CERTIFICATE

Certified that the dissertation entitled "**Outcome of Liver resection in Children**" is the original work undertaken by **Dr G Krishna Kumar** under our guidance and supervision, in the Department of **Paediatric Surgery**, Institute of Child Health, Madras Medical College, Chennai, during the period of his postgraduate residency in MCh Paediatric Surgery from 2003-2006.

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G Krishna Kumar

Contents

Introduction :

Liver tumors account for 1% of all childhood malignancies. Surgical resection forms the main stay of treatment of liver tumors. History has witnessed transition of liver surgery from the primitive techniques of amputation and excision in 1716 to the modern era of anatomic hepatic lobectomy in.1952. The evolution of hepatic resection, from an imprecise removal of portions of the liver, accompanied by extensive hemorrhage, to a controlled anatomic procedure with acceptable risk, represents a major advance in modern surgery. Appreciation of the segmental distribution of blood vessels and bile ducts within the liver, was an important landmark in liver resection, which brought about the anatomic liver resection in vogue.

Improvements in surgical technique have brought about a sea of change in the perception of hepatic resection. Also, established long term survivals post resection have made a strong case for hepatic resection. Advances in life support, intensive care, anesthetic techniques, blood banking have contributed to the feasibility and safety of hepatic resection especially in neonates. Further, the recent developments in control of hepatic parenchymal bleeding such as laser, ultrasonic dissector, argon beam coagulator have improved the outcome of liver resection.

At our Institute, we have a considerable burden of liver tumors, as the Institute with about 600 beds, housing all Paediatric Specialities, with availability of chemotherapy drugs, attracts referrals from allover the country. We have attempted to review our Institutional experience in the treatment of liver tumours.

Review of literature

History

Berta, who amputated the protruding portion of the liver, in a patient with penetrating injury, did the first surgical removal of a portion of the liver in 1716. Barring few isolated reports (Bruns 1870, Lius 1886, Langenbuch 1888), formal liver resection was performed by Tiffany in 1890. Wendel has been credited with the first authentic case of near total right hepatic lobectomy in 1910. Lortat Jacob and Robert in 1952 used extrahepatic ligation of vessels for control of hemorrhage. The technique of primary hilar ligation was used in the performance of right hepatic lobectomy by Quattelbaum in 1953.Digitoclasia or finger fracture technique was described by Fineberg (1956), Tien Y Lin (1958).

Cantlie in 1898 initiated the concept of the functional liver anatomy, which was carried on to the culmination of the segmental liver anatomy by Couinaud in 1981. Martin and Woodman reported hepatic lobectomy for Hepatoblastoma in children in 1969. The importance of complete surgical resection of the primary liver tumour for cure was emphasized by the Surgical section of the American academy of Pediatrics in 1975. In 1990, Merine et al illustrated a case of successful resection of a large solitary liver cyst in right lobe of liver casusing significant pressure symptoms requiring resection at presentation in a neonate. Tagge et al in 1992 reported a series of 15 children, who underwent transplantation for hepatic malignancies.

Parker reported a case of an infantile liver lesion, probably Hemangioendothelioma, in 1880. Haig Kasabach and Katharine Merritt in 1940 described the interesting association of thrombocytopenic purpura with liver hemangiomas. Dehner and Ishak recognized 3 malignant vascular lesions of liver namely Angiosarcoma, Malignant epithelioid hemangioendothelioma and type 2 hemangioendothelioma. Transformation of type 2 Hemangioendothelioma to Angiosarcoma was described by Kirchner(1981), Selby(1992), and Awan(1996). Luks (1991) in his work, stated that Mesenchymal hamartomas are the second common benign hepatic tumours in children.

Malignant transformation of nonparasitic cysts was reported by Pliskin (1992) and Weinmann (1996). Inflammatory pseudo tumours are uncommon lesions in liver with fewer than 20 case reports in world literature (Passalides 1996, Hsiao 1999, Lee DuBoir 2001).

Digitoclasia employed as the basic technique in liver resection concerns with hepatic parenchymal division by finger fracture with intrahepatic ligation of all vascular elements step by step without prior vascular control (Ton That Tung, 1957). Bismuth in 1982 combined the basic techniques of Ton That Tung and Lortat Jacob, to temporarily occlude the hilum, and proceed with parenchymal resection, to end in hepatic vein ligation within the liver.

The maneuver of occlusion of vascular inflow by hepatic pedicle clamping at the hepatoduodenal ligament, as described by Pringle in 1908, is effective in minimizing blood loss during parenchymal resections.

The wide use of Pringle maneuver attests to the procedural efficacy, safety and ease of performance. Makuuchi`s hemihepatic vascular occlusion aimed at limiting the ischemic damage only to the side of the liver undergoing resection indicated in patients who tolerate liver ischemia poorly. Total hepatic vascular exclusion consisting of the combined vascular inflow and outflow occlusion, reduces operative blood loss markedly, with the added advantage of extended caval resection, in case of tumour involvement of the inferior vena cava.

Described in 1966 by Heaney et al, this procedure has adverse hemodynamic effects at times. Fortner et al in 1970 reported major liver resection by using total vascular isolation and hypothermic perfusion. This procedure is claimed to make possible the undertaking of complex liver resections for which portal and hepatic vein dissections are needed. Pichlmayr et al improved Fortner`s technique by using the University of Wisconsin solution as the perfusate in insitu hypothermic liver perfusion in 1990.

Liver anatomy

Developments in the understanding of hepatic anatomy have been of vital importance in liver resection. Morphologically, as the liver lies in the abdominal cavity, it is split into a large right and a small left lobe by the falciform ligament extending from the anterior abdominal wall. The morphological description, however, does not correspond to the surgical anatomy of the liver and studies by Tung, and most importantly by Couinaud, on the functional anatomy of the liver have paved the way to safe hepatic resection.

Division of the portal inflow divides the liver into two, a right and left hemiliver, along the principal plane (Rex-Cantlie line) that passes through the gall bladder bed towards the vena cava and through the right axis of the caudate lobe. Further subdivisions of the portal inflow divide each hemiliver into 2 subdivisions termed sectors and then each sector into 2 subdivisions termed segments.

The divisions of the portal vein are mirrored by divisions of the bile duct and hepatic artery forming a ‘portal trinity’, and hence the liver can be divided into segments, each of which has its own ‘portal trinity’ supplying it. The 3 major hepatic veins (right, middle, and left) lie between the 4 sectors in the 3 main fissures or scissuras, right, main, and left, respectively, and each vein drains the sectors on either side of it. The functional anatomy is not visible on inspection of the liver.

The right hepatic vein separates the two sectors of the right hemiliver which lie anterior and posterior. The right anterior sector is subdivided into segments V (inferior) and VIII (superior) and the right posterior sector is subdivided into segments VI (inferior) and VII (superior). The left vein separates the 2 sectors of the left hemiliver, which lie anterior and posterior. The left anterior sector is divided into two segments, III and IV.

The left posterior sector is the one exception to the rule as it only has one segment, segment II. The caudate lobe is a distinct anatomical segment and is labelled segment I. It receives branches of the portal trinity from the right and left liver and drains independently into the vena cava.

The right vein drains into the vena cava independently, but the middle and left veins usually join and drain into the vena cava as a single vein. There are usually a few small veins draining into the vena cava from behind the liver. Occasionally there can be 2 or 3 inferior right hepatic veins of moderate size and these can provide significant drainage. If these are not recognized and torn during hepatic resection, bleeding may be profuse.

As each segment of liver has its own supply from the portal trinity, independent of the other segments, they can be resected independently of other segments. In practice, it is easier to remove some segments together. Although the intersegmental planes are not visible on the surface of the liver, segments can be defined by occluding the inflow to that segment thus rendering the segment ischaemic and demonstrating the functional division on the liver surface.

It has been recognised that Glisson’s capsule extends as a condensation of fascia around the biliovascular branches of the portal trinity (Glissonian sheaths). Couinaud and more recently Launois and Jamieson have noted that the fascia continues within the liver parenchyma up to the segmental divisions. The surgical implication is that if the supply to an individual segment is approached from within the liver, mass ligation of a sheath, will devascularise the segment. This is simplified even further by the use of a stapler.

The nomenclature of hepatic resection remains confusing with differing terminology used in the literature. The contrast is between the American terminology of Goldsmith and Woodburn and that of Couinaud. It is important that precise descriptions of what part of liver is to be resected are used.

Liver tumors

Of all liver masses in children, two thirds are malignant, Hepatoblastoma accounting for the majority of malignant tumors.

