

# Management of liver diseases and liver transplantation in India

**Prof Anupam Sibal**  
**Group Medical Director, Apollo Hospitals Group**  
**Adjunct Professor of Paediatrics**  
**School of Medicine**  
**University of Queensland, Brisbane, Australia**  
**Senior Consultant**  
**Pediatric Gastroenterologist and Hepatologist**  
**Apollo Centre for Advanced Pediatrics**  
**Indraprastha Apollo Hospital**

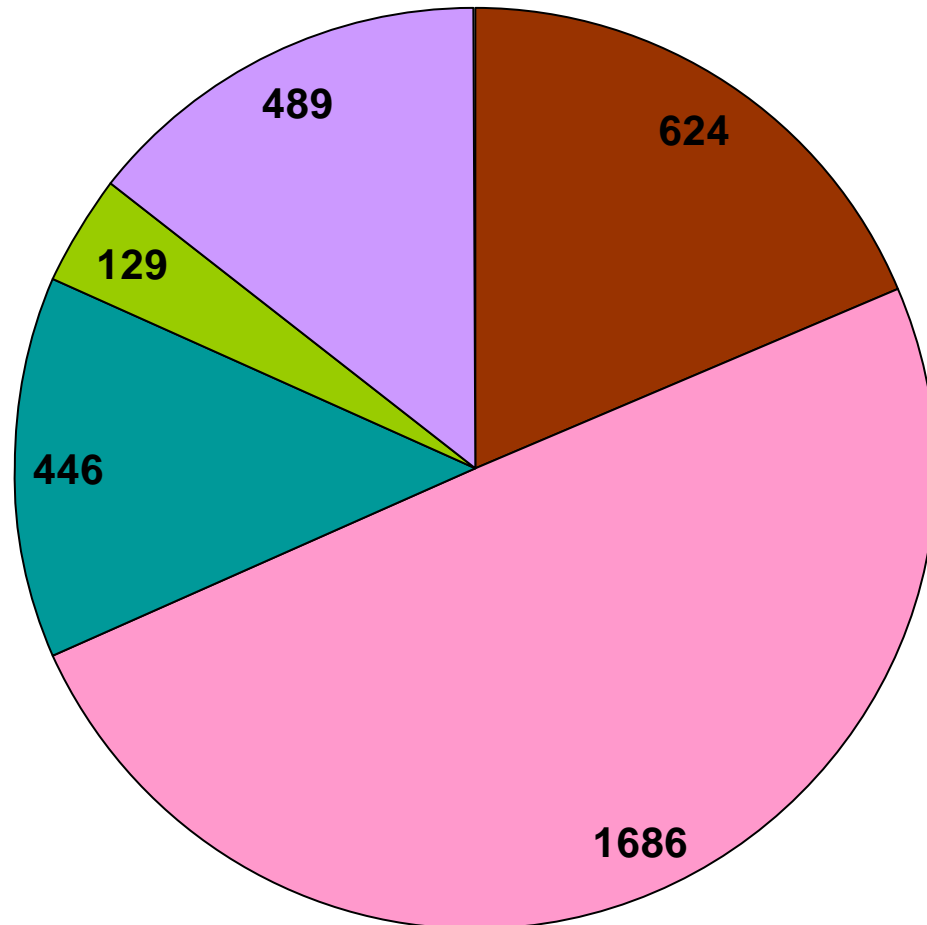
**Dr Vidyut Bhatia**  
**Pediatric Gastroenterologist and Hepatologist**  
**Apollo Centre for Advanced Pediatrics**  
**Indraprastha Apollo Hospital**



