

The Etiologies of Adrenal Insufficiency in 73 Thai Children: 20 Years Experience

Prapanrat Osuwannaratana MD*,
Saroj Nimkarn MD*, Jeerunda Santiprabhob MD*,
Supawadee Likitmaskul MD*, Pairunyar Sawathiparnich MD*

* Division of Pediatric Endocrinology, Department of Pediatrics,
Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok

Background: Adrenal insufficiency (AI) is an event caused by an inadequate secretion or action of adrenal hormones. It can be classified as primary (1°) and secondary (2°). AI may result in severe morbidity and mortality when undiagnosed or ineffectively treated.

Objective: To determine the etiologies of AI in Thai children

Material and Method: Data of children with AI presented to the authors' pediatric endocrine service between 1982 and 2002 (20 years) were retrospectively collected and analyzed.

Results: AI was diagnosed by clinical and laboratory data in 73 children (31 boys and 42 girls). Sixty-two (84.9%) patients had 1° AI while 11 (15.1%) had 2° AI. The majority of patients with 1° AI (87.1%) were diagnosed with congenital adrenal hyperplasia (CAH). Other causes of 1° AI were uncommon such as ACTH unresponsiveness (4.8%) and no definite diagnosis (8.1%). Most children with 1° AI presented with hyperpigmentation. Causes of 2° AI were as follows: panhypopituitarism (63.6%), isolated ACTH deficiency (9.1%), and low birth weight (27.3%).

Conclusion: In the present study, CAH was the most common cause of 1° AI while panhypopituitarism was the most common cause of 2° AI. Other causes of AI were quite uncommon. Definite causes of AI have not yet been identified in some children. Further clinical observation and special tests including molecular studies in these children are warranted for diagnostic and prognostic importance.

Keywords: Adrenal insufficiency, Children, Etiologies, Congenital adrenal hyperplasia

J Med Assoc Thai 2008; 91 (10): 1544-50

Full text. e-Journal: <http://www.medassocthai.org/journal>

Adrenal insufficiency (AI) is a relatively rare disorder. It can be classified as 1° (primary) or 2° (secondary). 1° AI occurs when the adrenal gland itself is dysfunctional. 2° AI occurs when lack of corticotropin-releasing hormone (CRH) secretion from hypothalamus or adrenocorticotrophic hormone (ACTH) secretion from pituitary gland is responsible for hypofunction of the adrenal cortex.

Clinical presentations of AI depend on the types of deficient adrenal hormones. Signs and symp-

toms of glucocorticoid (GC) deficiency are abdominal pain, hyperpigmentation, failure to thrive, weakness, anorexia, nausea, vomiting, hypoglycemia, hypotension, and shock. While signs and symptoms of mineralocorticoid (MC) deficiency are dehydration, nausea, vomiting, salt craving, hyponatremia, hyperkalemia, and metabolic acidosis. Hyponatremia and hyperkalemia are common in 1° AI due to deficient aldosterone secretion. Hyponatremia is occasionally seen in 2° AI, presumably due to water retention. AI is a potentially fatal disease if unrecognized, delayed diagnosed or inappropriately treated. Death usually results from hypotension or cardiac arrhythmia secondary to hyperkalemia.

There have been a few reports regarding the etiologies of AI in children. A review of 103 children

Correspondence to: Sawathiparnich P, Division of Pediatric Endocrinology, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, 2 Prannok Rd, Bangkok 10700, Thailand. Phone & Fax: 0-2419-7000 ext 5676, E-mail: sipry@mahidol.ac.th

with 1° AI by Perry et al at the Sainte-Justine Hospital, Montreal, Canada showed that CAH was the most frequent cause of 1° AI⁽¹⁾. A report of 16 patients by Simm et al. showed that autoimmune adrenal insufficiency and adrenal hypoplasia congenita were the most common causes of 1° AI⁽²⁾.

The present review will illustrate the etiologies of both 1° and 2° AI in children who presented with signs and symptoms of AI to the Department of Pediatrics, Siriraj Hospital over 20 years. The author will further discuss clinical presentation of these children with AI in detail.

