Fahner CJ, Reid GE, Simpson RJ. (ExoCarta 2012) Database of exosomal proteins, RNA and lipids. *Nucleic Acids Res*. 40: D1241-D1244.
- Huang X, Yuan T, Tschann en M, Sun Z, Jacob H, Du M, Liang M, Dittmar RL, Liu Y, Liang M, Kohli M, Thibodeau SN, Boardman L, Wang L. (2013) Characterization of human plasma-derived exosomal RNAs by deep sequencing. *BMC Genomics*. 14: 319.
- Lazaro-Ibanez E, Sanz-Garcia A, Visakorpi T, Escobedo-Lucea C, Siljander P, Ayuso-Sacido A, Yliperttula M. (2014) Different gDNA content in the subpopulations of prostate cancer extracellular vesicles: apoptotic bodies, microvesicles, and exosomes. *Prostate.* 74: 1379-1390.
- Kim MS, Haney MJ, Zhao Y, Mahajan V, Deygen I, Klyachko NL, Inskoe E, Piroyan A, Sokolsky M, Okolie O, Hingtgen SD, Kabanov AV, Batrakova EV . (2017) Development of exosome-encapsulated paclitaxel to overcome MDR in cancer cells. *Nanomed.* 12(3): 655-64.
- Christianson HC, Svensson KJ, van Kuppevelt TH, Li JP, Belting M. (2013) Cancer cell exosomes depend on cell-surface heparan sulfate proteoglycans for their internalization and functional activity. *Proc. Natl. Acad. Sci. U.S.A.* 110(43): 17380–5.
- Stephens L, Ellson C, Hawkins P. (2002) Roles of PI3Ks in leukocyte chemotaxis and phagocytosis. *Curr. Opin. Cell Biol*. 14: 203-13.

Image

# Bullets in Inaccessible Areas

**Dr. Bhabatosh Biswas[1], Dr. Rajarshi Basu[2], Dr. Rupak Bhattacharjee[3], Dr. Subir Basu Thakur[4]**

Localization and surgical retrieval of bullets from the chest as well as abdomen often becomes a nightmare for the surgeon.

A 38 years old male presented with shock after bullet injury at right lower lateral Chest. He had diabetes, obesity and COPD. The patient was resuscitated. Chest X-ray revealed One bullet in right chest and the other bullet in rightsubhepatic area.

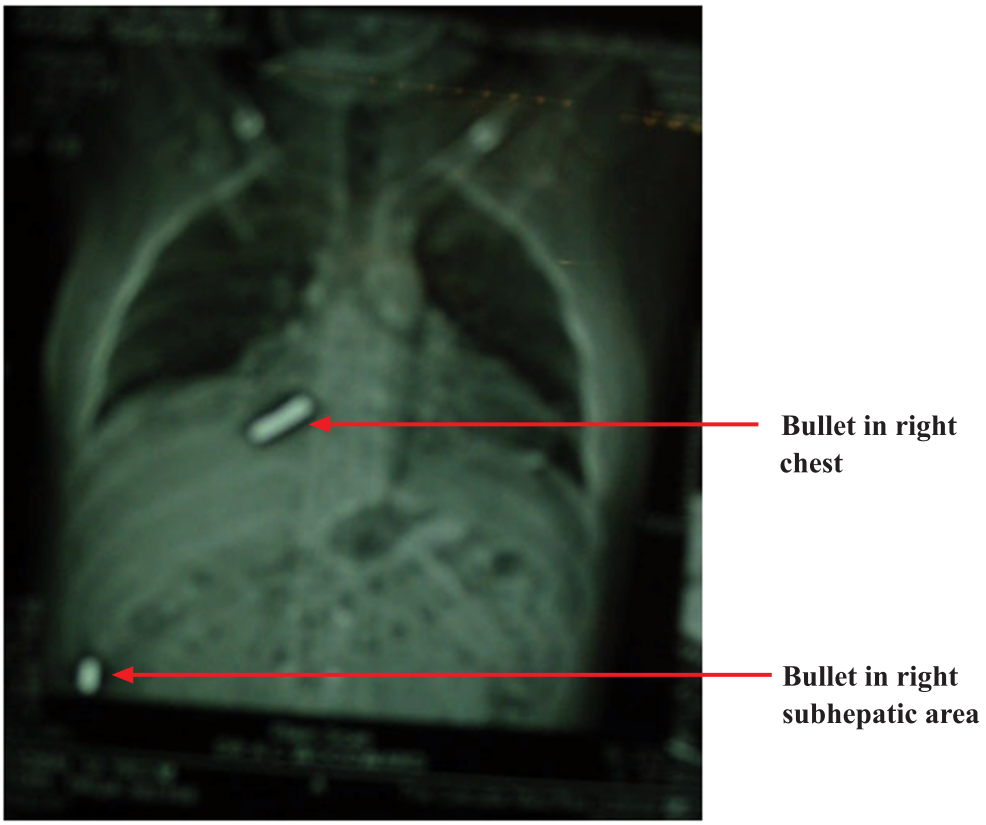
CT scan of thorax with upper abdomen revealed two bullets in surgically inaccessible areas.