# Hepatobiliary referrals

## 1.10.97 – 30.06.2011

n = 3374



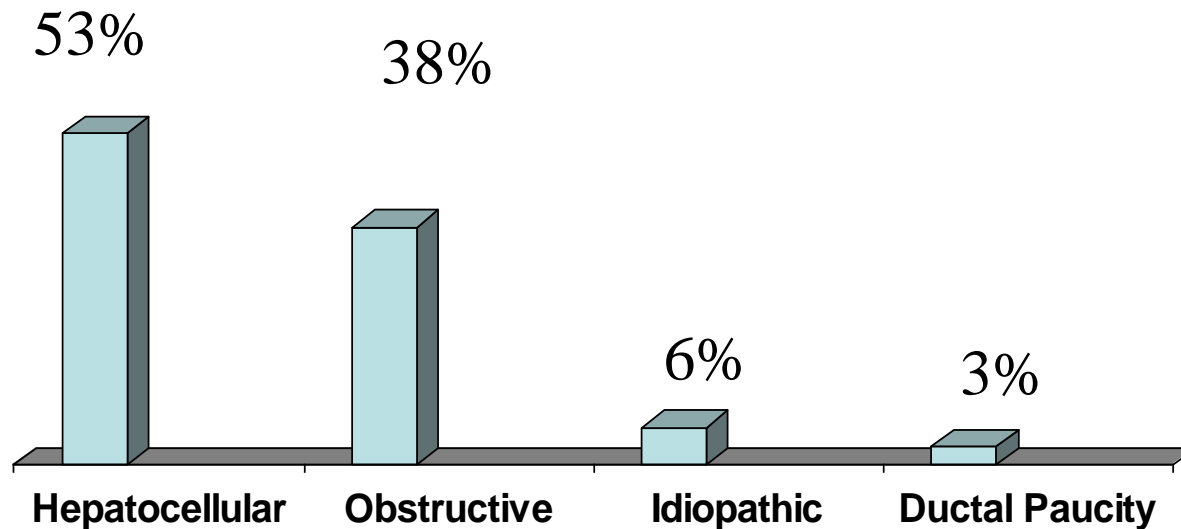
- Neonatal Cholestasis
- Acute Liver Disease
- Chronic Liver Disease
- Fulminant Hepatic Failure
- Miscellaneous



# Neonatal cholestasis

8 medical centres, n = 1008

30% of hepatobiliary disorders



*Indian Pediatrics 2000*



# Late referral for biliary atresia – missed opportunities for effective surgery

Age at referral	Rate of success
< 8 weeks	86%
> 8 weeks	36%

*Mieli-vergani, Lancet 1989*



# Biliary atresia – the Indian scenario

**33 days for a baby with neonatal cholestasis to seek medical attention for the first time**

**100 days to reach a tertiary centre**

***Consensus Report on Neonatal Cholestasis Syndrome***

***Indian Pediatrics 2000***



# Yellow alert campaign

**All babies in whom jaundice persists for more than 2 weeks should see a doctor**

**urine test**

**blood test**



# Results of the campaign

Parameters	1992 -1995	1999 – 2002	2002 - 2004
Number of NCS cases per month	1.5	1.8	3.2
Mean age at presentation of BA (days)	132	122	97
Delay in BA referral (days)	121	107	78