Material and Method

Data of children who presented with signs and symptoms of AI to the Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand for a period of 20 years (1982-2002) were retrospectively collected. Clinical presentation and laboratory data were reviewed. Children presented with hyperpigmentation, hypoglycemia were determined to have GC deficiency, while children presented with hyponatremia, hyperkalemia and metabolic acidosis were determined to have MC deficiency. Since nausea, vomiting, abdominal pain, weakness, or hypotension can be associated with either GC or MC deficiency, they were not used to classify types of deficient adrenal hormones.

Results

Seventy-three children diagnosed with AI (31 boys and 42 girls) were included. Among children with AI, 62 (84.9%) had 1° AI while 11 (15.1%) had 2° AI.

1° adrenal insufficiency (n = 62) (Table 1)

Among children with 1° AI, 54 (87.1%) were diagnosed with CAH while three (4.8%) were diagnosed with ACTH unresponsiveness. However, five (8.1%) patients with 1° AI did not have final diagnoses.

All children with CAH presented with mixed GC and MC deficiency. Children with ACTH unresponsiveness presented with GC deficiency alone. Poor weight gain, hyperkalemia, metabolic acidosis and skin hyperpigmentation were the most common signs and symptoms (> 90%) in children with 1° AI (Fig. 1).

Congenital adrenal hyperplasia (CAH)

Fifty-four children were diagnosed with CAH (21-OH deficiency in 53 and lipoid CAH in one). All patients with CAH presented with salt-losing. The diagnosis of 21-OH deficiency was confirmed by

elevated serum 17-OH progesterone either randomly or after 250 mcg ACTH stimulation tests. All girls with 21-OH deficiency presented with ambiguous genitalia. The patient with lipoid CAH had female genitalia and bilateral palpable gonads at inguinal area. Chromosome study revealed 46, XY. 250 mcg ACTH stimulation test revealed low levels of all adrenal hormones.

ACTH unresponsiveness (n = 3)

Familial glucocorticoid deficiency (FGD) (n = 2)

Two children were clinically diagnosed FGD. They were siblings (1 girl and 1 boy). Both presented with recurrent hypoglycemic seizures and darkening of skin at 1.5 years of age in the boy and 2 5/12 years of age in the girl. Both had inadequate cortisol response after 250 mcg ACTH stimulation tests and during hypoglycemic crisis. The girl and the boy were followed-up until 21 8/12 and 19 8/12 year old. They entered puberty normally and had normal pubertal progression.

Triple A syndrome (n = 1)

A 9 10/12 year old boy had classic triads of Allgrove syndrome, which were alacrima, achalasia, and presumably ACTH unresponsiveness. He presented at 3 months old with hyperpigmentation, frequent vomiting, drowsiness, fever and diarrhea. Serum ACTH was high (430 pg/ml) and there was no rising of serum cortisol during hypoglycemic episodes. Alacrima was found at 2 years after initial presentation.

Achalasia was diagnosed by Barium swallowing after 8 years of initial presentation.

No definite causes (n = 5) (Table 3)

The definite diagnoses were not made in five children (4 boys, 1 girl) with 1° AI. Hyperpigmentation was observed in each individual. The mean age of onset was 9.0 ± 3.6 years. Possible diagnoses are shown in Table 3.

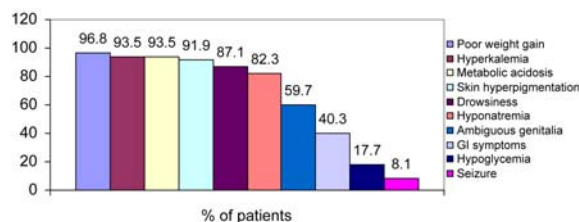


Fig. 1 Clinical signs and symptoms of children with 1° AI at initial presentation

Three boys presented with only GC deficiency at 5, 7, and 10 years of age whereas another 5 year-old boy presented with combined GC and MC deficiency. A one-month old girl who presented with both GC and MC deficiency had a history of multiple consanguinity and infant death in her family.