Benign tumors include

Hemangiomas	Inflammatory pseudo tumour
Hepatic cysts	Hemangioendothelioma
Teratoma	Mesenchymal hamartoma
Angiomyolipoma	Adenoma
Focal nodular hyperplasia	Biliary cystadenoma

Malignant tumors include

Hepatoblastoma	Histiocytosis
Hepatocellular Ca	Leukemia
Angiosarcoma	Leiomyosarcoma
Hemangioendotheliosarcoma	Lymphoma
Embryonal sarcoma	Neuroblastoma

Hepatoblastoma has noted associations with several syndromes such as Beckwith-Wiedemann syndrome, Familial adenomatous polyposis, Li Fraumeni syndrome, Prader-Willi syndrome and Trisomy 18. Similar notorious associations of Hepatoma include Tyrosinemia I, Glycogen storage disease type I, Alagille syndrome, Alpha1 antitrypsin deficiency. Hepatic tumors have been postulated to occur with the association of Neurofibromatosis, Tuberous sclerosis, Ataxia telengiectasia and Fanconi`s anemia.

Other reported links include Hepatitis B, Total parenetral nutrition, foetal alcohol syndrome, post radiation (Wilms tumour) and post chemotherapy (acute lymphoblastic leukemia).

Histopathological subtypes of Hepatoblastoma include fetal, embryonal, mixed mesenchymal, macrotrabecular and anaplastic or small cell types. The importance of subtyping is the association between prognostic risk and subtype.

Studies have attested to the fact, that foetal subtype is associated with an improved prognosis. In contrast, patients with anaplastic variety usually do poorly. Interesting associations observed to occur with Hepatoblastoma are the presence of thrombocytosis and extramedullary hematopoiesis. Ability to secrete interleukin 1, erythropoietin and stem cell factor may probably account for the presence of thrombocytosis.

Liver regeneration

The capacity of liver to regenerate has been recognized long back, as demonstrated by the greek legend of Prometheus.

Liver growth is a multistep process in which both growth stimulating and inhibiting factors are involved. Although all liver cells retain the ability to replicate, in normal conditions only a few hepatocytes undergo proliferation. This situation changes when the functional liver mass is reduced by surgical resection or noxious stimuli such as virus, toxin.

There is a burst of proliferation with the regenerative process leading to full restoration of hepatic mass over a period of 6 weeks.

Several factors have been identified to be involved in the modulation of hepatic regeneration including –

Initiators – ions, nutrients, hormones

Progressors –T3, TGF alpha, HGF

Augmenters – Insulin, IGF II, FK 506, Cyclosporin A, ALR (Augmenter of Liver Regeneration)

Inhibitors – TGF beta, IL 1,6

It has been found that some degree of hepatic regeneration occurs with every transplant and the factors controlling the regeneration reside principally in the recipient environment.

Investigations

Preoperative evaluation is an essential prerequisite to the safe performance of liver resection. The management protocol should be based on studies, which would establish the respectability of the lesion, based on the relationship to the vital structures. Evaluation of metastatic disease outside the liver is also mandatory. Estimation of hepatic reserve based on radionuclide studies would form an important tool in the background of cirrhosis.

Ultrasonography has stood the test of time as the major diagnostic tool as it is noninvasive, inexpensive, quick to perform, and can be manipulated into any plane so as to optimize visualization of anatomic structures.

Recent improvement in the use of Ultrasound has improved respectability rates, when applied laparoscopically and per operatively. Use of Ultrasound in the intraoperative setting has improved resolution with increased sensitivity to identify parenchymal vascular anatomy and extent of tumour involvement, helping in surgical decision making.

With the development of ultrasound probes designed for use through Laparoscopic ports, the technique of Laparoscopic Ultrasonography has emerged as a sensitive staging technique, determining respectability of tumour and also assists in the performance of liver resection. Doppler Ultrasonography can identify occult metastases based onhepatic perfusion index – ratio of hepatic arterial inflow to total liver inflow (Leen et al). Also, through the identification of efferent tumoral vessels and characterization of intratumoural blood flow, Doppler Ultrasound can aid in the differential identification of regenerative hyperplastic nodules and tumour nodules.

Preoperative angiography can provide useful information in that a clear roadmap of the hepatic arterial anomalies is available and is of value in the surgical resectiuon from a technical standpoint.It is to be noted that hepatic arterial anomalies can occur in upto 50% cases. Carbon dioxide Ultrasound Angiography is a recent innovation utilizing a mixture of CO_2 microbubbles and the patient`s blood, as slow injection into hepatic artery. It is claimed that the micro vasculature appears enhanced accentuating the image of neoplasms not easily seen using standard ultrasound.

Computed tomography has proved its superiority over sonography in view of higher sensitivity less operator dependence better anatomic definition easy interpretation. Newer techniques such as spirl scan mode and arterial portography have increased the imaging sensitivity and increased the ability to predict the presence and exrtent of the lesions in liver in particular neoplastic lesions. Information on diffuse diseases of the liver, hepatic vasculature and cirrhosis are reliably provided by CT. Portal vein thrombosis lends itself to prompt detection by CT. Another area where CT plays an important role is the assessment of tumour burden based on three dimensional volumetric informnation and automated CT based techniques which provide accurate estimatiuon of percentage hepatic rep[lacement by tumour, for assessment and monitoring of patients.

MR imaging with Gadolinium chelate injection intio the superior mesenteric artery and use iof the FLASH- fast low angle shot technique has been shown to have high sensitivity for imaging of liver tumors providing superior quality images.

Liver function tests, Tumour markers (alpha foeto protein), Isotope studies, Laparoscopy, Sonographic guided biopsy form the complete armamentaria for investigation of liver tumors.

Liver resection techniques

A number of abdominal incisions can be used for liver resection. A bilateral subcostal incision provides good access and usually is made by extending an exploratory right subcostal incision to confirm there is no unexpected peritoneal disease. An upwards extension to the bottom of the sternum to form a Mercedes-Benz incision can be made to allow wider access. A costal retractor such as a Rochard may be used.

A mid-line incision with a right costal extension is also practical. Following an exploratory laparotomy, the liver is mobilized from its peritoneal attachments. The falciform ligament is divided, with particular care superiorly where the hepatic veins enter the inferior vena cava. The right coronary ligament, with its anterior and posterior leaves around the bare area of the liver and its fused caudal extension as part of the triangular ligament, is divided to mobilize the right liver. The left triangular ligament is divided to mobilize the left liver, though for extensive right-sided resections, it may be preserved to prevent liver rotation and venous outflow occlusion post resection.

The main hepatic pedicle can be approached from outside or from inside the liver substance. The extrahepatic approach was first described by Lortat-Jacob and co-workers in 1952 in a report of a right hemihepatectomy. The free edge of the lesser omentum is opened, the portal vein, hepatic artery, and common bile duct followed up to their divisions, and the appropriate side dissected and divided. Dissection can be time consuming and anatomy may vary. Division may be high and close to the porta hepatis. Misidentification and ligation of the wrong vessels may devascularise an area of liver that is not planned to be resected. The hepatic veins may be dissected extrahepatically in the case of both the right vein and the middle/left vein, whether combined or prior to their joining. The veins are wide and accidental damage may result in catastrophic and uncontrollable haemorrhage.

The hepatic pedicles may be approached directly by the anterior intrahepatic approach. This was first described by Tung and involves dissection of the hepatic parenchyma along the hepatic fissures and ligation of the pedicles directly within the liver. The problems are that the fissures are not identifiable on the liver surface and, prior to pedicle ligation, there are no identifiable boundaries between the segments. There may be considerable haemorrhage as the pedicles are ligated after paren-chymal dissection. This method is necessary to ligate a portal triad to an individual segment and intra-operative ultrasound can aid identification of the appropriate portal triads. The hepatic veins may also be ligated within the liver substance.

The advantage is that this reduces the risk of damaging the vein, but the disadvantage is that ligation of the vein tends to have to be late in the resection and hence haemorrhage may again be considerable.

The hepatic pedicles may be approached by the posterior intrahepatic approach described by Launois and Jamieson which utilizes the Glissonian sheaths. Incisions of the liver capsule around the porta hepatis allow limited intrahepatic dissection. Dissection along the sheaths around the portal triads provides access to the main trunk sheaths supplying an entire hemiliver, further within to sectorial divisions, and then to segmental divisions. Clamping of these divisions may be used to confirm identification by devitalisation of the supplied segment(s) and the appropriate sheath may then be ligated. Excellent results have been reported with this method.

Hepatic vascular control

The potential of severe haemorrhage during liver resection and the resulting morbidity has already been mentioned. Bleeding maybe a particular problem during parenchymal transection. A number of techniques of hepatic vascular control of inflow and outflow are available and, though liver resection can be performed without vascular control, the use of vascular control can result in very low blood losses. Alternative techniques to reduce parenchymal bleeding such as use of a hepatic tourniquet or instruments to compress the parenchyma are not generally used.

