

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

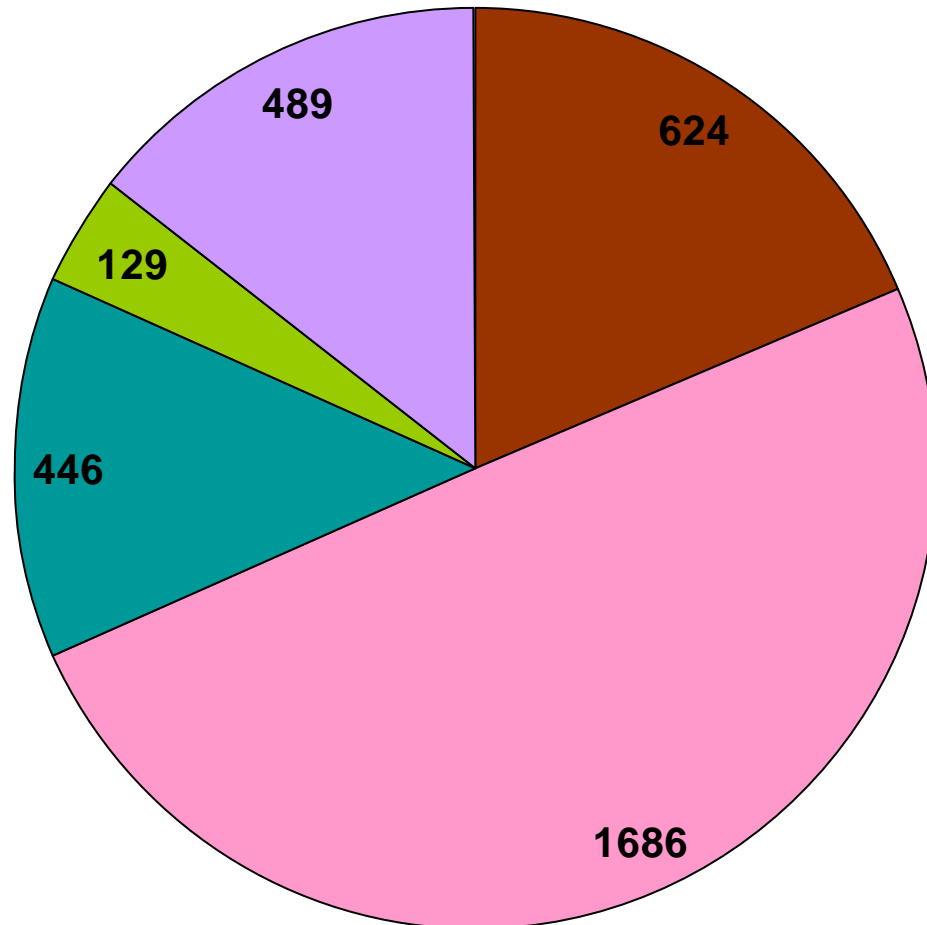
Dr Vidyut Bhatia
Pediatric Gastroenterologist and Hepatologist
Apollo Centre for Advanced Pediatrics
Indraprastha Apollo Hospital



