

Factitious administration of analogue insulin to a 2 year old child

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Introduction:

Hypoglycemia precipitated by factitious insulin administration in a Type 1 diabetic presents a unique diagnostic challenge, in that it has to be distinguished from other forms of hypoglycaemia such as by hyperinsulinism, insulinoma, insulin sensitivity and beta cell recovery "honeymooning". Diagnosis is based on circumstantial evidence, keen clinical observation and biochemical tests.

We present a case of recurrent hypoglycemia in a 2 year old child. Despite the best efforts, she was noted to have significant hypoglycemia, as depicted below.

Case Report:

2-year old girl presented to the hospital with 2 weeks symptoms of weight loss, polydipsia and polyuria.

First admission:

- At diagnosis, commenced on subcutaneous insulin injections.
- Family received primary education and achieved the competencies for self-management of diabetes
- Discharged and then received contact as per protocol; and subsequently received over and above standard contact (telephone and clinic).

Second admission Day 109 post-diagnosis:

- Admitted with low blood glucose of 3 mmol/L.
- Intravenous glucose infusion required to establish normoglycaemia.
- Extensive re-education of her parents completed to ensure they had appropriate knowledge and awareness for treatment of acute onset hypoglycaemia.

Third admission Day 115 post-diagnosis:

- Re-admitted with low blood glucose level of 1.5 mmol/L.
- Poor response to standard hypoglycemia management necessitating intravenous glucose to maintain normoglycaemia.
- Discharged the following day.