This is the original technique described by Tung with direct dissection through the liver parenchyma to the inflow and outflow of the area to be resected with no other vascular control.

It has the advantage of no risk of erroneous ligation of hilar structures, but, unless performed quickly, bleeding is substantial from the transection surface,particularly if coagulation is impaired such as with cirrhosis. Identification of the hepatic fissures may also be problematic as perfusion of the hepatic segments remains uniform during transection.

The extrahepatic approach to the hilar vessels and hepatic veins described by Lortat-Jacob does provide vascular haemorrhage as the pedicles are ligated after paren-chymal dissection. This method is necessary to ligate a portal triad to an individual segment and intra-operative ultrasound can aid identification of the appropriate portal triads. The hepatic veins may also be ligated within the liver substance. The advantage is that this reduces the risk of damaging the vein, but the disadvantage is that ligation of the vein tends to have to be late in the resection and hence control prior to transection of the liver parenchyma.

The advantages are that the area to be transected is well demarcated prior to transection as it is devascularised, and that intra-operative haemorrhage is minimal. The disadvantages are that inappropriate ligation at the porta hepatis is possible and dissection of the hepatic veins may be difficult, with the risks of severe haemorrhage and air embolism. It is also not possible if resection of a segment alone is undertaken.

Temporary vascular occlusions of the liver

A number of techniques of occlusion of hepatic inflow are available which may be combined with occlusion of hepatic outflow.

Total inflow occlusion

Pringle first described total clamping of the hepatic pedicle or the Pringle maneuver in 1908 to reduce hepatic haemorrhage secondary to trauma. It is probably the most common method of minimizing blood loss during parenchymal resection and involves 'en masse' clamping of all the structures of the hepatic pedicle present in the free edge of the lesser omentum with a non-crushing clamp. Nagasue *et a*l. and Kim *et a*l. have compared hepatic resections of cirrhotic livers with and without the Pringle maneuver and have shown a significant reduction in intra-operative blood loss, postoperative complications, and mortality in the group in which the Pringle maneuver was used.

Studies in which both cirrhotic and non-cirrhotic patients underwent hepatic resections also demonstrated a significant improvement using the Pringle maneuver. Inflow occlusion does result in a haemodynamic response with an increase in systemic vascular resistance and a corresponding increase in heart rate and mean arterial pressure, but this is usually well tolerated in both non-cirrhotic and cirrhotic patients.

Opinion on the safe duration of clamping varies. For a long time, the original description by Pringle of 15–20 min of inflow occlusion was considered the limit in a normal liver. Huguet *et a*l.56 reported no major com-plications or mortality in a series of resections with inflow occlusions times of 25–65 min with a mean of 38 min.Since then, a number of authors have reported continuous occlusion times of up to 60 min with few complications, and this is generally considered the safe upper limit for normal livers.

Continuous occlusion up to 90 min has been reported, although this duration of warm ischaemia is associated with a significant number of major complications such as transient hepatic insufficiency and encephalopathy.
Use of techniques to lower the central venous pressure (CVP) to 0–5 cm during transection has a dramatic effect on reduction of blood loss. Lowering the CVP to below 5 cm significantly reduces blood loss, and has resulted in groups demonstrating very low intra-operative blood losses. Melendez *et a*l. have done this by positioning the patient head down and restricting fluid replacement until the resection is completed. Rees *et a*l. used a combination of epidural anaesthesia and intravenous nitroglycerine for vasodilatation. Air emboli may occur during hepatic surgery, and the risk of this is increased with lowering of the CVP.

The hepatic fissures and segmental divisions are not visible on the liver surface. Clamping of the inflow as described above, allows ischaemic demarcation of the area of liver to be resected and indicates the appropriate line of resection. In segmental resection, segmental inflow ligation may not be possible prior to parenchymal transection and the line of resection must be estimated

The line of division needs to be 5–10 mm to the side of the line of ischaemic division along the hepatic fissures to avoid damage to the hepatic veins which usually lie within the fissures. The liver capsule is divided with knife or diathermy. The aim is to divide the parenchyma and leave the hepatic veins and larger branches of the hepatic sheaths containing divisions of bile duct, portal vein and hepatic artery. Small branches less than 1 mm may be diathermied, but larger branches are clipped or ligated. Segmental branches or the main hepatic veins may easily be stapled.

Meyer-May described the use of Kocher-like clamps to crush liver parenchyma in 1939 and haemostatic clamps such as Kelly clamps are still used by some units to crush small areas of parenchyma, leaving the vessels intact. Lortat-Jacob used the handle of a scalpel and Lin described the use of finger fracture to remove parenchyma. Ultrasonic dissection has been developed using a CUSA (Cavitron ultrasonic aspirator). This is an acoustic vibrator, perfused with saline, which disrupts the liver parenchyma by producing a cavitational force. Diathermy is also in-built into the tip. This has been shown to be very effective for division of parenchyma with low blood losses.

The use of other instruments such as water-jet dissection or ultrasonic cutting have also been reported.

Following division of the parenchyma, any form of vascular occlusion is released. Any residual bleeding vessel on the divided liver surface is then controlled. Use of argon beam coagulation can be valuable as it can plug vessels by creating a surface coagulum. Fibrin glue has been shown to be valuable in sealing the liver surface. The falciform ligament must be reconstituted if the right liver is resected to prevent torsion of the residual liver, although no ligament reconstruction is necessary for a left-sided resection.

There has been a limited application of laparoscopic hepatic resection and, although the results have been satisfactory with successful resections in a small group, the numbers are too small to make any conclusion as to its application on a wider scale.

Liver transplantation :

The final court of appeal for unresectable liver tumour without systemic spread is liver transplantation. Favourable results for transplantation in children with hepatoblastoma, whose disease is localized to the liver have been reported (Superina and Bilik 1996, Douglas 1997). Though this enthusiasm must be tempered in those with stage 4 hepatoblastoma, as recurrence is almost universal.

At times, even benign liver tumors can cause significant morbidity in children. Howard reported 20% mortality of the children with benign tumors in his series. With present survival rates of post liver transplant approaching 90%, children with unresectable or untreatable benign tumours are to be offered the option of liver replacement. Primary liver transplantation has been in the cards as an option, but significant controversies exist owing to the shortage of the availability of donor livers. Howard recommends transplantation for highly select group of children, with isolated liver tumours, with caution. The devised strategy for these children is 4 cycles of anterior chemotherapy followed by transplantation and early post transplant consolidation therapy with 2 more cycles of chemotherapy. In a rare instance, as evidenced by Tepetes (1995), orthotopic liver transplantation is the only therapeutic option available for an extensive unresectable benign tumour.

Recent advances :

Excessive bleeding during liver resection may require time consuming hemostasis with attendant complications resulting in increased post op morbidity and mortality. Hence researchers were hard pressed for newer methods to control bleeding. This led to the emergence of modern gadgets, which achieved controlled parenchymal resection with reduced blood loss compared to the finger fracture techniques.

These include

i. Ultrasonic dissection (Cavitron UltraSonic Aspirator – CUSA)

ii. Ultrasonic cutting (Harmonic scalpel)

iii. Hydrodissection

iv. Argon Beam Coagulation (ABC)

v. Laser dissection / cutting

vi. Cryotherapy

vii. Radiofrequency electrodissection

Using Ultrasonic dissection, damage to vessels, ducts can be avoided while fat or glandular parenchyma is separated. Due to sonic vibration at 25,000/sec, a cavitational effect is obtained, the ultrasonic high energy converting water to steam. More the water content, more the resultant cavitation effect, causing fragmentation of parenchymatous cells and fat. The advantage lies in the fact that structures with significant amount of collagen namely the vessels, ducts and nerves are left intact for careful ligation eliminating the risk of bleed and thus achieving effective hemostasis.

The glisson`s capsule requires incision by cautery before sonic dissection as the liver capsule has low water content.Harmonic scalpel is an innovative modification of the sonic dissector with increased frequency of the vibrating tip to the tune of 55,000 Hz. The device cuts when the tip is vibrating in the harmonic range and also achieves coagulation effect.

Hydrojet dissection has been reported as a quick and efficient technique for disrupton of the liver parenchyma during liver resection. Varying effects are produced on the liver – deep, sharp cutting of all the structures is achieved at close quarters, while washing and gentle separation of structures is achieved on placing the probe at a distance.