Hepatobiliary referrals

1.10.97 – 30.06.2011

n = 3374



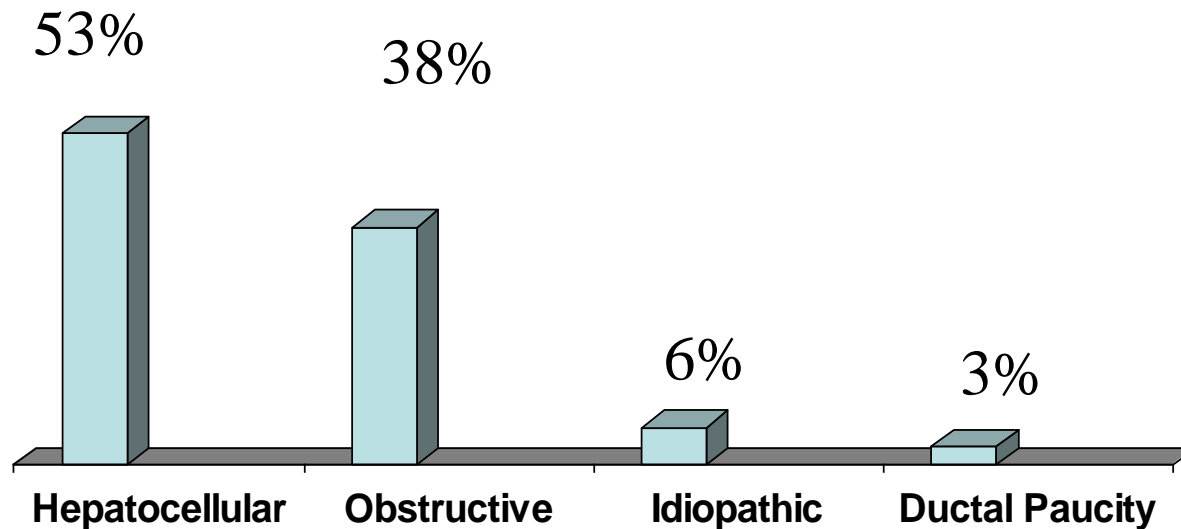
- Neonatal Cholestasis
- Acute Liver Disease
- Chronic Liver Disease
- Fulminant Hepatic Failure
- Miscellaneous



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

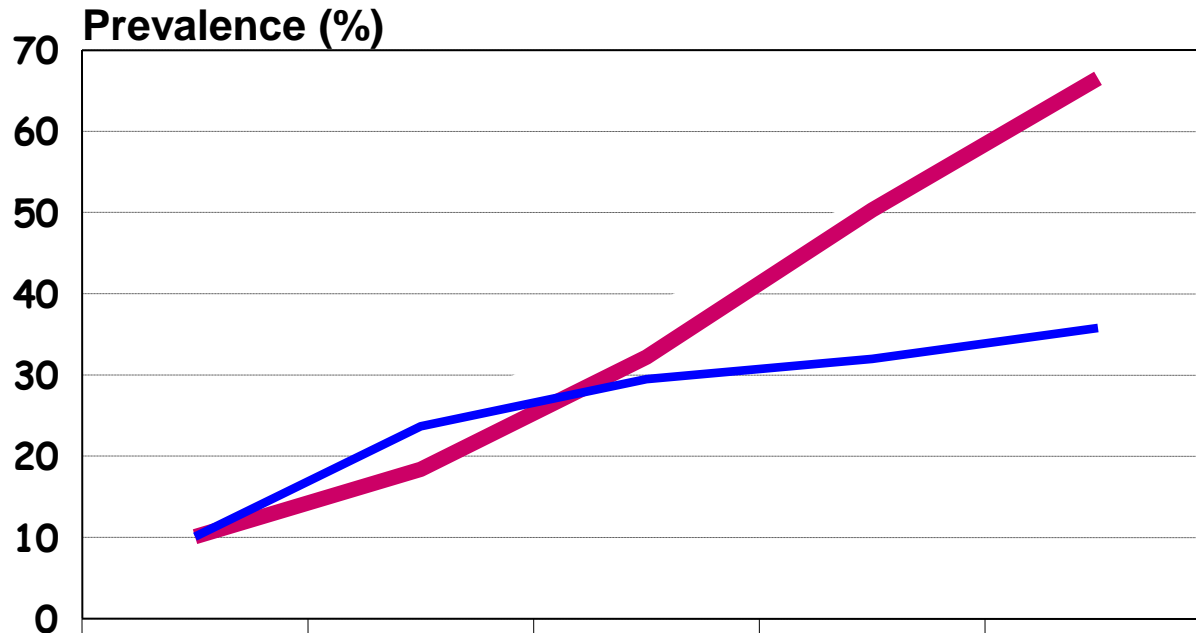
HEV constitutes an important cause for acute sporadic hepatitis and liver failure

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)



	6-24 mo	25-48 mo	49-72 mo	73-96 mo	97-120 mo
Observed prevalence	10.1	23.7	29.5	32	35.8
Projected prevalence	10.1	18.4	32.2	50.3	66.5