2° adrenal insufficiency (n = 11) (Table 2)

Causes of 2° AI in the presented patients were panhypopituitarism (63.6%), isolated ACTH deficiency (9.1%) and low birth weight infants (27.3%). All children with 2° AI presented only with GC deficiency. Hypoglycemia and drowsiness were the most common presenting signs and symptoms (100%) in children with 2° AI (Fig. 2).

Panhypopituitarism (n = 7)

Panhypopituitarism was the major cause of 2° AI (66.7%). Magnetic resonance imaging of pituitary glands and brain showed septo-optic dysplasia in three, pituitary aplasia or hypoplasia in three, and frontonasal meningoencephalocoele in one.

Isolated ACTH deficiency (n = 1)

A boy (age 6 5/12 years) first presented at 2 3/13 years old with hypoglycemic seizure. No rising of

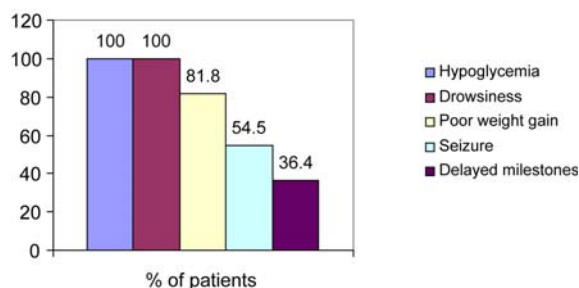


Fig. 2 Clinical signs and symptoms of children with 2° AI at initial presentation

serum cortisol was observed during hypoglycemic episodes. No hyperpigmentation was noted. Growth hormone response to hypoglycemia was normal. The patient had normal growth and thyroid function. MRI of the pituitary gland was normal.

Immaturity of hypothalamic-pituitary-adrenal axis (HPA axis) in preterm infants (n = 3)

Two preterm boys (born at 28 and 36 weeks) presented with neonatal hypoglycemia at the second day of life, which lasted for 3 and 4 weeks. They had no micropenis or prolonged jaundice. Their serum

Table 1. Etiologies, types of adrenal hormone deficiency, age of onset and age at diagnosis of 62 children with 1° AI

Causes of 1° AI	n	%	Age of onset (mean ± SD)	Age at diagnosis (mean ± SD)	GC def alone	MC def alone	GC + MC def
CAH	54	87.1	32.3 ± 66.4 days	61.1 ± 46.9 days	-	-	54
21-OH deficiency	53	85.5	52.3 ± 51.2 days	120.9 ± 111.8 days	-	-	53
Lipoid hyperplasia	1	1.6	14 days	30 days	-	-	1
ACTH unresponsiveness	3	4.8	1.9 ± 0.5 years	2.3 ± 1.1 years	3	-	-
Familial GC deficiency	2	3.2	2.0 ± 0.7 years	2.5 ± 1.5 years	2	-	-
Allgrove syndrome	1	1.6	1.7 years	1.9 years	1	-	-
Unknown	5	8.1	9.0 ± 3.6 years	11.1 ± 3.5 years	2	-	3

GC = glucocorticoid, MC = mineralocorticoid, def = deficiency

Table 2. Etiologies, age of onset and age at diagnosis of 11 children with 2° AI

Causes of 2° AI	n	%	Age at onset	Age at diagnosis
Panhypopituitarism	7	63.6	1.9 ± 1.4 years	3.4 ± 2.0 years
Septo-optic dysplasia	3	27.3	1.3 ± 1.9 years	1.5 ± 1.9 years
Pituitary hypoplasia	3	27.3	1.3 ± 1.1 years	3.0 ± 3.5 years
Frontomeningocoele	1	9.1	0.5 months	0.7 months
Low birthweight	3	27.3	2 ± 1 days	18 ± 6 days
Isolated ACTH deficiency	1	9.1	2.3 years	2.3 years

Table 3. Clinical and biochemical characteristics of 5 patients with undetermined causes of primary AI and their differential diagnosis

