

AFFORDABLE LIVER TRANSPLANTS CONCLAVE 2019

DATE: 2nd August

VENUE: THE LALIT HOTEL, MUMBAI

CONTEXT

In 2016, Mr. Pravin Agarwal embarked on the ambitious journey of developing India's paediatric liver transplant space with a vision that every child in need of a liver transplant should have access to one, irrespective of their socio-cultural-economic background. TPAF started as a funder for facilitating paediatric liver transplants and over the last three years has widened the scope and reach to become an ecosystem enabler for affordable liver transplants. Having enabled over 100 transplants, and still counting, TPAF is committed to making paediatric liver transplants more accessible and affordable.

Last year, the Affordable Liver Transplants Conclave underscored the importance of **creating a common platform** to share best practices, disseminate information on available sources of funding, and consolidate efforts made by various non-governmental organisations in this space. The discussion on the potential barriers to treatment brought out the challenges patients face, the reasons for clinicians' reluctance to referrals, and the lack of awareness among physicians and patients alike. Few people know that a liver transplant is now an affordable solution with a high success rate and good post-surgical outcomes. The power of collaboration was evidenced through the emergence of innovative solutions by the coming together of various stakeholders from different parts of the ecosystem.

Over the last year, TPAF has worked to address the challenges regarding the affordability and accessibility of paediatric liver transplants. To lower the cost of the transplant, TPAF partnered with super-specialty hospitals in cities across India to facilitate surgeries at a fixed cost. TPAF has collaborated with other funders like JEET Foundation, Tata Trusts and Mission Muskaan. The TPAF model leverages crowdfunding and has facilitated the collection of funds amounting to ~INR 8 Cr cumulatively. To raise awareness regarding the availability of funding for paediatric liver transplants among the medical fraternity, TPAF partnered at conferences for liver transplant surgeons, paediatric gastroenterologists and transplant coordinators. TPAF is now leveraging digital platforms to connect with various ecosystem players and reach more people through social media.

The theme for 'Affordable Liver Transplants Conclave 2019' was to make quality liver care available to all. To improve the outcomes of paediatric liver transplants we invited surgeons from across the world to share best practices, to prevent liver transplants we deliberated on methods of early detection and the prospect of leveraging technology for it, and to deepen the engagement we discussed ways to provide long-term support to children/families who have undergone liver transplant.

SUMMARY OF PANEL DISCUSSIONS

PANEL 1

Title: *Measuring the outcomes of paediatric liver transplant and setting the benchmark to international standards*

BACKGROUND

As an ecosystem influencer, TPAF is committed to facilitating dialogue among various teams involved in paediatric liver transplants and improving the outcomes of transplant surgeries. The one- and three- year survival rates of children who underwent paediatric liver transplants across six centres in the USA is 95.5% and 87.7% respectively. While few independent institutions and hospitals track their patients post transplants and claim good success rates, this data is not captured at the national level in India. The average self-reported success rate of 12,300 liver transplants performed across seven centres in India is 93%. The success rate of TPAF-supported transplants is ~90%. TPAF is synonymous with high-quality care and driven to raising the benchmarks of success and survival rates. In Panel 1 of ALTC 2019 four leading transplant surgeons with a cumulative experience of over 100 years across the world were invited to share their learnings along the journey. The discussion was aimed at identifying best practices and understanding good and achievable outcomes of liver transplants given the Indian context.

PANELISTS DETAIL

Panelists	Profile
Dr. Sonal Asthana (Moderator)	<i>Senior Consultant,</i> Department of Hepatobiliary Surgery and Multi-organ Transplantation, Aster CMI Hospital
Dr. Anil Dhawan (Voice conference)	<i>Director,</i> Paediatric Liver GI and Nutrition Center and MowatLabs King's College Hospital
Dr. Darius Mirza	<i>Transplant and HPB Surgeon,</i> Apollo Hospitals, Navi Mumbai <i>Professor of HPB and Transplant Surgery,</i> University Hospital Birmingham <i>Founder,</i> JEET Transplants