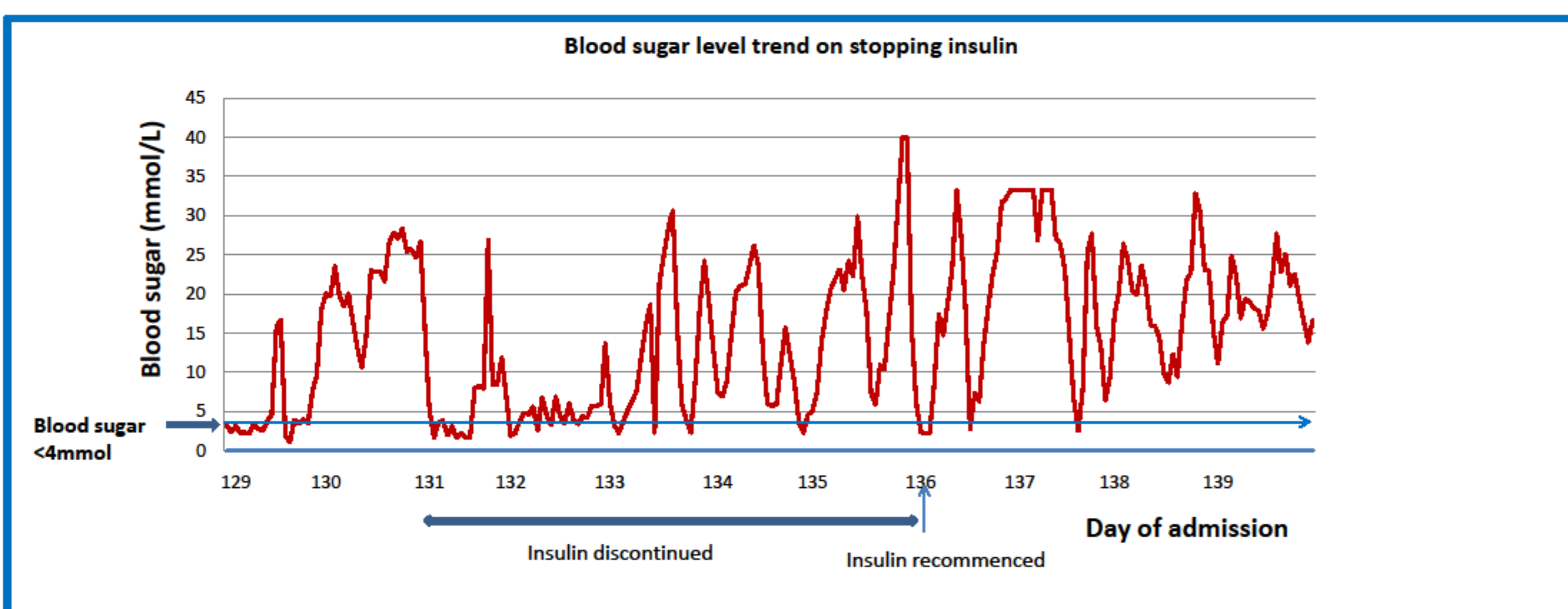
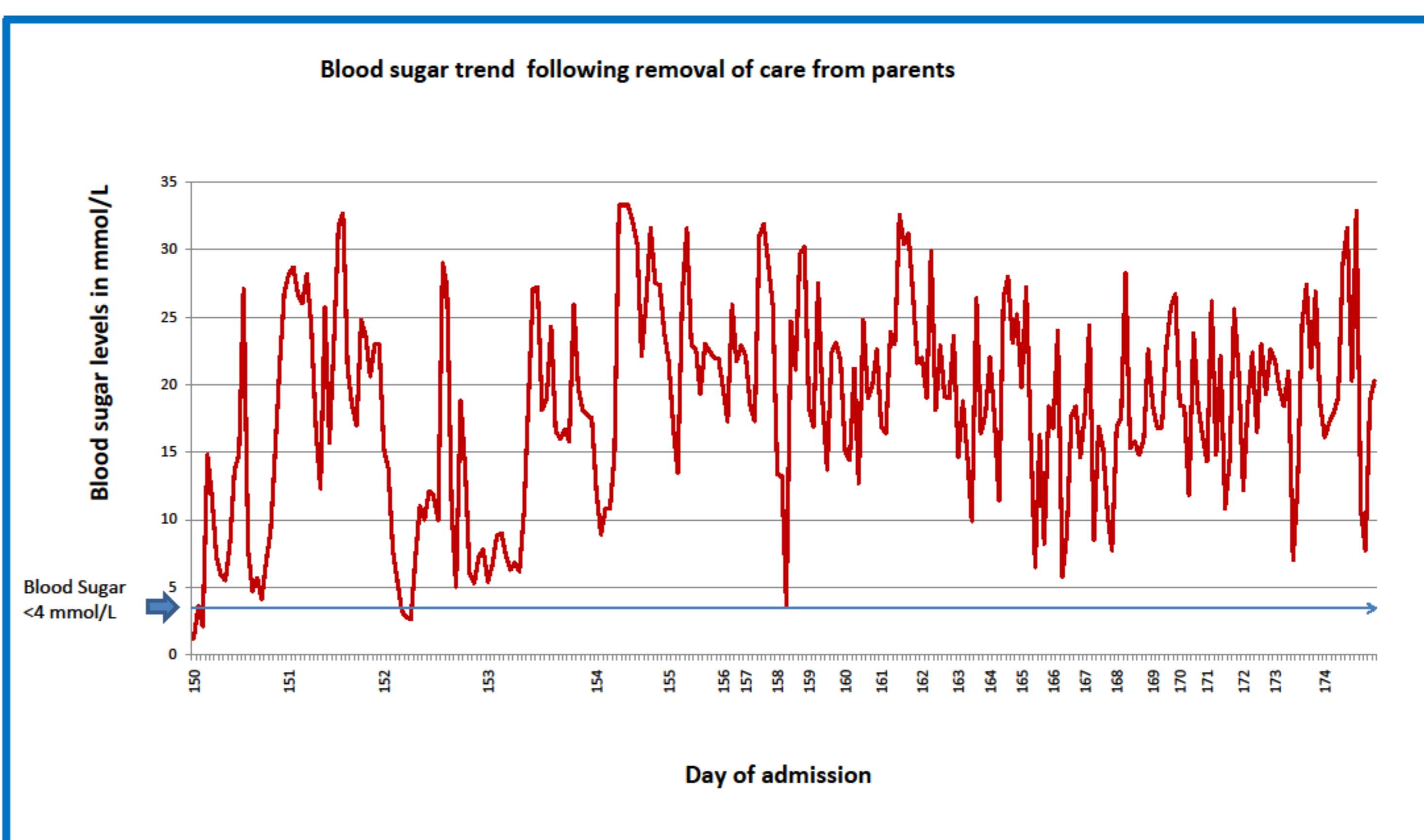
Fourth admission Day 128 post-diagnosis:

- Re-admitted with low blood glucose level 2.0 mmol/L. Emergency resuscitation required with IV glucose infusion to achieve normoglycaemia.
- Repeated attempts to stop IV glucose infusion over 2-3 days failed due to extreme glucose excursion (blood glucose >15mmol/L and < 2.0 mmol/L).
- All insulin ceased day 131 (4 days post admission) secondary to persistent hypoglycaemia.
- Intensive glucose monitoring continued (see graph below).
- Insulin recommenced day 136 (9 days post admission) due to hyperglycaemia.
- Unpredictable significant but not extreme hypoglycaemia persisted.