The Argon Beam Coagulator is a technological improvement over its predecessor – the electrocautery, in that more effective coagulation and hemostatsis is attained. Gentle flow of Argon conducts radiofrequency current to the target tissue, resulting in an eschar of uniform depth, and allowing coagulation within the vessel wall. Smoke production seen in electro-cautery usage, is absent in ABC, as also the fact that it clears blood from the surface of target tissue, allowing better visualisation and localization of the bleeding site. Nd:YAG, CO_2 lasers facilitate liver resection by combination of coagulation and vaporization, although the effect is cutting rather than coagulation on larger vessels in 2mm range resulting actually in increased blood loss.

Use of Cryotherapy probes and Radiofrequency ablation has been in the experimental stage, being advocated for application in treatment of unresectable liver tumours.

Aim :

i. To study the pattern of presentation of liver tumours in our Institute

ii. To study the histopathological profile of liver tumours

iii. To analyse the outcome of liver resection

Materials and methods :

The study was a combined retrospective and prospective collection of children operated for liver lesions.

Inclusion criteria for the study - all children who underwent liver resection were included in the study from January 1999 – January 2005.

Exclusion criteria were cases not operated or liver resection done for causes other than neoplasms, like trauma. Informed consent was obtained from the parents of the children, for inclusion in the study.

Cases that died or lost for follow up were identified. Otherwise, all cases were followed up on a periodic basis i.e - immediate post surgery every monthly till 1 yr, 3 monthly once for II yr, 6 monthly once for III yr, annually thereafter.

Children underwent a complete clinical examination during the follow up visit.

Relevant investigations including chest Xray, Ultrasonography of abdomen, complete blood counts, liver function tests and tumour markers were carried out during the follow up visits, to ensure detection of loco regional recurrence of the malignant neoplasms.

If Ultrasonography of abdomen was not satisfactory, in view of high index of suspicion of tumour recurrence, CT abdomen was done. The follow up cases were discussed in a tumour board, conducted once weekly, comprising of a team of specialists including Medical oncologist, Radiotherapist, Pathologist and Surgeon. Similarly, all the new tumour cases were discussed by the Tumour Board panel, to achieve a consensus opinion regarding surgery with or without chemotherapy.

Results :

The study comprised of 21 cases, over a period of 6 years. In our Institute, we register about 5-6 new cases of liver tumors annually. Approximately, 750 new cases were identified to have malignancies per year of which liver tumors account for about 1-2 %.

Age distribution

Of the 21 cases, most of them were within the age group of 1-2 years (33%). 6 of the children were infants, of whom 2 were neonates.

Between 2-3 years, 3 children were enrolled in the study. Older children formed a minority as evidenced by the group of 4-5 years consisting of 2 children (10%). 10% were between 6-7 years and 5% were between 8-9 years of age. The youngest child was 3 weeks of age (fig 3) and the oldest was aged 8 years. Overall, 80% of the children were below 3 years of age forming a considerable majority over children more than 4 years of age (5 children, 20%).

Among the study group, 10 were boys and 11 were girls, with an almost equal male-female ratio.

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Clinical presentation

The most common presenting complaint was abdominal mass / distension of abdomen, seen in 19 out of 21 children (90%). 5 of the children presented with anorexia (23%). Fever was present in 23% of the children. 20% of children were labeled as failure to thrive in view of inappropriate anthropometry, height and weight for age. 10% of the study group had significant weight loss. Pain abdomen was the presenting complaint in 2 children (10%). Uncommon but interesting presentation in the study group was pseudo-precocious puberty in 2 children (10%). One of them was diagnosed to have adrenocortical tumor with secondaries liver (fig 4), and the other was a beta HCG producing Hepatoblastoma.

All of them had a palpable mass or hepatomeagaly. 60% of them were anemic at presentation. None of the children were icteric, although altered liver enzymes were present in 55% of cases. Prothrombin time and biochemical parameters were within normal limits in all the cases.

Ultrasonography and CT scan was done in all the cases for delineating the liver tumour and assessing the operability of the lesion

Tumour markers

Alpha foetoprotein, Beta Human Chorionic Gonadotropin assay were performed in all the cases. Excluding 5 cases, rest of the 16 cases (70%) showed abnormality in the marker profile. Alpha foeto protein was grossly elevated above (30,000 ng/mL) in 6 cases (33%). In 5 of the children the levels were between 10,000 – 30,000 ng/mL. The levels were between 1,000 – 10,000 ng/mL in about 3 cases (15%). 10% cases showed mild elevation to the tune of < 1,000 ng/mL. Beta Human Chorionic Gonadotropin levels were elevated in only 2 cases.

Histopathology profile

The majority (85%,18 out of 21 cases) were found to be malignant on histopathological examination. 15% of the cases were identified as benign liver tumours. Of the 3 cases reported benign, 2 were Hemangioendotheliomas and one was Hepatic adenoma.

Among the malignant tumors, Hepatoblastomas form the bulk of the group, accounting for 66% of cases, i.e 14 cases out of 21 cases. One of them was a Hepatocellular Carcinoma and one was a malignant mesenchymal hamartoma. 2 of them were Adrenocortical carcinomas with secondaries liver.

Surgical procedures

Pre operative preparation of all the cases involved hydration with 10% dextrose and vitamin K. Anemia was corrected before taking up for surgery. Chevron incision was used in 8 cases and midline laparotomy was done in 2 cases. The commonly employed incision was bilateral rectus cutting incision in 12 cases (55%).

Surgical procedure involved exposure and liver mobilization by cutting the ligaments and taking vascular control. Finger fracture method was used for parenchymal resection and ligation of the large vessels and ducts done at the end of the procedure.

Among the 21 cases, 16 (85%) of the children under went anatomical resections. Non anatomical resections were undertaken in 4 cases. Re-resections were performed in the children who underwent non anatomical resection, in view of residual disease. In 2 children, concomitant adrenalectomy and liver resection were performed for Adrenocortical ca with liver metastases.

Majority of the anatomical resections were right hepatectomies (9 children out of 16). Less than 50% of the anatomical resections were left lhepatectomies. Only one of them underwent segmentectomy. In 5 cases, Pringle`s maneuver was performed for reducing blood loss.

Blood utilization

The use of finger fracture technique was associated with increased blood loss and hence replacement in the form of blood utilization was generally on the higher side.

Barring 3 cases, the vast majority (18 out of 21 cases) were transfused with blood. Range of blood utilization varied from 100mL to 5 pints. On an average, 1 pint was transfused per child. Among the 18 children who received transfusion, the transfusion was done on the basis of preoperative anemia and anticipated increased blood loss in 10 cases. Hence, significant blood loss requiring transfusion was only in about 8 cases.

Post-operative complications

Immediate complications in the early post-operative period (< 1 week) were noted in 8 children (30%).

Minor complications like wound infection, gaping, fever and ileus were not included in this. Bile leak was seen in 3 cases, of which 2 subsided gradually over 2 wks and subsided without any intervention. One of the children who had persistent bile leak required intervention.

Significant post-operative hemorrhage was observed in 5 cases, 3 of them being managed with fresh whole blood and plasma transfusions. In 2 cases, the bleed was severe and could not be controlled, and they expired eventually after prolonged stay in the intensive care unit.

In 6 cases, late complications were recorded, beyond the first post-operative week. One developed an incisional hernia, and the other child manifested bilioentero cutaneous fistula, requiring intervention. 4 children went on to develop recurrences, which were identified within 6 months post-operative follow up. Three of the children with recurrences did not respond to second line chemotherapy and expired while awaiting for re-operation. One of the children with recurrent liver tumour refused further treatment.

Chemotherapy

Of the 21 children, 15 received chemotherapy. 6 of the children did not receive chemotherapy in view of the histopathology report.

The children who were not subjected to chemotherapy include 2 Hemangioendotheliomas, 2 Adrenocortical tumors with secondaries liver, 1 Hepatic adenoma, 1 Hepatocellular carcinoma.

The chemotherapy regime consisted of Vincristine, 5 FluoroUracil and Cisplatin.

We submit the children for chemotherapy, within 10 days of surgery and continue 6 cycles of chemotherapy. Among the 15 children who received chemotherapy, only 2 of them were subjected to 2 cycles of neo adjuvant chemotherapy in view of doubtful resectability, based on imaging studies. Later, these children were followed up with 4 more cycles of chemotherapy post resection.

Outcome

Of the 21 cases studied, 13 of them are asymptomatic (65%) at the time of conclusion of the study. 20% of the study cases expired, 3 of them due to recurrence of tumour and 2 of them developing uncontrolled hemorrhage in the immediate post-operative period.

Two cases (10%) were lost for follow up. Among the cases on follow up, 4 of them were at the end of first follow up year.