No.	Sex	Age of onset	Age now (years)	Signs and symptoms at presentation	Signs and symptoms during F/U	Lab	Possible diagnoses
1	Female	1 month	4 4/12	Hyperpigmentation, poor weight gain, alteration of consciousness, seizure	Normal growth and development during GC therapy	- Chromosome: 46, XX - No rising of serum cortisol after ACTH stimulation test - Normal female genitalia - HypoNa, hyperK, metabolic acidosis	Adrenal hypoplasia congenita
2	Male	5 years	15 3/12	Hyperpigmentation, poor weight gain, alteration of consciousness	Normal puberty	- Hypoglycemia - No rising of serum cortisol after ACTH stimulation test - HypoNa, hyperK, metabolic acidosis - Negative thyroid antibodies - Normal adrenal ultrasound	Autoimmune adrenailitis Adrenal hypoplasia congenita X-linked ALD
3	Male	7 years	19 4/12	Hyperpigmentation, poor weight gain, alteration of consciousness, seizure	Normal puberty	- Hypoglycemia - Normal electrolytes - No rising of serum cortisol after ACTH stimulation test - Normal thyroid function	Autoimmune adrenailitis Familial GC deficiency X-linked ALD
4	Male	5 years	13 9/12	Hyperpigmentation, poor weight gain, alteration of consciousness, seizure	Progressive learning problem mutism Memory deficit Depression	- Hypoglycemia - Normal electrolytes - No rising of serum cortisol after ACTH stimulation test - Normal adrenal sonography - Normal thyroid function	X-linked ALD
5	Male	10 years	20 9/12	Hyperpigmentation, poor weight gain	Normal puberty	- Hypoglycemia - High serum ACTH level - No rising of serum cortisol after ACTH stimulation test - Normal electrolytes	Autoimmune adrenailitis Familial GC deficiency X-linked ALD

cortisol levels were low during hypoglycemic episodes. Glucocorticoid replacement were started and then discontinued at 3.8 months and at 2.6 years of age. One boy had 1 mcg ACTH stimulation test done after discontinuation of glucocorticoid. Serum cortisol response was normal. Both children grew normally (until 7 months and 4 2/12 years old) with no signs and symptoms of hypoglycemia. Both had normal thyroid function tests.

A girl (2 5/12 yr old) presented with neonatal hypoglycemia at the third day of life. She was a near term SGA infant. Hypoglycemia persisted for 4 weeks. Her serum cortisol was low during one hypoglycemic episode. Glucocorticoid replacement was started with complete resolution of hypoglycemia. She had normal growth and development with normal thyroid function. MRI of the pituitary gland was normal. She was still on a maintenance dose of glucocorticoid at the age of 2 5/12 years.

Discussion

In the authors' 20-years-experience retrospective study, the authors have demonstrated that 21-OH deficiency CAH was the most common cause of 1° AI (87.1%) while panhypopituitarism was the most common cause of 2° AI (63.3%).

In the present study, all patients with CAH presented with adrenal crisis and high serum 17-OH progesterone either during crisis or after 250 mcg ACTH stimulation test. They were all identified as classical salt wasting form of 21-OH deficiency except one patient who was diagnosed with lipoid CAH. The mean age of diagnosis of 21-OH deficiency CAH was at 4 months of age while the mean age of onset of signs and symptoms was at almost 2 months of age. The diagnosis could have been made earlier by newborn CAH screening, which is unavailable in Thailand⁽³⁾. 12.9% of the presented patients with 1° AI were diagnosed with non-CAH causes, which were familial glucocorticoid deficiency (FGD) in two siblings, Triple A syndrome in one. The definite diagnoses were not made in 8.1% of patients with 1° AI.

The present findings are quite similar to the previous study by Perry et al who reported that CAH was the most common cause of 1° AI in children (71.8%) while 6% of their patients did not have definite diagnoses⁽¹⁾.

Triple A or Allgrove syndrome, a rare cause of 1° AI was diagnosed in a boy who presented with classic triads consisting achalasia, alacrima and ACTH-resistant adrenal insufficiency. Achalasia is usually the initial symptom that brings the patient to

medical attention⁽⁴⁾. Interestingly, our patient initially presented with 1° AI at a very young age (3 months). Alacrima and achalasia appeared much later. AAAS gene localized at 12q13 is responsible for this disorder. The product of this gene is called ALADIN (Alacrima-Achalasia-adrenal Insufficiency-Neurological disorder) protein⁽⁵⁾.