VATS retrieval of bullets were performed under Image Intensifier guide.

One bullet was found deeply imbedded in the right Cardiophrenicarea and the other was deeply imbedded in the right Retroperitoneal area.

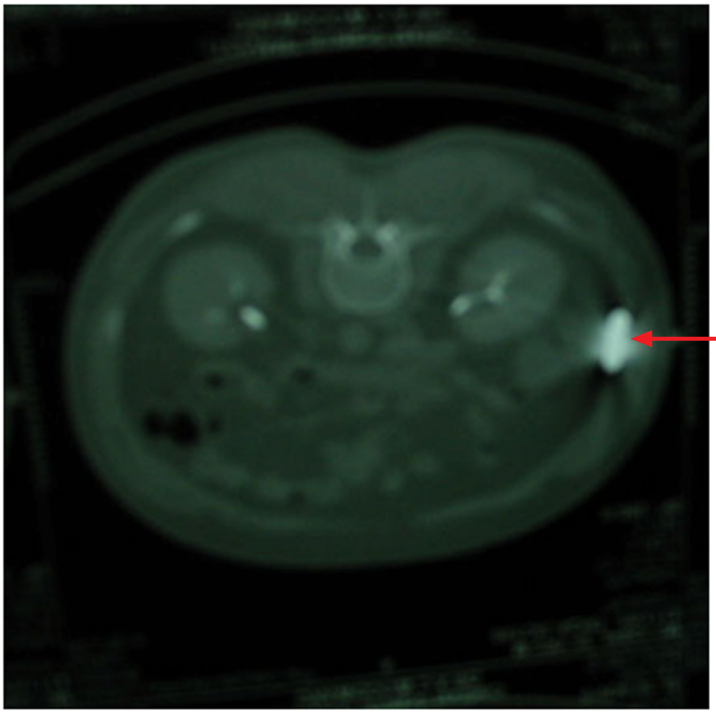
Both the bullets were localized under Image Intensifier and were retrieved by VATS.

The patient was discharged on the 3rd day uneventfully.



