Outcome of Organic Acidemia in Indian Children.

Dr. Anil B. Jalan[1],Nutan Telawane[1],Rupali Shinde[2], Dr. Debjani Dasgupta[2], Dr. Adolf Muehl [3]

1- NIRMAN, Navi Mumbai Institute of Research in Mental and Neurological Handicap, India. 2- The Institute of Science, Dept. of Biochemistry, Mumbai, India. *3-Biochemical Genetics and Newborn Screening Laboratories, University Children's Hospital, Vienna, Austria*

Introduction: - With a population of over 1 billion and annual birth rate of about 28 million babies, the number of children born with Inborn error of Metabolism is expected to be quite high. In absence of any formal newborn screening it is impossible to even guess the number of actual babies born alive with any IEM. As regards Organic Acidemia M. Muranjan et.al. has shown an incidence of 32 out of 231 children (13%) with Organic Acidemia and overall mortality of 9.3 %. In our view this appears to be very low. In actual practice we see much higher rate of mortality and morbidity in India. Also this data does not provide any clue to the Organic Acidemias with universally bad outcome v/s those with better outcome.

Objective: - was to assess the relative incidence of Organic Acidemias amongst all children referred for study of Inborn Error of Metabolism, including sick newborns. Also we planned to study the overall mortality and neurological morbidity. We also wished to identify disorders with uniformly bad outcome against those with much better outcome. Since the awareness amongst Indian Pediatricians and General practitioners regarding IEMs is quite limited, we intend to identify few common Organic Acidemias and their outcome in general, so that they can discuss with parents regarding the possible outcome and need for urgent and proper treatment.

Subjects and method: We selected 1,844 children from Jan. 2000 to 31st March 2007 referred for diagnostic workup of IEM. Of these we had 88 children with Organic Acidemias. This number is not representative of true incidence of any IEM in India, as these were all referred cases, so there was a selection bias from the Pediatrician's side and also selection bias for sex (male children more often investigated properly than female children) and socio-economic condition (affluent class opting for detailed investigations and proper treatment than those from poorer section of the community). However it does provide an opportunity to understand relative incidence of some IEMs and also the natural course, as most of these disorders are investigated only after symptoms appear and almost always the treatment is delayed due to late investigations and poor availability of special diets and medicines needed to treat such conditions. All these children received basic metabolic screen like Ammonia, Lactate, Blood Sugar level, ABG, Electrolytes and anion gap, TMS of blood for Carnitine/Acyl carnitine profile, Urine GC-MS for Organic Acids, Biotinidase enzyme assay by colorimetry and Urine Orotic acid by HPLC. Some of the children, especially those with MSUD and GA Type I also were subjected to Neuroimaging by MRI and MRS. Diagnosis was made based on the biochemical profile along with clinical picture. No DNA based diagnosis was performed as those are not available in India and exporting DNA outside is not an economical option for most of the Indian patients.

Results :-	N=88	CNS Aff.	Expi-red	Normal CNS
Overall	**88**	**38 43.2 %**	**33 37.5 %**	**17 19.3 %**
MMA	13	7	3	3
PA	11	5	6	0
GA Type I	10	10	0	0
F.D.Pase def.	9	0	3	6
Biotinidase def.	8	1	2	5
MSUD	7	0	7	0
GA Type II	7	0	7	0
IVA	6	3	2	1
β Ketothiolase def	5	4	0	1
3 Methyl Gluta-conic Aciduria	4	3	0	1
Multiple Carboxylase def.	2	0	2	0
SSADH	2	2	0	0
HMG Co A Lyase def.	2	1	1	0
2 Ethyl Hydra-crylic Aciduria	1	1	0	0
Canavan's Dis.	1	1	0	0

Discussion:- As it is very clear from the above results, the out come of MSUD and GA type II is uniformly bad with 100 % mortality in Indian situation. Where as GA Type I has 100 % neurological affection. However disorders like Biotinidase deficiency, FDPase deficiency has relatively better prognosis. Relative incidence MMA and PA is quite high in India, and outcome is not very satisfactory with very high mortality and morbidity. Only some forms of MMA (especially those B12 responsive) have better outcome. In our study overall mortality was 37.5 % (33/88) which is much higher than those reported by other workers from India. This might be due to inclusion of all very sick newborns referred for IEM workup as our Centre specializes in diagnosis and management of Critically ill newborns.

Conclusion: - Organic Acidemias are common in Indian children. Unfortunately they are detected late, only after the symptoms have appeared. Most of the times, diagnostic facilities are not available immediately and cost of special diets and medicine is beyond reach of most of the Indian patients. In such a situation the mortality is unacceptably high and those who survive have high rate of neurological affection and other complication.

References: -

1. M.Muranjan, Clinical Features of Organic Acidemias; experience at tertiary Care Centre in Mumbai, Indian Paediatrics 2001: 38: 518 – 524.