5. **Pharmacokinetics** was not consistent with the last recorded dose of Novorapid (Aspart) or Actrapid (Human soluble insulin) given, which suggested that both these types of insulin would have been expected to be eliminated from the body by the time of blood collection.

This led to the most likely probability of insulin being administered by a third party. Safeguarding procedures were followed and all care was removed from parents to conduct appropriate investigation and secure the safety of the child.

Following removal of care from parents to hospital delivered care, only one further episode of transient hypoglycaemia was recorded, which was not of the pattern of previous episodes. This transient hypoglycemia was easily corrected by consumption of orange juice, compared to previous low blood sugars requiring intravenous dextrose; as depicted in the graph below.



Discussion:

- This case demonstrates the difficulty in defining the medical causes of hypoglycaemia and subsequent exclusion of all other causes bar that of fabricated illness by third party insulin administration and its legal implications.
- Suspicion arose when despite extensive re-training and education of parents, the child had repeated admissions to the hospital with unexplained hypoglycaemia, not responding to conservative management.
- The Insulin/C-peptide ratio can give vital clue to the underlying diagnosis.
- Factitious insulin administration is a difficult diagnosis to make; admission and consultation is usually necessary before the diagnosis can be confirmed.
- Hospitalization may be warranted to keep the child safe from further abuse.
- The average length to establish a diagnosis usually exceeds 6 months²; 3 ½ months in our case.

Investigations: On Admission:

Blood glucose	30.7mmol/L
Glucosuria	500mg/dl
Ketonuria	≥ 160mg/dl.
HbA1C level	94mmol/mol (Ref range: 20-43mmol/mol)
Positive IA2 antibody level	184 IU/ml (Ref range: 0-10IU/ml)
Anti-GAD antibody level	<5U/ml (Ref range: 0-10U/ml)
Islet cell antibody levels	Equivocal

Comment: Pattern consistent with the Type 1A Diabetes

Investigations: Day 132:

1. High blood insulin 286 pmol/L
2. Low c-peptide < 33pmol/l (Ref range: 298-2350 pmol/L)

Comment: Low c-peptide level is consistent with the external administration of insulin as the molar ratio of insulin to C-peptide is >1¹, as opposed to beta cell recovery in a newly diagnosed young infant.

Confirmatory Investigations (Sent for expert external opinion) :

1. **High blood insulin** 270 pmol/L
2. **Low C-peptide** <94 pmol/L
3. The insulin result obtained after **PEG precipitation** was 120 pmol/L
4. **Mass spectrometry**^{3,4,5} yielded a positive result for the insulin derivative Aspart, which contains the amino acid substitution Pro(B28)Asp.

Comment: Results not consistent with autoimmune mediated hypoglycaemia (i.e. Insulin Antibodies binding insulin and releasing it at an inappropriate time to cause a low blood glucose) as the C-peptide level is suppressed and the insulin result after PEG precipitation is not low enough. In cases of autoimmune hypoglycaemia, the insulin result post PEG precipitation is less than 10% of the non-treated insulin result. However, in this case, it was 44%.

Conclusions:

- 1) Factitious illness is an uncommon situation, but can have devastating long term consequences and can sometimes be fatal to the children/infants. It is therefore recommended to initiate prompt investigations and management once clinical suspicions are confirmed.
- 2) C-peptide ratio should be carefully assessed in these cases, as it can give vital clue to the underlying diagnosis.
- 3) Managing a case of fabricated illness requires multidisciplinary team effort of doctors, nurses, child protection agencies, police and law; all working together in unison and following strict child protection policy to ensure a correct chain of evidence and protection the safety of the child.

Recommendations for management of fabricated illness:

- A cautious but vigilant approach is when required when fabricated illness is suspected.
- It is essential to approach social care and court to ensure safety of the child.
- Consider constant hospital delivered care, whilst investigations are ongoing.
- A review of medical records of all other siblings is mandatory.
- Consider long term psychiatric help and support for the perpetrator after appropriate psychiatric evaluation.
- Multidisciplinary team approach is crucial to ensure prevention of long term consequences which could prove fatal to the children/infants.

References:

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