Dr. Naresh Shanmugum	<i>Paediatric Hepatologist, Gastroenterologist and Nutritionist,</i> Dr Rela's Institute and Medical Centre
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SUMMARY OF DISCUSSION POINTS

Defining success of a paediatric liver transplant

- Setting benchmarks for success of transplants is difficult since there is a lack of data transparency and while success is reported frequently, failures are not always reported. Some challenges of setting global benchmarks are
 - *Scant data availability:* Registry data collected is usually incomplete and only there is independently published units is available. Data from the available sources suggests that
 - 5-year survival in the UK is 90%
 - 5-year survival in France is 87%
 - 5-year survival in Switzerland is 91%
 - 5-year survival in Canada is 82%
 - US – 5-year data not available
 - *Discrepancies in available data:* There is vast variability in the definitions considered and hence non-uniformity in the data collected. For example, graft success is evaluated by liver enzymes while degrees of fibrosis are not captured. Besides this, the data is dated and across different time periods. Long-term data collected of patients 12-25 years after transplants between 1988-2014 shows that:
 - Mortality rate post liver transplant is 20%
 - Re-transplantation is required in 78% of the cases
 - And 53% suffer chronic rejection
- Focus should move from mere survival to ***meaningful survival*** where the patient is contributing to the society. There is a biological reason for cognitive development and a need to take care of patients when they are vulnerable.
 - Individual factors (disease and biology) are not alterable, and behaviour is alterable to an extent. Medical factors such as graft health, liver biochemistry, metabolic syndrome and renal dysfunction need to be addressed as do cognitive function, such as ensuring completion of the child's education
 - Social well-being (education and mental health) is important and a study indicated that 35% patients suffer mental health problems (depression) which affects their quality of life
- Paediatric transplant success has been over 90% in the UK and yet increasing marginally each year. Though it will never be 100, striving for improvement is important

Setting benchmarks for transplants in the Indian context

- The Indian transplant ecosystem is where the UK was 30 years ago but growing rapidly and there are few centres that are doing great work, with outcomes comparable to international standards. An estimated 250 children get liver transplants in India each year while the need is 2 per million per year. About 50% of the patients cannot afford the costs due to poverty and the gap is ~900 children, although the cost of transplants and medication is low in India
- **Stakeholders involved:** In the UK, the Government takes responsibility of the child (for eg, a health worker follows up with the parents if they miss a visit). In India, the child's survival depends on the parents' commitment to the child and the doctor's engagement with the child and family. The surgeon needs to take ownership of the child's survival years after transplant and patient can't make excuses or miss any consults
- **Education and training infrastructure:** In India, most surgeons are first generation (Indians who are trained abroad and return to India to practice) and it might take up to 10 years before we have home-grown surgeons
- **Availability of donors:** Since the rates of deceased donors is low rates. The UK has witnessed an increase cadaveric transplants due to a governmental push. Sensitisation and awareness are clear drivers to increase the number of transplants
 - Though the number is only ~70% of Spain's rate, number of transplants in the UK has gone from 2660 to 4039 while the waiting list has reduced from 8012 to 6044 between 2009-10 and 2017-18 and there is 81-85% utilisation of livers (retrieval from stage of identification)
 - Most are brain-dead donors since non-heart beating transplants require a huge amount of faith required in the system and doctors; India should aim at increasing brain-dead donors
 - UK had 1574 deceased organ donors in FY 17-18. Getting an estimated 4473 organ transplants from a population of 65 million highlights the potential funnel. Indian has 100x potential (accounting for affordability)
 - In the UK the time taken to assess the patient is long but wait for organ is ~ 1 month, especially fast for those with blood groups A&B
- **Cultural factors:** A transplant surgery places a significant financial burden on the families of over 50% of the children in need. In this scenario, a gender bias is observed towards providing surgery to the male child. Besides this, the seniors in the family get involved in the decision making and time is lost in convincing the family to opt for transplant
- **Compliance is an issue:** Post-transplant the family has to make significant lifestyle changes for the child, perform periodic tests and follow up with the doctors regularly. This is exhausting and there is no support in the post-transplant ecosystem.