*Sharma, Poddar et al  
J Gastroenterol Hepatol, 2004*



# Hepatitis A

## Changing epidemiology

**Low and intermediate areas mixed with high endemicity areas**

**A decrease in immunity against hepatitis A**

**Increasing the number of children and adolescents who are now susceptible to HAV**

**Local epidemics**

*Mathur et al, IJMR, 2008*



# Apollo data

**Anti HAV body was studied in 100 children over a period of 1 year in the age group 2- 12 years**

**Overall seroprevalence was 49 %**

**Proportional increase in seroprevalence with age**

**Seroprevalence inversely proportional to socio economic status**



# Hepatitis E

**Children are exposed to HEV since early infancy and the rates increase with advancing age**

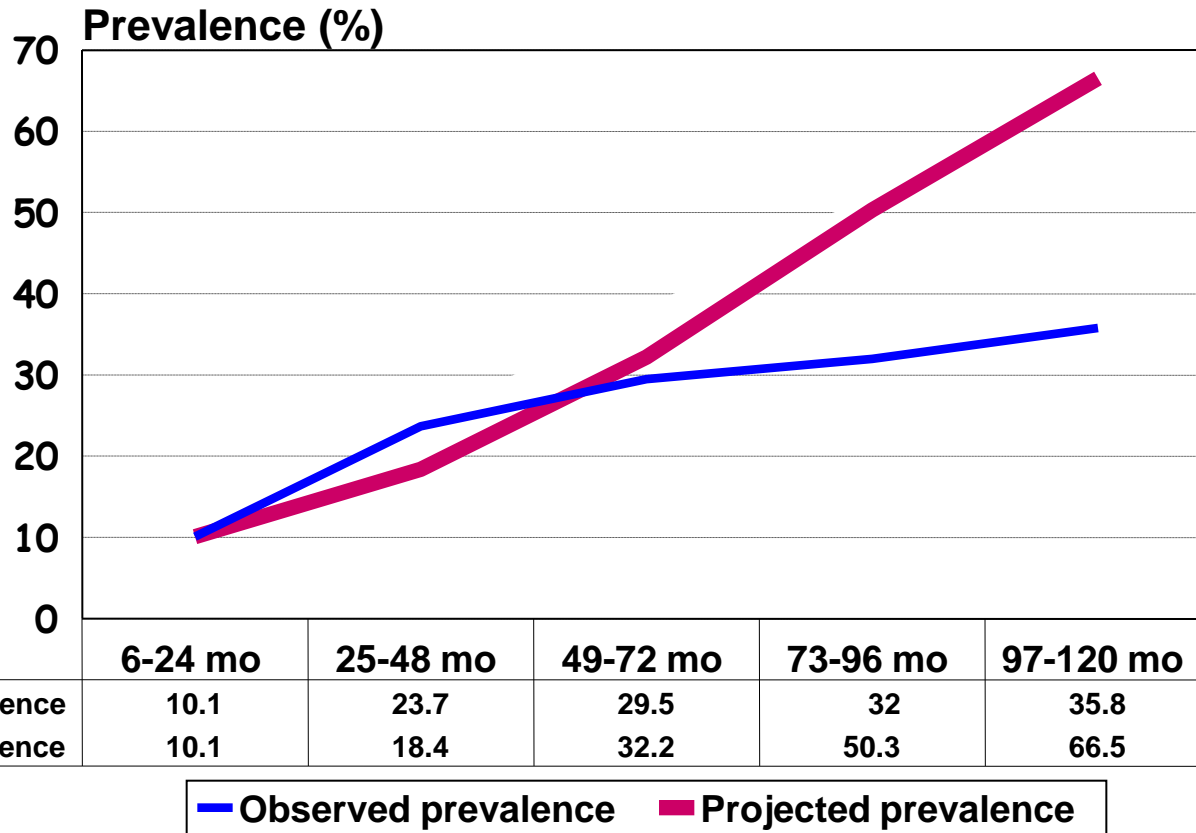
**HEV constitutes an important cause for acute sporadic hepatitis and liver failure**

**Co-infections with Hepatitis A and Salmonella occur frequently**

*Acharya et al, 2006, NMJI*



## Weaning off of anti-HEV IgG antibodies: Projected vs Observed (n=2070)



*Mathur Arora et al*  
*Indian Pediatr 2001 May;38(5):461-75*



# Acute liver disease

<b>Hep A</b>	<b>1331</b>
<b>Atypical hep A</b>	<b>217</b>
<b>Hep E</b>	<b>86</b>
<b>Hep B</b>	<b>30</b>
<b>Acute pres Wilson's disease</b>	<b>22</b>



# Fulminant hepatic failure - 129

<b>Hep A</b>	<b>61</b>
<b>Cryptogenic</b>	<b>41</b>
<b>Hep A and E</b>	<b>11</b>
<b>Hep A and B</b>	<b>6</b>
<b>Hep E</b>	<b>6</b>
<b>Hep B</b>	<b>3</b>
<b>Poisoning</b>	<b>1</b>