.Two cases have completed 2 year follow up while another 2 cases have completed 3 year follow up. 25%(5 out of 21 cases) of the total study cases have completed successfully 5 year follow up and they are disease free till date.

Discussion:

Our study found a 1-2% incidence of malignant liver tumors, which is in accordance with the SEER program cancer registry of the Bethesda cancer institute. Also, our annual resection rate of 3 per year is the same as that reported by Young et al.

In our study, the median age at diagnosis was 18 months, for Hepatoblastoma, which is consistent with the reports of Exelby et al and Lack et al. According to Tomlinson, only 5% of Hepatoblastoma cases were seen in children older than 4 yrs of age, whereas we had not encountered any Hepatoblastomas in children older than 4 years. .Weinberg et al reported a male predominance in Hepatoblastoma with a ratio of 1.4 : 1 to 2:1. In contrary, our study found a relative female preponderance of 1.3 : 1.

In the series reported by Exelby et al, the most frequent clinical presentation was the presence of an abdominal mass accounting for 68% of cases.

We observed 90% cases with abdominal mass / distension. Pain abdomen (10%) and weight loss (10%) were uncommon features of presentation noted in our series. Though consistent with our findings, the series of Exelby reported a slight higher percentage of these features – pain abdomen 19%, weight loss 23%.

Literature records that alpha foeto protein is markedly elevated in more than 90% of Hepatoblastomas and in many cases of Hepatocellular carcinoma. Our study noted marked increase in alpha foeto protein in 88% of cases of Hepatoblastoma. Levels were abnormal in 1 case of Hepatocellular carcinoma and 1 case of Hemangioendothelioma.

Histopathological profile of our series revealed Hepatoblastoma as the commonest variety of tumour(65%). Other lesions were less common including 10% Hemangioendothelioma, 10% secondaries liver and 5% each of Adenoma, Malignant mesenchymal hamartoma, Hepatoma. Finegold et al recorded 43% of cases in their series as Hepatoblastoma, followed by 23% Hepatoma, 6% mesenchymal hamartoma, 2% adenoma.

Malignant tumors accounted for 85% (18 of 21 cases) in our series. This pattern of majority of malignancies among the liver tumors is observed in the literature with a quoted 66%. The single case of Hepatocellular carcinoma noted in our series was incidentally the oldest patient (8 yr old boy) in our series.

The youngest child in our study was a 3 week old neonate with Hemangioendothelioma.

Surgical resection is the most important therapeutic modality of liver tumors. Resection is curative for most of the benign tumors including adenoma and mesenchymal hamartoma.

Treatment of Hemangioendothelioma is controversial, as a variety of alternative therapies to surgery are available namely arterial embolization, steroids, interferon and Cyclophosphamide, though with varying degrees of success. The PRETEXT staging system based on the number of liver sectors involved is helpful in determining the tumor resectability. Features that limit surgical resection of Hepatoblastoma include bilobar involvement, porta hepatis involvement and bulky lymphadenopathy.

We use the triple drug regime consisting of Cisplatin, 5FU and Vincristine for chemotherapy of Hepatoblastoma, after submitting the patient to surgical resection. In accordance with the Pediatric Oncology group, we had adopted this regime, which is supposed to produce a 67% 4yr survival rate. Recent trials have reported the use of other regimes, including Cisplatin & Doxorubicin, Ifosfamide, Cisplatin & Doxorubicin with supposedly high overall survival rates of 75% at 5 years.

Prognostic factors determining survival post resection include complete tumour resection, degree of mitotic activity, pure foetal histology, reduction in the alpha foeto protein level, diploidy and proliferation index. Identification of the high risk individual for Hepatoblastoma, based on the presence of the known associations like Beckwith Wiedemann syndrome may facilitate early detection and enhance the ability to cure with limited therapy.

It has been found out that in infants with Tyrosinemia type I, known to be at very high risk for Hepatoma, when treated with a chemical NTBC, the incidence of carcinoma was notably diminished,

The most recent POG study achieved a survival of 90% in early stages of Hepatoblastoma with a significant fall in survival in advanced stages (67%). We in our series have achieved a 2 yr survival rate of 60%. All the 13 children are thriving well with good weight gain. Our recurrence rate of 14% was probably due to the non-anatomical resections undertaken in those children. 10% of our study cases were lost for follow up. Among the 3 recurrences, 2 were hepatoblastomas and one was adrenecortical ca with liver secondaries.

Liver transplantation is fast catching up as an effective and attractive treatment modality for unresectable malignant tumors, in view of the improved survival post transplant.

So much so, that even large benign tumors deemed unfit for resection, have been successfully taken up for transplantation.

Newer modalities which would be available in future, for treatment of Hepatoblastoma are Chemoembolization with thrombogenic agents containing Cisplatin or Doxorubicin, viral transfection vectors to specifically attack and destroy the malignant cells, and anti alpha foeto protein antibodies.

Conclusion :

I. Annual burden of new liver tumors registered in our Institute is 1-2% of the total number of malignancies

II. Commonest liver tumor seen in our study is Hepatoblastoma, predominantly seen in age group less than 4 years

III. Anatomical liver resections preferable to non anatomical resections

IV. Outcome of liver resection is good with 60% 2 yr survival rate

Further long term studies are required, to establish the role of neo adjuvant chemotherapy in liver tumors. Need to use vascular occlusion techniques, in the reduction of blood loss requires to be defined.

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Table 1 Age, Gender and histopathological profile

Age group	Male	Female	Total
< 1 yr	2 HPB	3 HPB, 1 HE	6
1-2 yrs	3 HPB	4 HPB	7
2-3 yrs	1 HPB, 1 HE	1 HPB	3
4-5 yrs	1 Ad Ca	1 Adenoma	2
6-7 yrs	1 Ma Me Ha	1 Ad Ca	2
8-9 yrs	1 Hepatoma	-	1
	10	11	21

HPB - Hepatoblastoma, HE - Hemangioendothelioma Ad Ca - Adrenocortical Ca with liver metastases, Ma Me Ha - Malignant Mesenchymal Hamartoma

Table 2 Histopathology profile

Benign tumors 3 (15%)	Malignant tumors 18 (85%)
• Hepatic adenoma 1 • Hemangioendotheioma 2	• Hepatoblastoma 14 • Malig Mesench Hamartoma 1 • Hepatoma 1 • Adrenocortical Ca with sec liver 2

Table 3 Clinical features

Presentation	Number of cases
Mass abdomen / distension	19 (90%)
Anorexia	5 (23%0
Fever	5 (23%)
Failure to thrive	4 (20%)
Weight loss	2 (10%)
Pain abdomen	2 (10%)
Pseudo precocious puberty	2 (10%)

Table 4 Alpha foeto protein profile

Levels ng/mL	Cases
> 30,000	6 HPB
10,000 – 30,000	5 HPB
1,000 – 10,000	3 HPB
< 1,000	1 HE, 1Hepatoma
normal	1 Adenoma, 1HE, 1 MMH, 2 Ad Ca

HPB - Hepatoblastoma, HE - Hemangioendothelioma Ad Ca - Adrenocortical Ca with liver metastases, MMH - Malignant Mesenchymal Hamartoma

Table 5 Operative procedures

Procedures	**cases**
Right hepatectomy	**9 (44%)**
Left hepatectomy	**7 (33%)**
Segmentectomy	**1 (4%)**
Non anatomical	**4 (19%)**
Re resection	**3 (14%)**

Table 6 Post op Complications

Immediate	**Bile leak 3 (2 settled, 1 reoperated)**
	Bleed 5 (3 controlled, 2 died)
Late	**Recurrences 4 (3 died, I reoperated)**
	Incisional hernia 1

Table 7 chemotherapy

Neo adjuvant	**2 HPB**
Post op	**12 HPB, 1 Malig mesen hamartoma**
No Chemo	**6 – 1 HA, 1 Hepatoma, 2 HE, 2 Ad ca**

HPB - Hepatoblastoma, HE - Hemangioendothelioma Ad Ca - Adrenal Ca with liver metastases, HA – Hepatic Adenoma

Table 8 Outcome

Status	**cases**
Doing well	**13 (65%)**
Awaiting surgery	**1 (4%)**
Death	**5 (23%)**
Lost follow up	**2 (8%)**