— Observed prevalence — Projected prevalence

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



Acute liver disease

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



Fulminant hepatic failure - 129

Hep A	61
Cryptogenic	41
Hep A and E	11
Hep A and B	6
Hep E	6
Hep B	3
Poisoning	1



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

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



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 3rd
week**

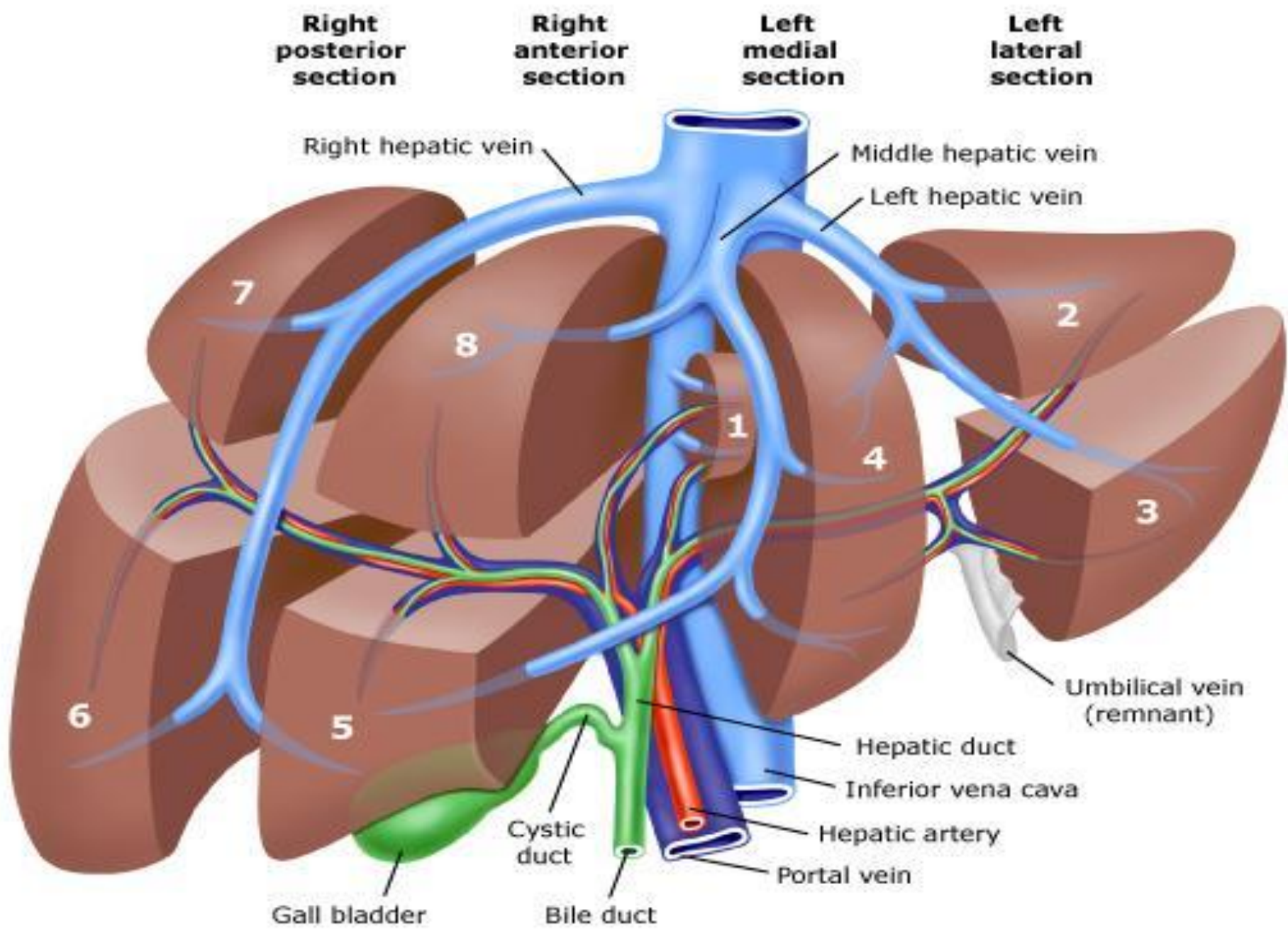
Choudhari et al, Emerg Infect Dis. 2002



Miscellaneous - 489

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