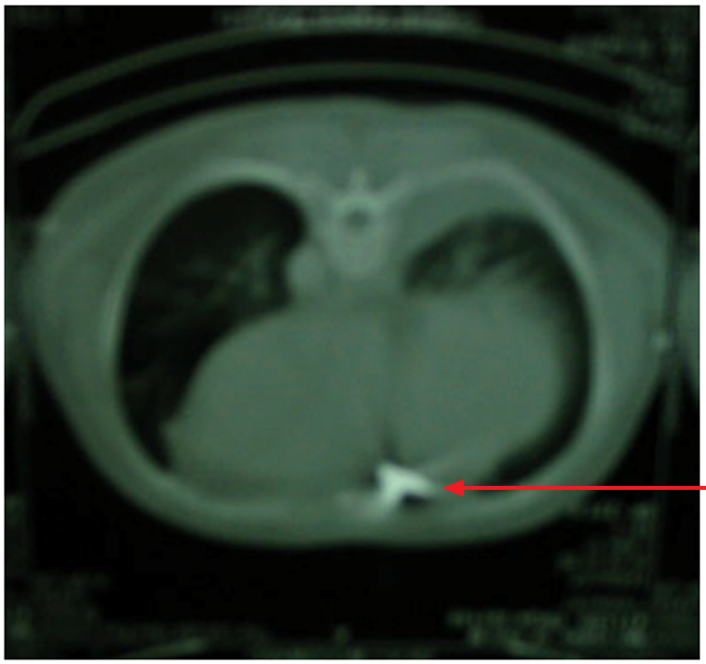

**Chest X-ray**

[1,2,3,4]Calcutta Medcal Research Institute, Kolkata



Bullet in right Retroperitoneal area

CT Scan of Thorax



Bullet in right Cardiophrenic area

CT Scan of Thorax

**Specimen of Bullets After Retrieval**

Image

# An Unique Case of Multisite Hydatid Cysts

**Dr. Prriya Eshpuniyani[1], Dr. Bhusan Thombare[2], Dr. Subhankar Pramanick[3]**

40/ F, no cormobidities presented with cough and lower abdominal pain. On investigation Plain CT scan of thorax and abdomen showed cystic lesions in right lung, liver and pelvis? Hydatid cyst. After adequate cover of Tab Albendazole she was taken up for Right posterolateral thoracotomy. Lung cyst was removed by Baretts method. Liver cyst was approached via Right phrenotomy and excised in toto. A lower midline abdominal incision was taken and pelvic cyst was excised in toto along with adhered appendix. HPE confirmed Hydatid cyst. Postoperative recovery was uneventful.

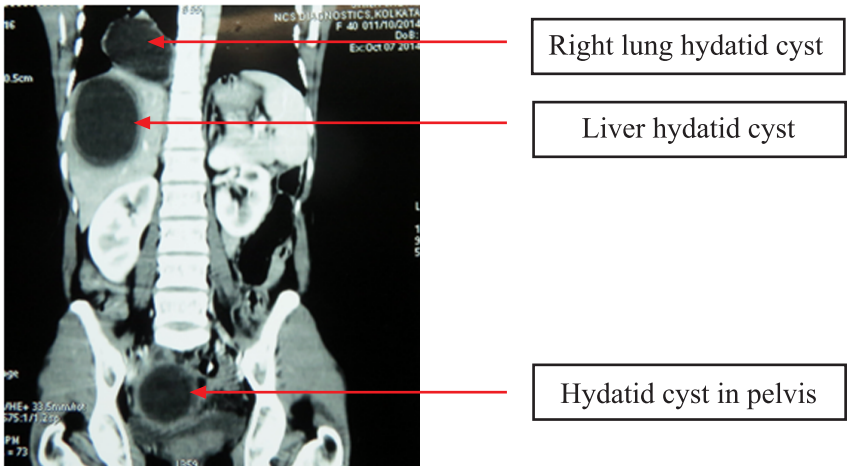



**Fig 1: CT Scan Showing Hydatid Cyst in Right Lung, Liver and Pelvis**

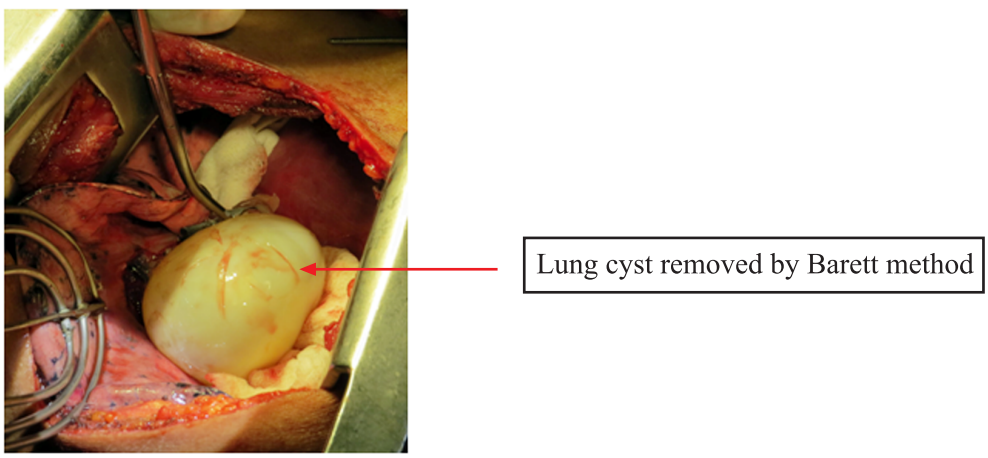



**Fig 2: Right Lung Cyst being Removed by Baretts Method**

[1,2,] CTVS, R. G. Kar Medical College & Hospital; [3,] CTVA, R. G. Kar Medical College & Hospital