# **Fulminant hepatitis A and G6PD deficiency**

## **n=19**

**Mean age 7.8 yr, range 6 –10 yr**

**Mean duration of symptoms 10 days**

**Anemia**

**High bilirubin**

**Mean 56.8 mg/dl, range 24.7 – 87 mg/dl**

**rapid rise in bilirubin (> 10 mg/24 hr in 6 cases)**



# Metabolic liver disease

**Up to one fourth of CLD patients may have metabolic etiologies**

**WD is the most common MLD in India**

**Almost 50% of metabolic liver disease in India**

**18 new mutations described**

**Exons 8, 12, 13, 15, 16, and 18 are hot spots for mutations in Indian WD patients**

*Kumar and Thapa et al, 2005  
Pediatric Liver Study Group of India, 1999*



# Alpha 1 antitrypsin

**57/58 children of neonatal cholestasis normal phenotype (PiMM)**

**1 patient had a normal variant (M1E)**

**no case of abnormal allele was detected**

**Out of 1250 liver disease patients**

**Z or S phenotype was not observed on phenotyping, PCR-Restriction Fragment Length Polymorphism, SSCP and sequencing**

**A1AT appears to be uncommon in North India**

*Arora et al, March 2010, Ind Pediatr*

*Khanna et al , 2006, Indian J Gastroenterol*



# Metabolic liver disease

**Reliable diagnostic facilities exist in few centers**

**Diagnosis**

**On the basis of clinical features and liver histology**

**ICC virtually non-existent**



# Etiology of chronic liver disease in Indian children

Etiology	Chennai n=236(%)	Pune n=117(%)	Chandigarh n=113(%)	Lucknow n=144(%)	MAMC n=38(%)	AIIMS n=161(%)
Viral	75 (32%)	2 (2%)	9 (8%)	15 (10%)	17 (45%)	29 (18%)
Autoimmune	0	7 (6%)	21 (19%)	4 (3%)	1(3%)	16(10%)
Metabolic	18 (8%)	50(43%)	24 (21%)	40(28%)	4 (11%)	34 (21%)
Others	6 (3%)	14(12%)	25 (23%)	3 (2%)	2 (5%)	33 (20%)
Unknown	137 (38%)	44(38%)	34 (31)	82 (57%)	14 (36%)	49 (30%)

*Indian J Pediatr. 1999*



# Hepatitis B

**HBsAg prevalence among general population ranges from 2% to 8%**

**Intermediate HBV endemicity zone**

**Number of HBV carriers estimated at 50 million**

**Genotypes A,D most common**

*Dutta et al, Virol J, 2008*



# Hepatitis C

**Affects approximately 1% of Indian population**

**12-13 million HCV carriers in India**

**HCV3 (3a/3b primarily) in 62%**

**HCV1 (1a/1b primarily) in 31% patients**

**Predominance of HCV3 significant in northern  
( $p=0.01$ ) and eastern ( $p=0.008$ ) regions**

**Types 2, 4, 5, and 6 were detected in 0.05-4.5%**

*Narahari et al, Infect Genet Evol. 2009*



# Chronic liver disease

<b>Hepatitis B</b>	<b>189</b>
<b>Cryptogenic</b>	<b>114</b>
<b>Hepatitis C</b>	<b>68</b>
<b>Wilson's</b>	<b>31</b>
<b>Choledocal cyst</b>	<b>26</b>
<b>AIH</b>	<b>18</b>



