# Tyrosinemia Type I: Clinical, Biochemical and Molecular Profile of Indian Patients.

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**Introduction: Tyrosinemia Type I (OMIM # 276700) also known as Hepato-renal Tyrosinemia. It is an autosomal recessive inborn error of metabolism, involving defect in FAH Gene (gene locus 15q23-25), resulting in deficiency of an enzyme "Fumaryl Acetoacetate Hydrolase". This results in accumulation of Tyrosine and Succinyl acetone in tissues.**

**Objective: - To determine clinical-biochemical and molecular profile and usefulness of NTBC in Indian children with Tyrosinemia Type I [HT1]**

**Subjects and method: In this paper we report experience during the period 2000-2006. 22 patients clinically suspected to have HT1, on the basis of hepatomegaly, jaundice and cirrhosis were studied. Of these 5 patients were confirmed to have HT1. Of these 5 children, 3 received NTBC treatment. The fifth patient [ LS ] was referred to us when he was already being treated with diet & NTBC on suspicion of HT1.**

**Results: - 5 Children were confirmed to have HT1, of these - 2 babies presenting before 3 months expired soon after diagnosis and NTBC could not be started. The remaining 3 children received NTBC and Tyrosine restricted diet and are clinically and biochemically better. At the time of presentation mean biochemical parameters were as follows – Pl. SA - 24.05, Pl. Tyrosine 700, Pl. Phe, 198, Pl. Methionine, 250.5 (all µm/L), Urine SA 335.25 (mmol/mol Creatinine) and AFP 153950. All 3-surviving children have shown reduction in AFP, SA, Tyr and Phe levels. Of the two expired children one showed IVS8-1g ->c/IVS8-1g ->c and other one has Q64H/Q64H mutation. Of the 3-surviving children, 2 are Q64H homozygote and in 1 no known mutation could be identified. However one child homozygous for Q64H presented at 1-month age expired within next month. Other two children showed late onset and good response to NTBC. One child showed irritability and hyperactivity probably that was NTBC induced, as dose reduction (from1 mgm/kg to 0.75 mgm/kg) led to disappearance of these symptoms.**

| No | | Age | Sex | PBG Syn. | Pl. SA | AFP | Pl. Tyr. | Pl. Phe. | Pl. Meth. | Ur. SA | Ur. SAA |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | S R | 3 M | F | 0.01 | 3.2 | 40400 | 428 | 163 | 32 | 71 | <1 |
| 2 | Y P | 3 Yrs | M | 0.02 | 38 | 9450 | 537 | 138 | 66 | 350 | 45 |
| 3 | M P | 40 D | M | 0.01 | 17 | 412000 | 970 | 221 | 469 | 330 | <1 |
| 4 | E P | 8 M | F | 0.01 | 38 | NA | 863 | 271 | 435 | 590 | 25 |
| 5 | L S | 8 Yrs | M | 0.58 | 0.14 | 5 | 965 | 175 | 43 | <1 | <1 |
| | Mean | | | | 24.05 | 153950 | 700 | 198 | 250.5 | 335.25 | |

| No | | Age | Sex | Mutation Analysis | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 1 | S R | 3 M | F | IVS8-1g ->c/IVS8-1g ->c | No Treatment | Expired |
| 2 | Y P | 3 Yrs | M | No Mutation Identified | Diet + NTBC [ Receives NTBC in the dose of 0.75 mgm / kg / day ] | Better |
| 3 | M P | 40 D | M | Q64H/Q64H | No Treatment | Expired |
| 4 | E P | 8 M | F | Q64H/Q64H | Diet + NTBC [ Receives NTBC in the dose of 1 mgm / kg / day ] | Better |
| 5 | L S | 8 Yrs | M | Q64H/Q64H | Diet + NTBC [ Receives NTBC in the dose of 1 mgm / kg / day ] | Better |

**Conclusion: - HT1 is common in India and Q64H is the commonest allele (6/10). Late onset HT1 has better prognosis. NTBC though costly, is very effective in treatment with good tolerance in the dose range of 0.75 – 1.0 mgm/kg/day. Only side effect observed so far is irritability in one child, which was does dependant.**

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