Transplant is a disease, not a cure and time of transplant decides outcomes

- Post-transplant the patient needs life-long care: from lifestyle changes to medication. Moving from chelatic agents to immunosuppressants is no progression
- *Biliary atresia* - the survival rates are higher when patients are transplanted early

- *Wilson's disease* - the survival rates are higher for older children. Though this is relatively uncommon but comparatively high in some pockets of the world.
 - Over-transplantation of Wilson's disease among adults (especially between 19-29 years) is observed in some countries and surgeons need to be educated that data shows while survival is 100% for children, 1- and 5-year graft survival rates are 89.5 and 85.5% respectively and patient survival rates are only 94.7 and 90.1% respectively for adults
- *Acute Liver failure (ALF)* - The liver is the only organ in the body that can regenerate and there is scope for innovativeness here
 - A study conducted between 1988-2007 tracking 108 patients shows that the 1- and 5-year survival rates for transplants done due to ALF are 82% and 76% respectively
 - The underlying aetiology leads to differences in mortality and morbidity post-transplant in case of ALF
 - In case of idiopathic ALF, it is 30% while AIH is 4%
 - In children auxiliary transplant has a much higher success rate (90%), and is preferred over non-auxiliary transplant (success rate <70%) - *Auxiliary transplants have better outcomes and should be adapted in more centres*

Infrastructural requirements for institutions

- A successful transplant is a team effort and a multi-disciplinary team is required with various departments involved - surgical and nursing team, paediatricians and gastroenterologists, physical and occupational therapists, dieticians and nutritional experts
- Every member must be adequately trained and experience and expertise must be considered
- Aim for benchmarks set by already established programs with tweaks for the India context
- Audit data since it is important to learn from mistakes and shortcomings to improve long-term meaningful survival

PROPOSED SOLUTIONS

- **Building the pre- and post-transplant care network**
 - A multidisciplinary approach needs to be taken for paediatric liver transplants with involvement and shared responsibility of several teams pre and post-transplant
 - Children in India are undernourished, and a transplant is a significant health risk; improving the nutritional status and vaccinating children will help cut the costs and improve outcomes of transplants by minimising hospital stay and reducing mortality and morbidity
 - Training of paediatricians in small cities and rural India to diagnose patients and for day-to-day care post transplants (needn't handle immunosuppressants) is important
 - Hub-and-spoke model with larger / private hospitals supporting smaller / public hospitals should be explored; a mentor-mentee arrangement will work well
- **Raising awareness and increasing deceased donor transplants**

- There is need for uniformity in the data collected and transparency in information shared to develop trust between the funders, care providers and community; building the transplant database will enable more transplants
- The trust-deficit between the community and clinicians prevents transplants; constant communication in the community through various media channels to raise awareness is important
- There is scope for increasing the number of organ donors through cultural sensitisation and raising awareness
- Creation of a national database of donors is important. In India, individual hospitals feel the “donor” is theirs; it belongs to the state
- **Innovating to facilitate more transplants**
 - There is scope for *surgical innovation* through split living donor transplants. This started in the EU the 1990s and a triple split is done successfully in several centres in the UK now
 - There is a learning curve in the three-split and outcomes are not good in the 0-20 range. A significant hike in the success rate is seen post 20-splits
 - Hepatocyte transplants in alginate beads for ALF attempted in March 2011 which showed 50% native liver survival and liver transplant avoidance
 - Paediatric liver transplants have excellent outcomes, but the skills are not easy. Few centres can manage the complexity, and, in the UK, it is consolidated within three centres only

SUMMARY OF PANEL DISCUSSIONS

PANEL 2

Title: *Early detection and prevention of Paediatric Liver Transplants: to reach children in need sooner along the patient journey*

BACKGROUND

Over the last year, The Pravin Agarwal Foundation had the privilege to interact with various doctors - paediatricians, gastroenterologists and paediatric hepatologists. Through these interactions and our analysis, we learnt that the incidence of Biliary Atresia (amounting to 64% as the cause for paediatric liver transplant) is close to 1 in 8000 live births in India. Keeping in mind that only about 250 children undergo a liver transplant every year, it is fair to assume that majority of the Biliary Atresia cases go undetected. The Foundation aims to collaborate with doctors, grassroots healthcare NGOs and healthcare technology companies to enable the early detection and prevention of chronic liver diseases like Biliary Atresia, Metabolic Liver Diseases and Acute Liver Failure at scale. Through this discussion, TPAF intended to get a better understanding of piloting a feasible intervention to reach children in need of liver transplants sooner along the patient journey.

