Introduction
Congenital hyperinsulinism (CHI) is the commonest cause of intractable hypoglycaemia in neonates and infants. Hyperinsulinemic hypoglycaemia occurs due to unregulated insulin secretion from β-cells of pancreas in relation to blood glucose levels.

Aim
- To describe clinical profile, molecular characterization, response to therapy and short term outcome in CHI.

Materials and methods
- Records of 27(15 F) children diagnosed with hyperinsulinism in last 10 years were studied.
- Clinical, hormonal and mutation details were analyzed in DR (Diazoxide Responsive) and DU (Diazoxide Unresponsive) group.
- Syndromic and transient cases were excluded.

PATIENT CHARACTERISTICS (n=27)

<table>
<thead>
<tr>
<th>Females (n) (%)</th>
<th>15 (55)</th>
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<tbody>
<tr>
<td>Mean Gestational age, weeks</td>
<td>37.3±0.99 (36-40)</td>
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<td>Mean Birth Weight, grams</td>
<td>3240±695 (1500-4600)</td>
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<td>Median Age of onset, days</td>
<td>3 (1-240)</td>
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<td>Diagnosed in neonatal period, (n) (%)</td>
<td>20 (74)</td>
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<td>Large for gestational age, (n) (%)</td>
<td>9 (33.3)</td>
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<td>Consanguinity (%)</td>
<td>8 (29.6)</td>
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<td>Mean of maximum GDR (mg/kg/min)</td>
<td>12.6±4.81</td>
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<td>Mean Blood Glucose at diagnosis (mg/dl)</td>
<td>30±11.5</td>
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<td>Mean Serum Insulin at diagnosis (mIU/ml) (range)</td>
<td>26.57 (3.6 - 300)</td>
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MOLECULAR CHARACTERIZATION* (ABCC8 & KCNJ11)

- 14/27
- 7/8 (87.5%) in DU
- 3/6 (50%) in DR

- 9 in ABCC8 gene, 1 in KCNJ11 gene
- 2 novel mutations – one in each ABCC8(p.V1361L) and KCNJ11(p.C142Y) gene.
- 1-de novo mutation
- 2 mutation positive children were infant of diabetic mother
- 3 mutations were paternally inherited
- 3 – AD inheritance, all in DR group
- 6 were heterozygous, 4 were homozygous mutations
- 2 children had atypical features (one with MIMD(Empty sella syndrome) and one with dystonia and late onset hyperinsulinism) – but were mutation negative

TREATMENT RESPONSE

- N = 27
- Diazoxide
  - Responsive (DR) 16
  - Unresponsive (DU) 11

- Octreotide (7)
  - (Mean Octreotide dose 21.6±6.3ug/kg/day)
  - Discharged & Follow up
    - Octreotide (5)
      - LAR (6)
      - Expired (1)
    - S.C. Octreotide (1)
      - Expired (1)
  - Near total pancreatectomy (4)
  - LAR (1)
  - Expired (1)

- Lost to follow up (2)

CHILDREN ON LONG ACTING OCTREOTIDE (LAR)

- Mean duration of follow up – 12.25 months (6-24)
- Mean age at starting LAR - 8.38 months (1-33)
- Mean age at last follow up – 18.37 months (6-47)
- Mean dose of LAR at last follow up – 21.52 ± 5.2 ug/kg/day
- Daily Octreotide stopped on 2nd dose of LAR
- Mean Height SDS at last follow up – -0.9±1.92
- Although 2 children had low IGF 1 level on follow up, all had normal growth velocity

Side effects
- Gall bladder pathology (5/8) – had stones, 2 had sludge
- On Ursodeoxycholic acid, 40% reduction in size of gallstones seen on follow up
- No significant differences in dose of LAR in patients with (23.40 ±4.15ug/kg/day) or without (18.40 ± 7.14ug/kg/day) GB pathology (p=0.35)
- Deranged liver functions with severe bacterial sepsis (1/8)

OUTCOME

- 33.3% (9/27) had normal milestones
- 59.2% (16/27) had delayed milestones with/without neurosensory affection
- 7.4% (2/27) expired

CONCLUSION
ABCC8 mutation was the commonest mutation found in our cohort.
40% of our children did not respond to Diazoxide of which 36% underwent near total pancreatectomy.
In all Diazoxide Unresponsive patients LAR was useful to maintain euglycemia.
Long term studies are required to emphasize the safety profile of LAR.

Reference

Conflict of interest : None