# Other diseases involving the liver



# Typhoid

**23-90% have mild to moderate hepatomegaly**

**1–16% are jaundiced**

**Hepatomegaly and jaundice resolve within 7–10 days**

**Transaminases resolve within 2–3 weeks**

**AST/LDH ratio < 9 helps distinguish from AVH**

*Kumar et al Indian J Pediatr 2007*  
*Jagdish et al Indian Pediatr 1994*



# Dengue

**Degree of liver injury varies from mild to FHF**

**Coagulopathy due to liver disease aggravates  
hemorrhagic manifestations**

*Nguyen et al Res Virol, 1997*  
*Mohan et al, J trop Pediatr, 2000*



# Dengue

**Transaminases may be elevated up to fivefold**

**Peak in the second week of illness**

**Gradual normalization by the third to fourth week**

**Hepatomegaly with tenderness**

**Jaundice is a less common symptom (15–62%) except in those with DHF or DSS**

*Nguyen et al Res Virol, 1997*

*Mohan et al, J trop Pediatr, 2000*



# Malaria

**Falciparum and vivax**

**Jaundice and hepatomegaly are more  
common in children (68%) vs adults (6%)**

**Jaundice usually unconjugated**

*Pooravaram, Ann Trop Pediatr, 2006*



# Tuberculosis

**Primary hepatobiliary TB**

**Disseminated TB**

**Congenital**

**Drug induced hepatotoxicity**

**4.28% in Western countries**

**11.5% in Indian studies**

*Consensus statement of IAP, 2008*



# Hepatobiliary ascariasis

**Highly endemic in Kashmir, central and south-west India**

**Enters the ampullary orifice from the duodenum**

**Less common in children**

**Acute cholecystitis, pancreatitis, cholangitis  
hepatic abscess**

*Zargar et al, Lancet 1990*



# Leptospirosis

**Western and southern parts of India**

**Liver disease is usually mild**

**Right upper quadrant pain, hepatomegaly,  
hyperbilirubinemia, modest elevation of  
transaminases**

**Jaundice appears by day 6, decreases by 3<sup>rd</sup>  
week**

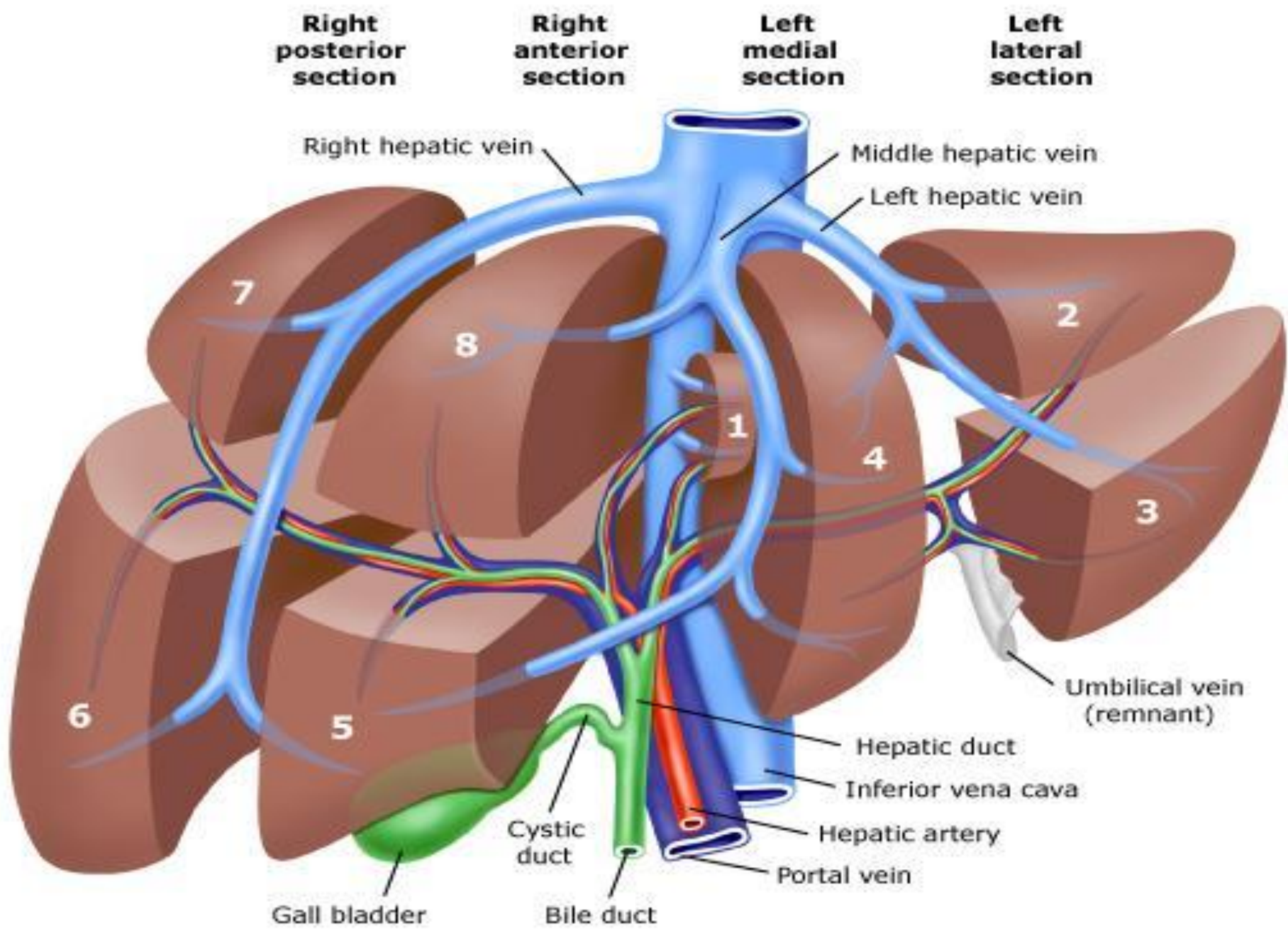
*Choudhari et al, Emerg Infect Dis. 2002*