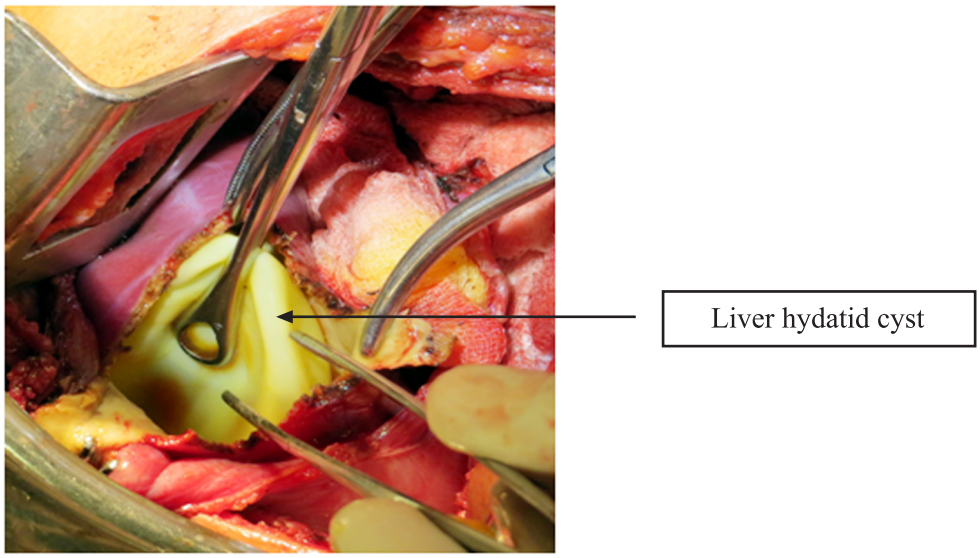



**Fig 3: Liver Hydatid Cyst Removed via Phrenotomy**

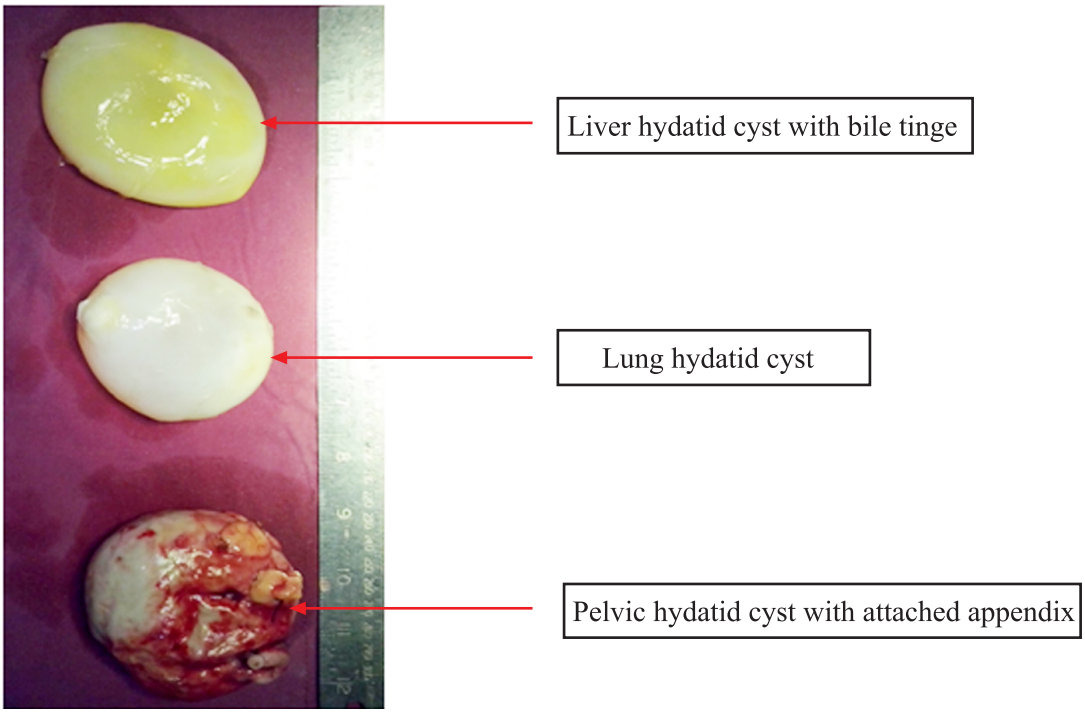



**Fig 4: Lung, Liver and Pelvic Hydatid Cyst**