Figure 1 : Age distribution of study cases

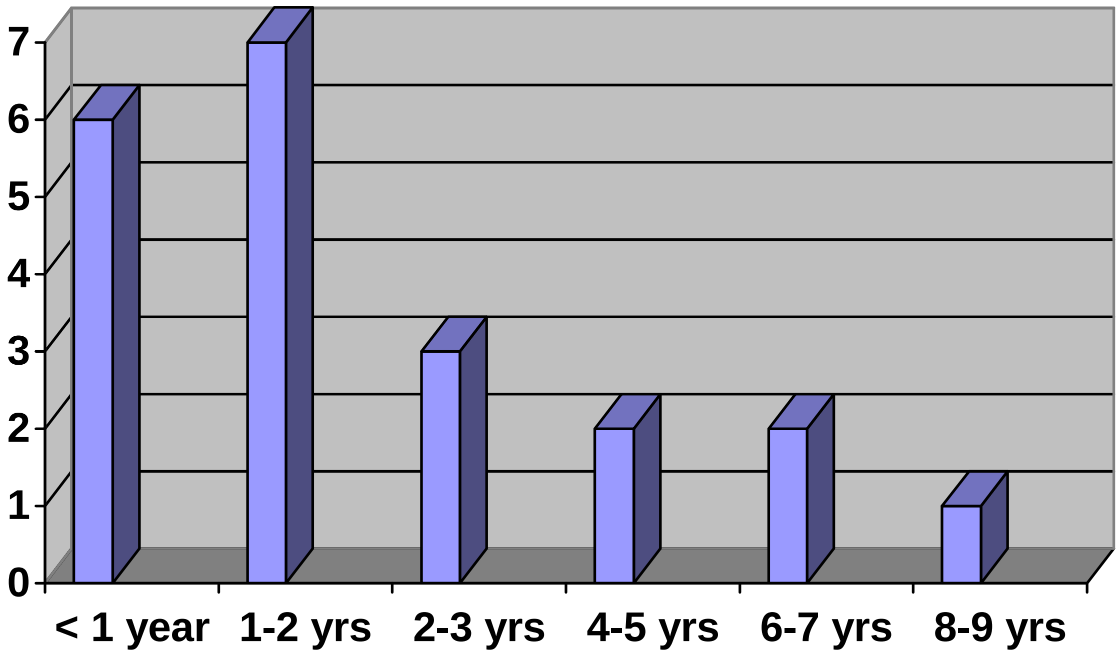


Figure :2 Follow up of study cases

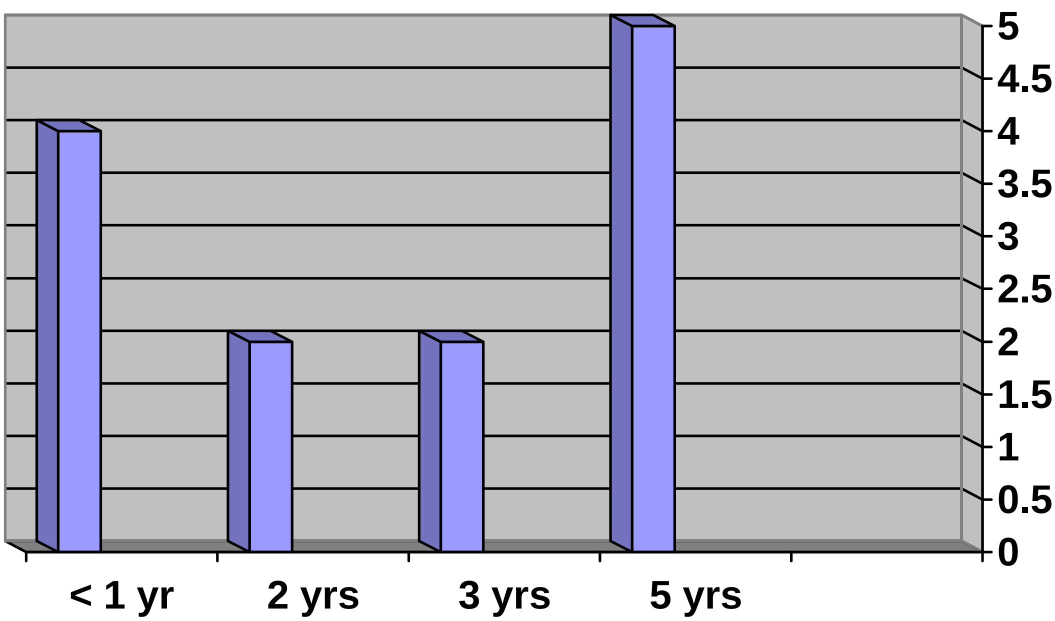
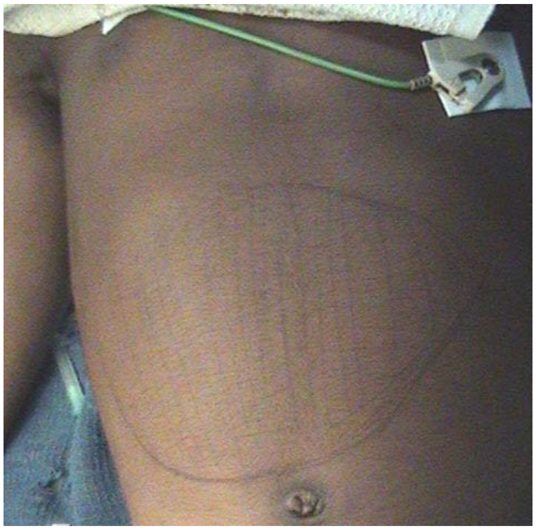