# Miscellaneous - 489

<b>Enteric/Malaria/Multi/Dengue</b>	<b>204</b>
<b>Breast milk jaundice</b>	<b>52</b>
<b>Drug induced</b>	<b>51</b>
<b>EHPVO</b>	<b>33</b>
<b>Inf Cyst</b>	<b>30</b>
<b>Gilberts Syndrome</b>	<b>29</b>
<b>Glycogen Storage Disease</b>	<b>19</b>
<b>Crigler Najjar Syndrome</b>	<b>18</b>
<b>Granulomatous hepatitis</b>	<b>15</b>
<b>Hepatoblastoma</b>	<b>13</b>
<b>HCC</b>	<b>10</b>
<b>Hydatid cyst</b>	<b>7</b>
<b>Caroli's</b>	<b>6</b>
<b>Obstetric</b>	<b>1</b>
<b>Toxocara</b>	<b>1</b>





# Need

**Need for LT in 30% of children with liver diseases**

**Cirrhosis (45%)**

**Biliary atresia (38%)**

**FHF (11%)**

*Mehrotra et al Indian Pediatr 1999*



# Need

**2 per million  
2500 children**



# Need for liver transplantation

<b>Satisfying criteria</b>	<b>358</b>
<b>NCS</b>	<b>214</b>
<b>FHF</b>	<b>56</b>
<b>Cryptogenic</b>	<b>39</b>
<b>Wilson's</b>	<b>13</b>
<b>PFIC</b>	<b>13</b>
<b>Hepatoblastoma</b>	<b>6</b>
<b>Tyrosinemia</b>	<b>5</b>
<b>Crigler Najjar</b>	<b>5</b>
<b>HCC</b>	<b>3</b>
<b>BCS</b>	<b>3</b>
<b>Congenital hepatic fibrosis</b>	<b>1</b>



# Liver transplantation in India historical landmarks

<b>11<sup>th</sup> Jan. 1998</b>	<b>1<sup>st</sup> pediatric attempt (cadaver)</b>
<b>15<sup>th</sup> Nov. 1998</b>	<b>1<sup>st</sup> successful pediatric liver transplant</b>
<b>17<sup>th</sup> Nov. 1999</b>	<b>1<sup>st</sup> successful left LRLT (pediatric) for FHF</b>
<b>17<sup>th</sup> July 2002</b>	<b>1<sup>st</sup> successful LR re transplant</b>
<b>March 2007</b>	<b>1st combined living related liver and kidney transplant</b>
<b>16<sup>th</sup> Nov. 2007</b>	<b>1<sup>st</sup> pediatric cadaver transplant</b>
<b>12<sup>th</sup> Aug. 2008</b>	<b>Youngest liver transplant in India</b>
<b>2009</b>	<b>Youngest Domino Liver Transplant</b>



Institute	Total	Living related	Cadaveric
Apollo	63	57	4
SGRH	50	48	2
Mediciti	22	22	0
Bangalore	33	31	2
Global Hospital	30	21	9
Amrita Institute	20	-	-
Army R&R	13	-	-