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

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



Liver transplantation in India historical landmarks

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



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

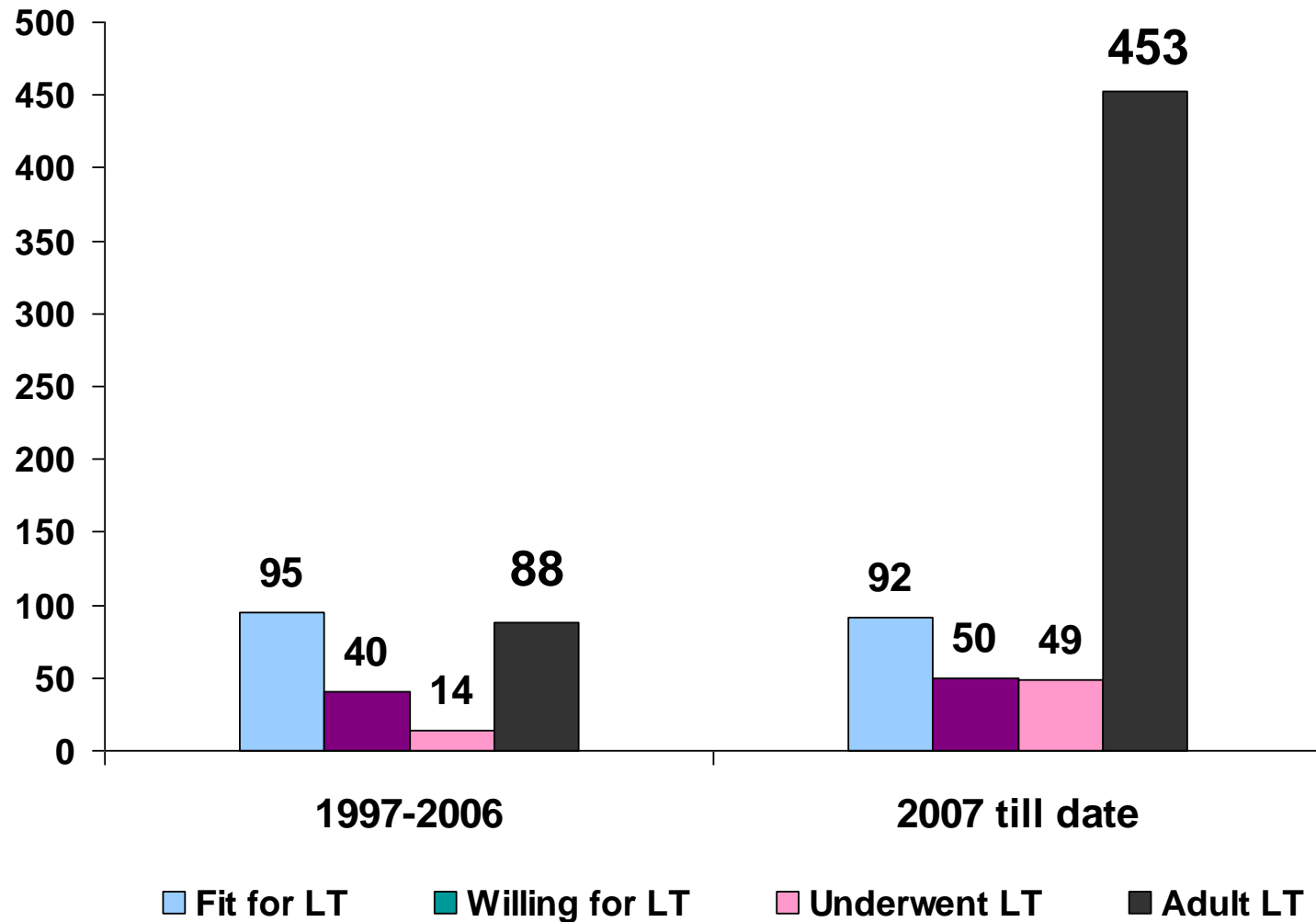
n = 63

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

**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

Centre for
Liver and Biliary Surgery

Indraprastha Apollo
HOSPITALS

Centre for
Liver and Biliary Surgery

1776
CORPORATE CHALLENGE

Centre for
Liver and Biliary Surgery

17795
CORPORATE CHALLENGE

17770
CORPORATE CHALLENGE

17776
CORPORATE CHALLENGE