The diagnosis of FGD was made in a pair of siblings (a boy and a girl). Both presented with recurrent hypoglycemic seizures and hyperpigmentation. Both of them were proved to have cortisol deficiency without MC deficiency. FGD is an autosomal recessive disorder in which unresponsiveness to ACTH leads to deficient secretion of cortisol. Although the authors did not perform a molecular analysis of ACTH receptor gene, the authors made a diagnosis based on clinical presentation, the history of two affected siblings and the evidence of cortisol deficiency without MC deficiency. Since MC production is mainly regulated by the renin-angiotensin-aldosterone system, it is rarely affected^(6,7). Mutation of the ACTH receptor is responsible for this condition⁽⁸⁾.

Among children with 1° AI whom the final diagnosis could not be determined (8.1%), based on clinical presentation and clinical course of each patient, the authors speculated that their differential diagnoses could be autoimmune adrenalitis, adrenal leukodystrophy (ALD), adrenal hypoplasia congenita (AHC), and FGD.

Autoimmune adrenalitis can be an isolated entity or a part of an autoimmune polyendocrinopathy syndrome (APS). It was suspected in patient no. 2, 3, and 5 who presented with 1° AI with or without signs of MC deficiency. Circulating autoantibodies against side-chain cleavage enzyme (SCC) and 17 α -hydroxylase are relatively specific for APS patients⁽⁹⁾. However, these biochemical markers are not widely available in Thailand.

X-linked adrenoleukodystrophy (ALD) was highly suspected in a boy (patient no. 4) since he had 1° AI and progressive neurological impairment. Mutations have been found in the ALD gene encoding a membrane transport protein, which is involved in the import of VLCFA coenzyme A synthetase into the peroxisome. ALD is associated with demyelination of the central or peripheral nervous system with or without AI⁽¹⁰⁾. MRI of the brain should be worthwhile in this particular patient to evaluate the presence of cerebral white matter disease. Since 1° AI may precede neurological function⁽¹¹⁾, X-linked ALD cannot be totally excluded in patient no. 2, 3, and 5.

AHC should be considered in a girl (patient no.1) and a boy (patient no.2) since both presented with combined GC and MC deficiency (salt wasting) during infancy and childhood. AHC is a rare inherited disorder that occurs in two distinct forms: X-linked and autosomal recessive. The X-linked recessive form is characterized by lack of the permanent adult cortical zone⁽¹²⁾ whereas, the autosomal recessive form is characterized by small adrenal glands composed almost entirely of permanent cortex with normal histology⁽¹³⁾. Patients frequently developed salt wasting and GC deficiency during infancy but these can present later in life⁽¹⁴⁾.

FGD should be considered in two boys (patient no. 3 and 5) who presented with hyperpigmentation, hypoglycemia due to hypocortisolemia without signs of MC deficiency. The details of FGD were discussed earlier.

In the present study, panhypopituitarism associated with structural brain anomalies was the most common cause of 2° AI. In contrast, previous data suggested that abrupt discontinuation of glucocorticoid therapy was the most common cause of 2° AI⁽¹⁵⁾. This observed difference could be accounted for by the limited numbers of the presented patients with 2° AI together with the fact that children with mild non-specific symptoms of AI may not come to medical attention.

Isolated ACTH deficiency, a very rare disorder was suspected in a boy who presented with hypocortisolism without any hyperpigmentation or electrolyte disturbance. Unfortunately, serum ACTH was not performed in this patient. During the follow up period, he did not have evidence of other pituitary hormone deficiencies. Clinical onset of isolated ACTH deficiency can vary from just after birth to 8 years of age⁽¹⁶⁾.

Three low birth weight (LBW) infants were diagnosed with immaturity of hypothalamic-pituitary adrenal axis. All of them required glucocorticoid treatment for the treatment of hypoglycemia. Glucocorticoid replacement was discontinued in two patients without any recurrence of hypoglycemia. Weaning of glucocorticoid treatment should be considered in the other patient. In premature infants, HPA axis is relatively hypoactive when compared to full-term infants. Pituitary ACTH response to stress may be immature. Moreover, the sensitivity of the adrenal glands to ACTH may be reduced in preterm infants⁽¹⁷⁾. All of these increase risks of hypoglycemia after birth.