# LT experience

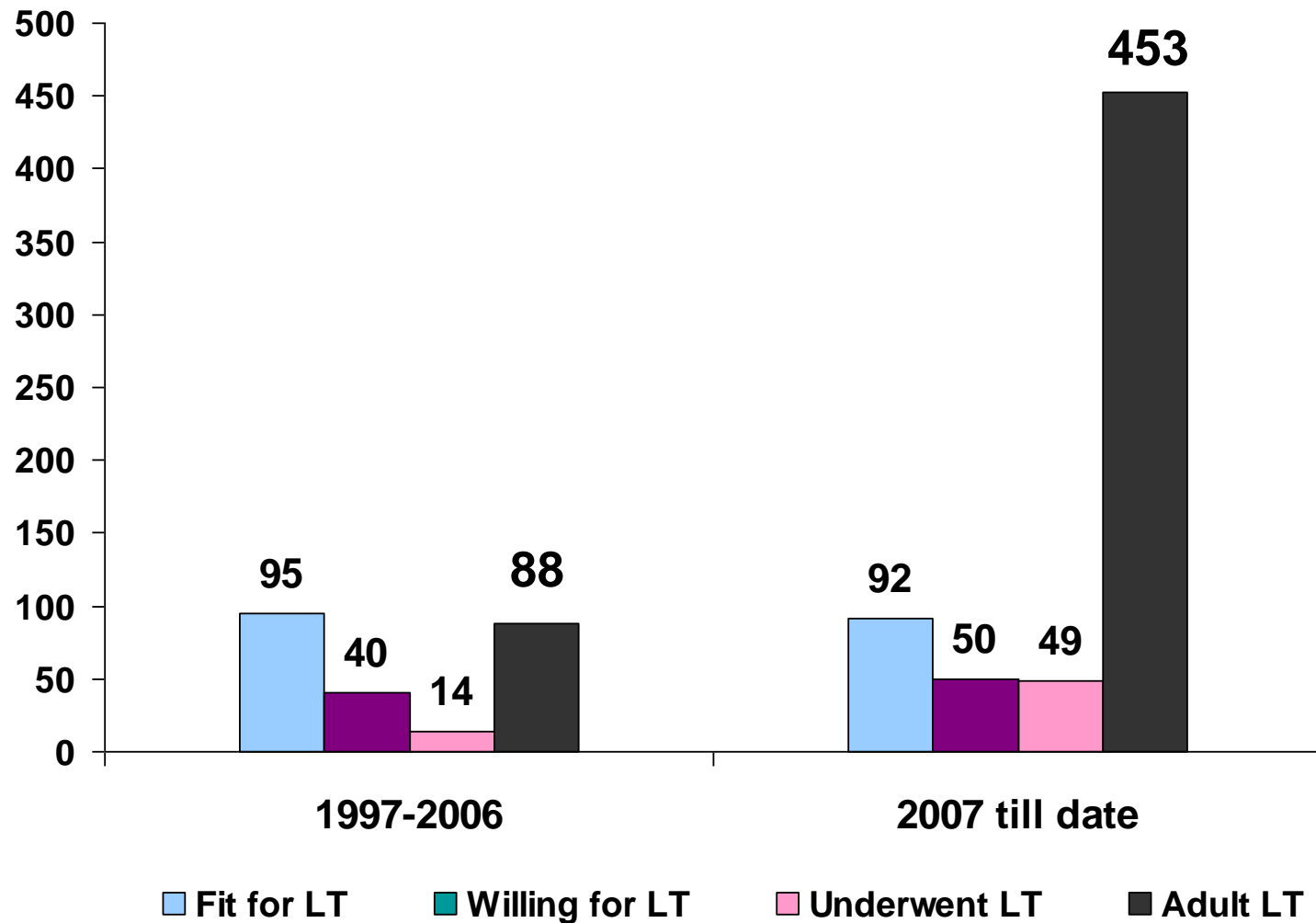
## n = 63

<b>BA</b>	<b>23</b>
<b>PFIC</b>	<b>7</b>
<b>Cryptogenic</b>	<b>7</b>
<b>FHF</b>	<b>7</b>
<b>Wilson's</b>	<b>3</b>
<b>BCS</b>	<b>3</b>
<b>Congenital hepatic fibrosis</b>	<b>3</b>
<b>NNH</b>	<b>2</b>
<b>Tyrosinemia</b>	<b>1</b>
<b>PVT</b>	<b>1*</b>
<b>Hep C</b>	<b>1</b>
<b>HCC</b>	<b>1</b>
<b>Crigler Najjar syndrome</b>	<b>1</b>
<b>Poisoning</b>	<b>1</b>
<b>AIH</b>	<b>1</b>

*\*One re transplant*



# The watershed



# What has contributed to success?

**Better intra and post operative monitoring**

**Improvements in intensive care**

**Standardized post transplant care**

**Fewer complications**

**Better immunosuppression**



# What has changed?

**Greater awareness**

**public**

**medical community**

**Improving outcomes**

**expanding indications**

**smaller babies**

**Greater acceptance**

**Cost has come down to £ 16000-20000**



# Building the bridge





Indraprastha Apollo  
HOSPITALS

Indraprastha Apollo  
HOSPITALS

Centre for  
Liver and Biliary Surgery

Centre for

Liver and Biliary Surgery

1776  
CORPORATE CHALLENGE

Centre for  
Liver and Biliary Surgery

17795  
CORPORATE CHALLENGE

17770  
CORPORATE CHALLENGE

17776  
CORPORATE CHALLENGE