Fig 3 Neonate with

Hypochondriac mass

Fig 4 Boy with Adrenocortical ca with Liver metastases



Mass abdomen

Premature Pubarche

Fig 5 Liver eviscerated with tumor

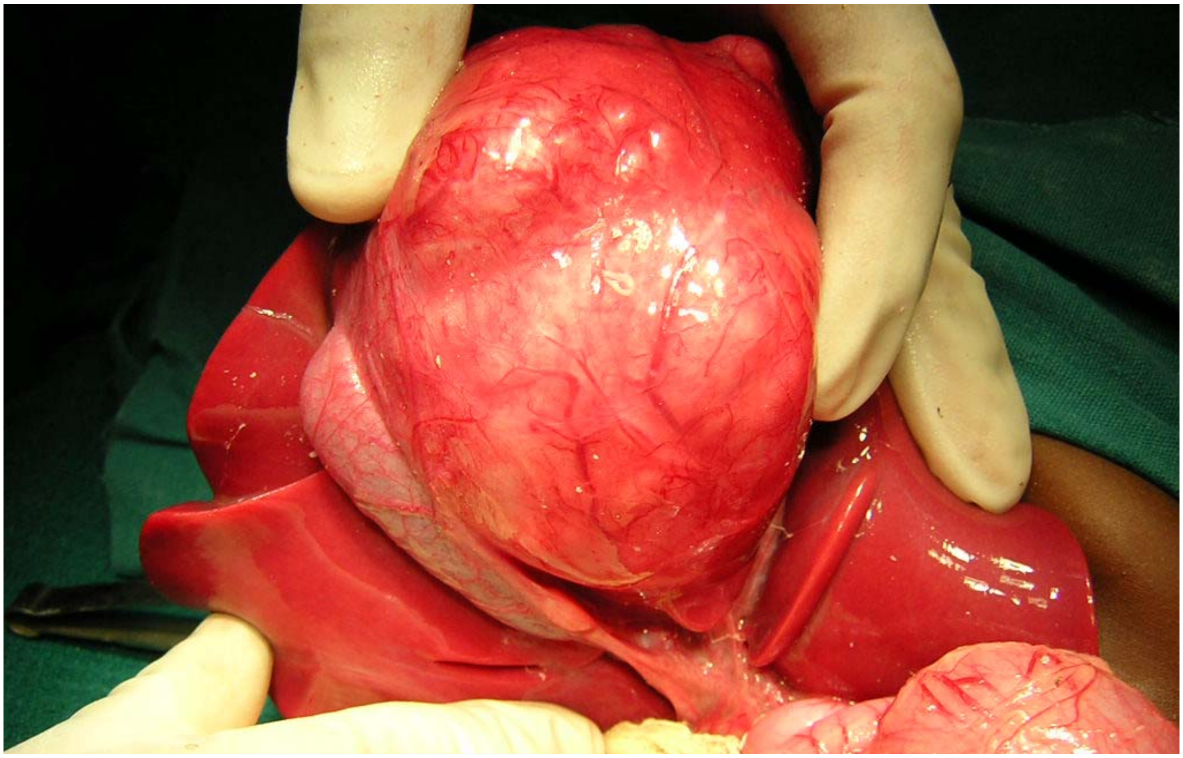


Fig 6 showing Right lobe liver mass

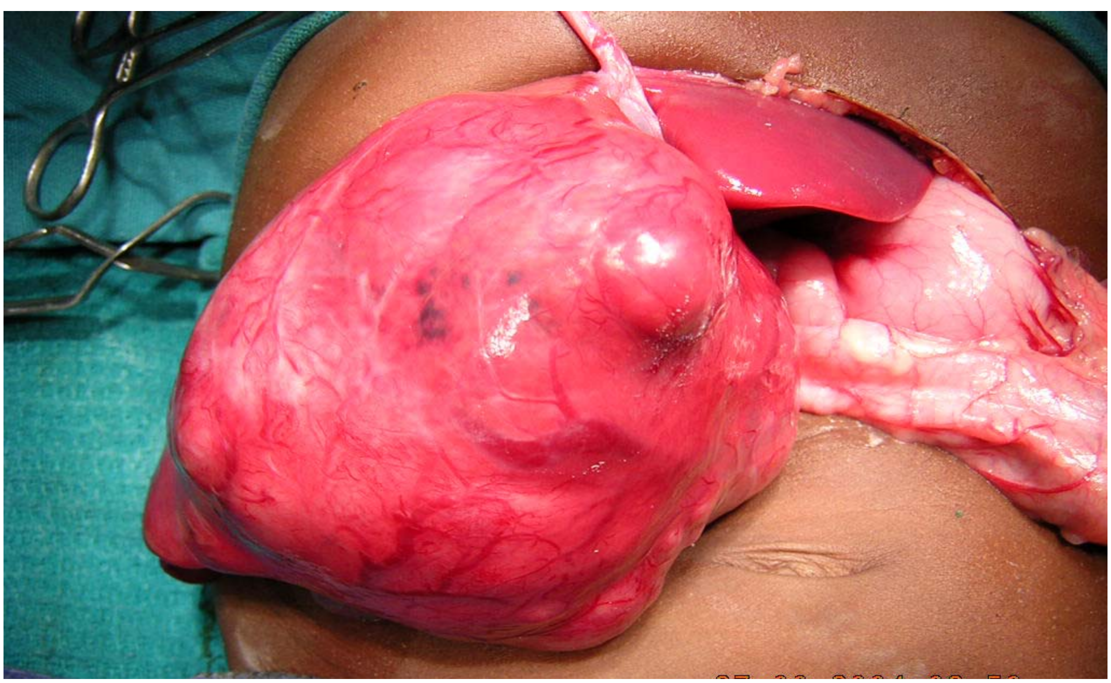


Fig 7 showing Left lobe liver mass

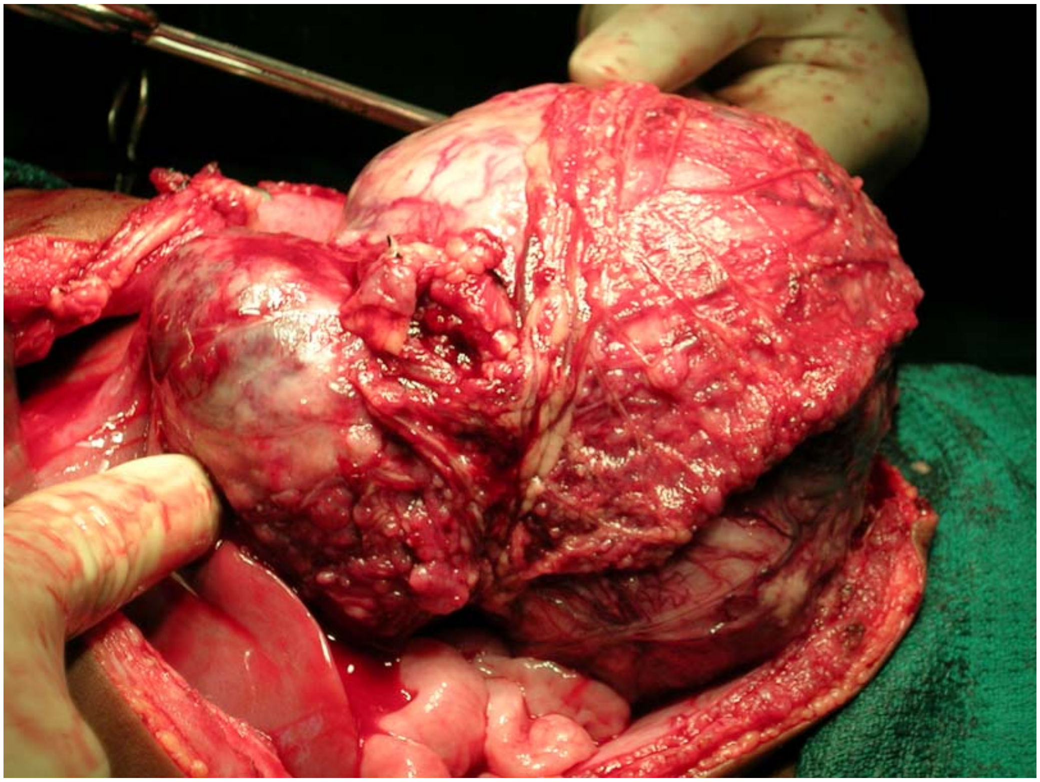


Fig 8 Vascular control taken prior to commencement of liver resection

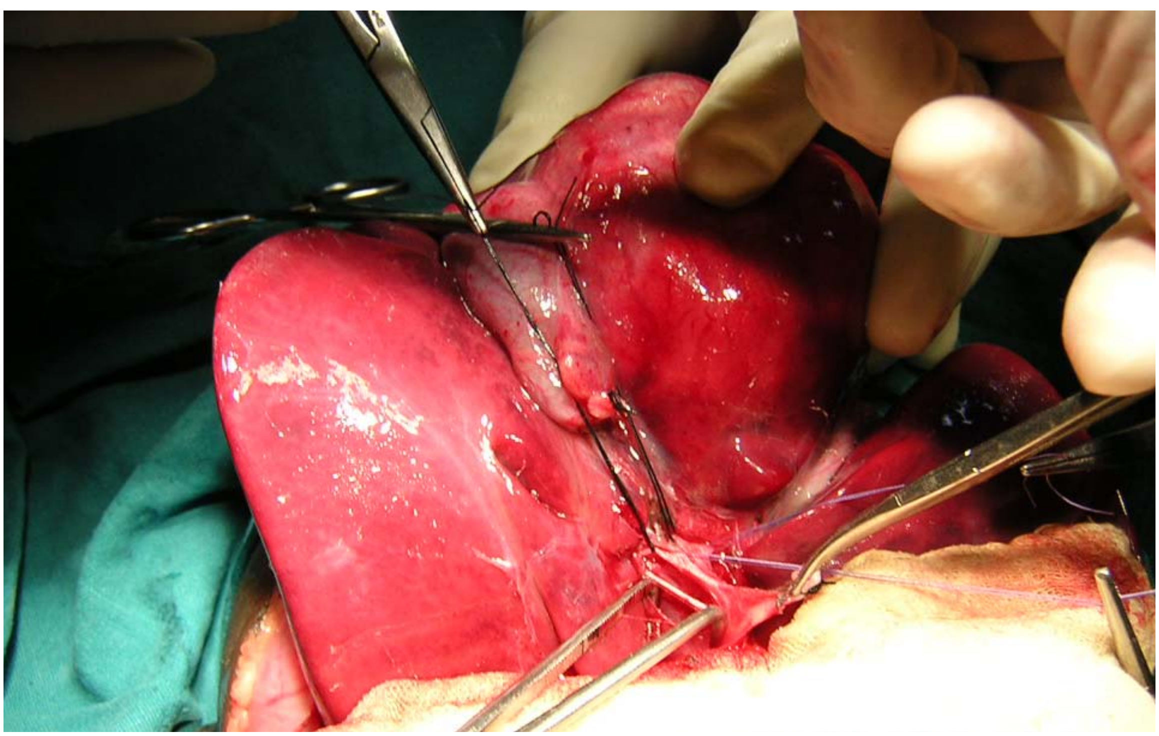


Fig 9 Post resection liver bed