In summary, CAH was the most common cause of 1° AI while panhypopituitarism was the most

common cause of 2° AI in the present study. The other causes of AI were relatively rare. Determination of definite causes of AI can be a great challenge to physicians. Clinical observation and special tests including biochemical and molecular studies in children with unidentified causes of AI are warranted for diagnosis and prognostic importance.

References

1. Perry R, Kecha O, Paquette J, Huot C, Van Vliet G, Deal C. Primary adrenal insufficiency in children: twenty years experience at the Sainte-Justine Hospital, Montreal. *J Clin Endocrinol Metab* 2005; 90: 3243-50.
2. Simm PJ, McDonnell CM, Zacharin MR. Primary adrenal insufficiency in childhood and adolescence: advances in diagnosis and management. *J Paediatr Child Health* 2004; 40: 596-9.
3. Pang S, Shook MK. Current status of neonatal screening for congenital adrenal hyperplasia. *Curr Opin Pediatr* 1997; 9: 419-23.
4. Huebner A, Elias LL, Clark AJ. ACTH resistance syndromes. *J Pediatr Endocrinol Metab* 1999; 12 (Suppl 1): 277-93.
5. Tullio-Pelet A, Salomon R, Hady-Rabia S, Mugnier C, de Laet MH, Chaouachi B, et al. Mutant WD-repeat protein in triple-A syndrome. *Nat Genet* 2000; 26: 332-5.
6. Shepard TH, Landing BH, Mason DG. Familial Addison's disease; case reports of two sisters with corticoid deficiency unassociated with hypoaldosteronism. *AMA J Dis Child* 1959; 97: 154-62.
7. Kelch RP, Kaplan SL, Biglieri EG, Daniels GH, Epstein CJ, Grumbach MM. Hereditary adrenocortical unresponsiveness to adrenocorticotrophic hormone. *J Pediatr* 1972; 81: 726-36.
8. Mountjoy KG, Robbins LS, Mortrud MT, Cone RD. The cloning of a family of genes that encode the melanocortin receptors. *Science* 1992; 257: 1248-51.
9. Chen S, Sawicka J, Betterle C, Powell M, Prentice L, Volpato M, et al. Autoantibodies to steroidogenic enzymes in autoimmune polyglandular syndrome, Addison's disease, and premature ovarian failure. *J Clin Endocrinol Metab* 1996; 81: 1871-6.
10. Mosser J, Lutz Y, Stoeckel ME, Sarde CO, Kretz C, Douar AM, et al. The gene responsible for adrenoleukodystrophy encodes a peroxisomal membrane protein. *Hum Mol Genet* 1994; 3: 265-71.
11. Moser HW, Moser AB, Smith KD, Bergin A, Borel J, Shankroff J, et al. Adrenoleukodystrophy: phenotypic variability and implications for therapy.

- J Inherit Metab Dis 1992; 15: 645-64.
12. Weiss L, Mellinger RC. Congenital adrenal hypoplasia - an X-linked disease. J Med Genet 1970; 7: 27-32.
 13. Phelan JK, McCabe ER. Mutations in NR0B1 (DAX1) and NR5A1 (SF1) responsible for adrenal hypoplasia congenita. Hum Mutat 2001; 18: 472-87.
 14. Kletter GB, Gorski JL, Kelch RP. Congenital adrenal hypoplasia and isolated gonadotropin deficiency. Trends Endocrinol Metab 1991; 2: 123-8.
 15. Arlt W, Allolio B. Adrenal insufficiency. Lancet 2003; 361: 1881-93.
 16. Metherell LA, Savage MO, Dattani M, Walker J, Clayton PE, Farooqi IS, et al. TPIT mutations are associated with early-onset, but not late-onset isolated ACTH deficiency. Eur J Endocrinol 2004; 151: 463-5.
 17. Bolt RJ, van Weissenbruch MM, Lafeber HN, Delemarre-van de Waal HA. Development of the hypothalamic-pituitary-adrenal axis in the fetus and preterm infant. J Pediatr Endocrinol Metab 2002; 15: 759-69.