PANELISTS DETAIL

Panelists	Profile
Dr. Sanjay Rao (Moderator)	<i>Senior Consultant and Head, Department of Paediatric Surgery, Narayana Health</i>
Dr. Shailendra Hegde	<i>Head-Clinical Services, Piramal Swasthya</i>
Mr. Reuben Fernandes	<i>Team lead, Atom360</i>
Dr. Priya Ramachandran	<i>Consultant - Paediatric Surgery, Dr. Rela's Institute and Medical Centre Founder, Ray of light foundation</i>
Dr. Aabha Nagral	<i>Consultant Gastroenterologist and Hepatologist, Apollo Hospitals, Navi Mumbai Vice-President, Maharashtra Chapter of the Indian Society of Gastroenterology (ISG)</i>
Dr. Sharat Verma	<i>Consultant - Paediatric Hepatologist, Gastroenterology & Liver Transplantation, Max Healthcare</i>

SUMMARY OF DISCUSSION POINTS

Paediatric Liver Transplant is the endpoint intervention for irreversible liver failure. The means to enable early detection and prevention of paediatric liver transplants is through developing preventive measures that reduce the risk from diseases like Biliary Atresia, Metabolic Liver Diseases and Acute Liver Failures which cause end-stage liver disease.

Biliary Atresia (BA):

- BA is a curable condition if detected in time and treated by the appropriate doctor. It is a myth that BA is diagnosed by doctors. In reality, the mother plays (or should play) a key role in diagnosing the disease
- If BA is diagnosed between the first three months of the child being born, the Kasai procedure can treat 80-90% cases
- The cadre of frontline healthcare workers including ASHA/ANMs/AWW are in constant interactions with children. Building their capability for the early detection of BA through the stool-chart and prolonged jaundice will enable appropriate and timely referrals

- Hospitals empanelled under the *Ayushman Bharat* scheme will have 'Ayushman Mitra', a person recruited to coordinate with the beneficiaries of the scheme and provide assistance to patients. Training the *Ayushman Mitras* to detect alarming stool will enable early detection and outreach in city-slums
- Technology-based algorithms have started outrunning humans indicating that with the usage of Artificial Intelligence, it is possible to execute a scalable solution to implement the stool chart

Metabolic Liver Diseases:

- Metabolic liver diseases include Wilson's Disease, Crigler-Najjar syndrome, Dubin-Johnson syndrome, Gilbert's disease and Hemochromatosis
- Majority of metabolic liver diseases are also rare diseases which are genetic and without a diagnosis, families lose more than one child to the same disease
- Almost 10% of the 60% institutional deliveries are conducted through ANMs making access to new-born screening for metabolic diseases limited along with the high costs associated with it
- The state governments of Delhi and Goa had made significant attempts in the past to adopt new-born screening within its public health policy but unfortunately, the intervention has not received adequate funding. It is debated that there is a need to shift the mindset of the policymakers to incorporate the mandate of new-born screening under *Rashtriya Bal Swasthya Karyakram* (RBSK) with the help of Natural Rural Health Mission (NRHM)
- India has a lot to learn from the USA as they have mandatory new-born screening for over 30 diseases

Acute Liver Failure - Immunisation

- Majority states in India have implemented pentavalent immunisation which includes screening for Hepatitis A and B
- Charting the patient journey post the detection of Hepatitis A and B is a challenge due to the lack of access to specialist doctors in remote regions
- A cost-benefit analysis of the impact of immunisation will make the need for stricter implementation of universal immunisation evident to healthcare policymakers to ensure

PROPOSED SOLUTIONS

- **Entrusting and empowering the child's biggest warrior - the Mother!**
 - Screening through stool charts is an effective means for the early detection of Biliary Atresia. For this, it is proposed that the **stool chart should be incorporated at the back of Mother-Child Protection Cards** which are issued by the government
 - **Training mothers and frontline healthcare workers** at the village level and Ayush Mitras at the city level to detect alarming stools using the stool chart will bring the child one step closer along the patient journey.