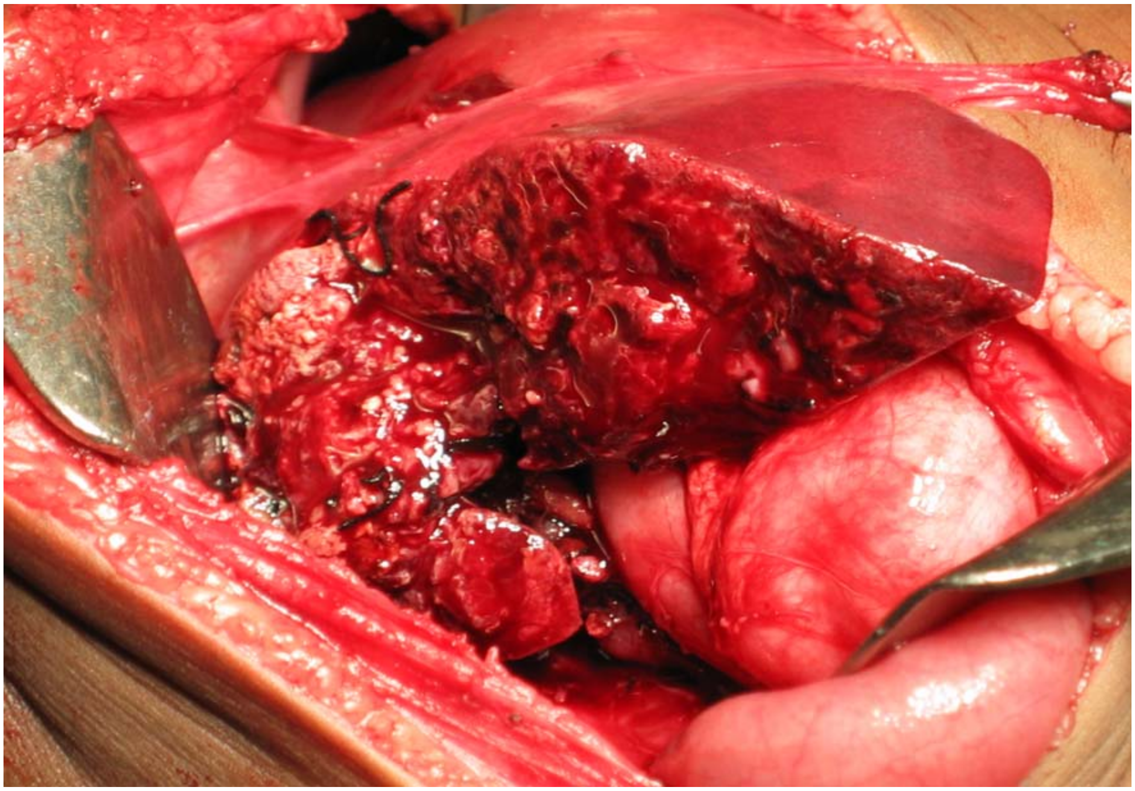


Fig 10 Digitoclasia in progress

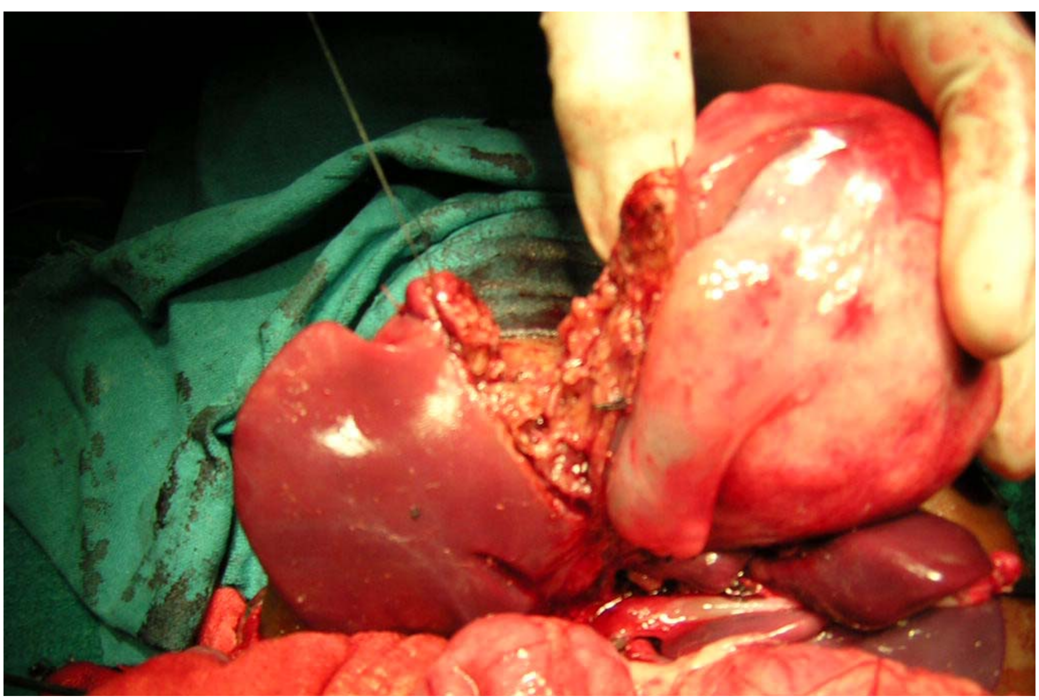
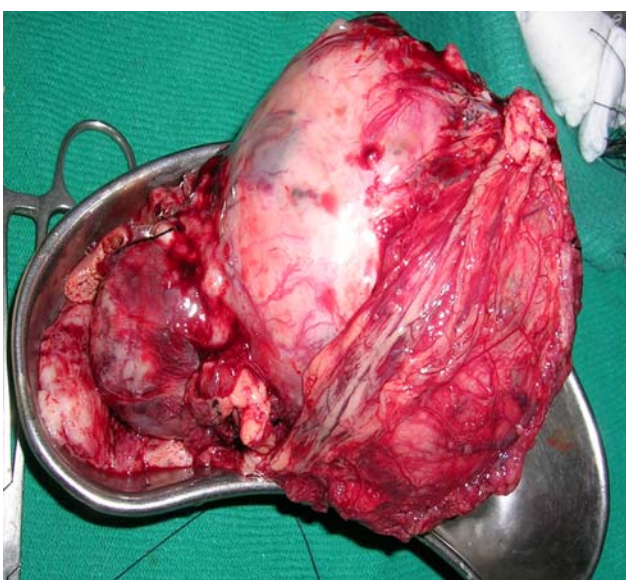


Fig 11 Resected Specimen

Segmentectomy specimen

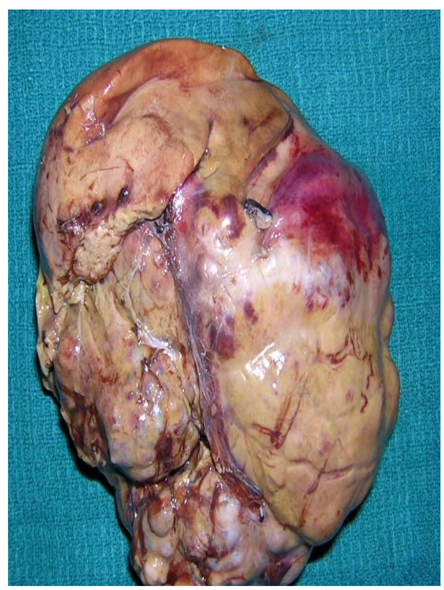
Right hepatectomy specimen

Specimen of Non anatomical resection



Left hepatectomy

specimen



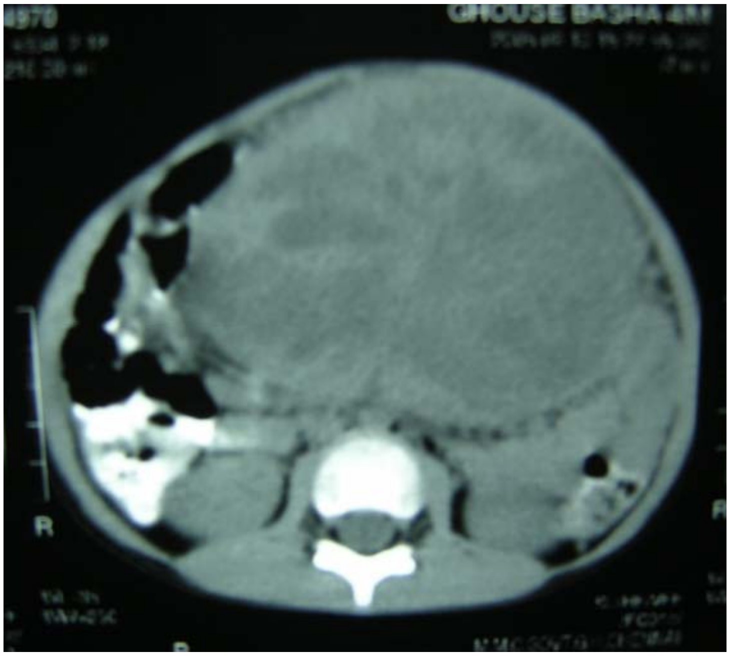


Fig 12 CT scan abdomen showing Left lobe liver tumor with necrosis

Fig 13 - Post resection, completed chemotherapy at 1 yr follow up