สาเหตุของภาวะต่อมหมวกไตทำงานน้อยในเด็กไทย 73 ราย: ประสบการณ์ 20 ปี

ประพาพรรัตน์ โอสวรรณรัตน์, สาโรช นิมภาณูจน, สุภาวดี ลิขิตมาศกุล, จีรันดา สันติประภพ, ไพรวัลยา สวัสดิ์พานิช

ภูมิหลัง: ภาวะต่อมหมวกไตทำงานน้อยเป็นภาวะผิดปกติที่เกิดจากต่อมหมวกไตหลังฮอร์โมนออกมาไม่พอกับความต้องการของร่างกาย หรือ ฮอร์โมนที่หลั่งออกมาไม่สามารถออกฤทธิ์ได้ตามปกติ ภาวะต่อมหมวกไตทำงานน้อยแบ่งออกเป็นชนิดปฐมภูมิ (เกิดจากความผิดปกติของต่อมหมวกไต, 1°) และทุติยภูมิ (เกิดจากความผิดปกติของไฮโปธาลามัส และ/หรือ ต่อมใต้สมอง, 2°)

วัตถุประสงค์: เพื่อประเมินสาเหตุของภาวะต่อมหมวกไตทำงานน้อยในผู้ป่วยเด็กไทย

วัสดุและวิธีการ: เป็นการศึกษาและวิเคราะห์ข้อมูลย้อนหลัง จากเวชระเบียนผู้ป่วยเด็กที่มาด้วยอาการและอาการแสดงของภาวะต่อมหมวกไตทำงานน้อยที่มารับการตรวจรักษาที่ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ตั้งแต่ปี พ.ศ. 2525-2545 (20 ปี)

ผลการศึกษา: มีผู้ป่วยเด็ก 73 ราย (เด็กชาย 31 ราย เด็กหญิง 42 ราย) ได้รับการวินิจฉัยว่ามีภาวะต่อมหมวกไตทำงานน้อยโดย 62 ราย (84.9%) มีภาวะต่อมหมวกไตทำงานน้อยชนิดปฐมภูมิ ขณะที่ 11 ราย (15.5%) มีภาวะต่อมหมวกไตทำงานน้อยชนิดทุติยภูมิ ผู้ป่วยที่มีภาวะต่อมหมวกไตทำงานน้อยชนิดปฐมภูมิ ส่วนใหญ่ (87.1%) เกิดจาก CAH สาเหตุอื่นพบได้น้อยเช่น ACTH unresponsiveness พบ 4.8% และที่ไม่ทราบการวินิจฉัยชัดเจนอีก 8.5% ผู้ป่วยมีภาวะต่อมหมวกไตทำงานน้อยชนิดปฐมภูมิมีสีผิวเข้มขึ้นเกือบทุกราย ส่วนสาเหตุของภาวะต่อมหมวกไตทำงานน้อยชนิดทุติยภูมิมีสืบเนื่อง panhypopituitarism (63.6%), Isolated ACTH deficiency (9.1%) ทารกที่มีน้ำหนักตัวแรกเกิดน้อย 27.3%

สรุป: ในการศึกษาครั้งนี้ CAH เป็นสาเหตุที่พบบ่อยที่สุดในผู้ป่วยที่มีภาวะต่อมหมวกไตทำงานน้อยชนิดปฐมภูมิ ส่วน panhypopituitarism เป็นสาเหตุที่พบบ่อยที่สุดของภาวะต่อมหมวกไตทำงานน้อยชนิดทุติยภูมิ สาเหตุอื่น ๆ ของภาวะต่อมหมวกไตทำงานน้อยค่อนข้างพบน้อย มีผู้ป่วยบางรายที่ยังหาสาเหตุของภาวะต่อมหมวกไตทำงานน้อยไม่ได้ ทั้งนี้ต้องอาศัยการติดตามลักษณะทางคลินิก และการตรวจพิเศษ เช่น การตรวจทางพันธุกรรม เพื่อการวินิจฉัยเฉพาะและเพื่อการพยากรณ์โรคต่อไป