- **Tele-medicine** may be leveraged for conducting the training along with a mass social media campaign to sensitise the patient community and the general public
- **Improving patient access to care:**
 - A **patient helpline** to counsel the patients before and after the new-born screening will reduce the patient disappearances along the patient journey
 - Awareness generation regarding government schemes aiding paediatric liver transplants through a mobile application
- **Collaborations and advocacy:**
 - Public-Private Partnership in various parts of the country wherein corporate doctors perform paediatric liver transplants in government facilities to build the capability of that facility by training residents and building its capability to manage post-transplantation care
 - There is a need for pushing advocacy movements that ensure that the mandate of treating rare diseases is taken up by the government through the allocation of an appropriate budget for the same

SUMMARY OF PANEL DISCUSSIONS

PANEL 3

Title: Provision of long-term support to children who have undergone paediatric liver transplants

BACKGROUND

For a paediatric liver transplant to be sustainable, the child needs a lifetime of medical care including access to immunosuppressants, follow-ups with the doctor and a hygienic environment. For this, it is important that the caregivers of the children who have undergone a liver transplant are aware regarding the latest developments in the ecosystem with respect to patient support organisations, government policy and financial aid, to ensure that they are able to provide the best in class care to their children. In order to provide holistic support to its beneficiaries, TPAF aims to bring together experts from patient support groups, funding organisations and doctors to brainstorm various avenues of collaboration for post-operative care.

PANELISTS DETAIL

Panelists	Profile
Srikrishna Shridhar Murthy	<i>CEO, Sattva Consulting</i>
Dr. Neelam Mohan	<i>Paediatric Gastroenterologist, Medanta The Medicity, Gurugram</i>

Sunayana Arora Singh	<i>Co-founder,</i> ORGAN (Organ Receiving & Giving Awareness Network) India
Prasanna Kumar Shirol	<i>Co-founder and Director,</i> Organization for Rare Diseases in India
Dr. Lalit Verma	<i>Paediatric Gastroenterologist,</i> Wockhardt Hospitals, Mumbai
Anoj Viswanathan	<i>Co-founder and President,</i> Milaap

SUMMARY OF DISCUSSION POINTS

There is a need to create a system for the management of post-transplant care for children. With advancements in medicine over the years, the medical fraternity has learnt the appropriate dosage of immunosuppressants; however, there is a need to look at the provision of the same in the long-term. Collaboration through communication between liver transplant teams across different hospitals is necessary to secure bulk deals for medicines and ensure that maximum children are able to procure the medicines at a cheaper rate. Post-transplant care is not merely for the patients but is also applicable to the parents/caregivers of children who have undergone a liver transplant as they facilitate the environment which enables speedy and sustainable recovery.

Post-Transplant Care

- Doctors are primarily concerned about discharging the patient within the first month of the transplant as this is the period wherein the maximum number of complications (*details below*) arise:
 - **Vascular complication** rate post paediatric liver transplant is close to 5-10% for expert transplant centres
 - **Metabolic issues** - cholesterol, fatty liver, thyroid
 - **Post-transplant lymphoproliferative disorder (PTLD)**
 - **Chronic rejection** as compared to a kidney transplant is relatively less. New research for protocol liver biopsy is in process
- Once the patient is discharged, one looks at the provision and management of immunosuppressants. With advancements in medicine over the years, the medical fraternity

has learnt the appropriate dosage of immunosuppressants; however, there is a need to look at the provision of the same in the long-term

- Data suggests that the two-, three- and four-year survival rate for children who have undergone a liver transplant is 95%, 93% and 92% respectively
- A system to ensure that there is **complete communication and commitment** between the patients, their caregivers and the transplant team is required for the successful management of the transplant
- All **transplant centres to work as a team**. Patients should have the liberty to follow-up with doctors at transplant centres across the country irrespective of where they underwent the transplant as this would **increase their accessibility to post-operative care**
- The **willingness to live** plays a crucial role in a transplant patient's recovery. This willingness can be **strengthened through the provision of emotional support** through patient support groups
- Measuring the success of the paediatric liver transplant through the World Health Organisation's definition of health - 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.' Hence, to measure the quality of life of children who have undergone a liver transplant, the following indicators should be used:
 - Physical health
 - Social well-being, life skills
 - Emotional well-being

Peer Support Groups

- **Strength of the family and the mindset of the patient** are the key levers for ensuring the success of the paediatric liver transplant
 - Family plays an important role for undertaking the liver transplantation journey for the child. During the course of this journey, **caregivers have numerous queries** and every **query cannot be discussed with the medical fraternity**
 - It is the family that is exhausted and collapses throughout the transplant journey. Therefore, it is required for organisations to look at providing emotional support to the caregivers by connecting them with their peers who have undergone a similar experience
 - Support is available for the transplant surgery itself. However, few organisations are supporting pre and post-operative care as a significant amount is required for pre-transplant diagnosis as well as post-transplant
 - When information is shared through a planned communication system, it transforms informal information into formal information
- A few initiatives to support rare disease patients in the long-term:
 - A helpline number for instant resolution of doubts along the patient journey
 - Long-term rehabilitation centre providing a conducive environment for recovery
 - *Rashtriya Arogya Nidhi* provides funding for liver transplants but limited to Below Poverty Line (BPL) families. Contribution at the policy level in terms of recommendations is necessary to increase the access to government funding

Funding support

- Since the time healthcare crowdfunding gained momentum in late 2014, over 1000 people have raised money for patients out of which 60% were children
- There is a strong difference between the funds collected through crowdfunding for paediatric liver and adult liver transplants as campaigns for children tend to raise 45% of the target amount which is much higher than the funds raised for adults. For TPAF supported cases, this the quantum of funds collected nearly doubles to ~87%
- There is a clear intent from donors across the world to support PLT
- PLT has the highest chances of meeting desired funding and acceptance amongst the donors as the symptoms are visible and the outcome of the surgery is noticeable in a relatively shorter timeframe as compared to other ailments like bone-marrow transplant and cancer
- The average contribution is ~1500 and more than 500 donors contribute towards a child's donors.
- Data generated by Milaap suggests that about 70% of the children who underwent liver transplant go back to school within one year

PROPOSED SOLUTIONS

- **Capability building of doctors:** Paediatricians to be trained for the micro-management of infections
- **Capability building of caregivers/parents:** It is essential to build the capacity of the caregiver's family through awareness generation and connecting them with others who are going through a similar phase in their life. Today, these conversations are happening on an ad-hoc basis and there is a pressing need to formalise them through the following interventions:
 - Creating collaterals in regional languages which contains all information regarding different aspects of the patient journey of a paediatric liver transplant. This collateral may be deployed through the patient support networks
 - **Impact stories of donor and recipients** of transplants through mainstream media like **radio shows** to be shared to reduce the apprehension for undergoing a liver transplant amongst the patient community
 - **Helpline number** to provide access to information regarding the various aspects of the transplant
- Creation of **nodal patient networks through peer support groups** at the hospital and city level to share success stories and seek medical and non-medical support through their peers and ecosystem enablers. Peer support group to have different verticals namely:
 - Medical support
 - Boarding and lodging support - rehabilitation homes
 - Socio-emotional support
 - Financial aid - *advisable to keep financial support separate*
- **Improving the nature of funding support**

- **Cost of the entire transplant to be explicitly stated.** In some states, an aspect of the post-transplant care is subsidised by the government or the hospital. Data suggests that the **propensity for donors to contribute for another campaign for the same child is less.** Hence, the campaign organiser should **raise what is absolutely required in one go**
- There should be a **periodic patient follow-up and update policy** as donors compel crowdfunding organisations for updates
- Bringing **different types of capital** from corporations and foundations to facilitate scholarships for children for their **educational needs**