Complication of steroid therapy in kidney diseases

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Table 2 Primary effects of glucocorticoids (GCs) [1]

Anti-inflammatory:	Inhibit inflammation by blocking the action of inflammatory mediators (transrepression), or by inducing anti-inflammatory mediators (transactivation)
Immunosuppressive:	Suppress delayed hypersensitivity reactions by directly affecting T-lymphocytes
Anti-proliferative:	Inhibition of DNA synthesis and epidermal cell turnover
Vasoconstrictive:	Inhibit the action of histamine and other vasoconstrictive mediators

DNA deoxyribonucleic acid.

Table 1 Common clinical uses of systemic corticosteroids

Field of medicine	Disorder(s)
Allergy and respirology	• Moderate to severe asthma exacerbations
	• Acute exacerbations of chronic obstructive pulmonary disease
	• Allergic rhinitis
	• Atopic dermatitis
	• Urticaria/angioedema
	• Anaphylaxis
	• Food and drug allergies
	• Nasal polyps
	• Hypersensitivity pneumonitis
	• Sarcoidosis
	• Acute and chronic eosinophilic pneumonia
	• Interstitial lung disease
Dermatology	• Pemphigus vulgaris
	• Acute, severe contact dermatitis
Endocrinology*	• Adrenal insufficiency
	• Congenital adrenal hyperplasia
Gastroenterology	• Ulcerative colitis
	• Crohn's disease
	• Autoimmune hepatitis
Hematology	• Lymphoma/leukemia
	• Hemolytic anemia
	• Idiopathic thrombocytopenic purpura
Rheumatology/ immunology	• Rheumatoid arthritis
	• Systemic lupus erythematosus
	• Polymyalgia rheumatica
	• Polymyositis/dermatomyositis
	• Polyarteritis
	• Vasculitis
Ophthalmology	• Uveitis
	• Keratoconjunctivitis
Other	• Multiple sclerosis
	• Organ transplantation
	• Nephrotic syndrome
	• Chronic active hepatitis
	• Cerebral edema

Serious complication of systemic corticosteroid as follows:

- Osteoporosis
- Adrenal suppression
- Hyperglycemia
- Dyslipidemia
- Cardiovascular disease
- Cushing’s syndrome
- Psychiatric disturbances
- Immunosuppression
- Growth retardation

Table 6 Major drug interactions with systemic GCs [1,8]

Interacting drug class	Effect	Recommendation/comment
Anticonvulsants (e.g., carbamazepine, phenobarbital, phenytoin)	• ↓ GC exposure and efficacy; may persist for weeks following discontinuation of anticonvulsant	• Closely monitor outcomes of concomitant use • GC dose alterations may be required
Anticoagulants (e.g., warfarin)	• May ↑ anticoagulant effects of warfarin and ↑ risk of GI bleeding	• Monitor INR closely • Significant alteration in warfarin dose will likely be required within 3–7 days of GC initiation
Antifungals (e.g., itraconazole, ketoconazole)	• ↑ GC exposure and toxicity	• Monitor concurrent use for signs of GC overdose (fluid retention, hypertension, hyperglycemia) • Dose alteration of methylprednisolone and dexamethasone may be needed (prednisone and prednisolone not affected to a clinically relevant degree by this interaction)
Antidiabetic agents	• GC initiation can lead to glucose dysregulation, thereby counteracting the effects of antidiabetic drugs	• ↑ frequency of BG monitoring when initiating GC therapy • Adjust antidiabetic therapy based on BG results
Antibiotics (macrolides) (e.g., clarithromycin)	• ↑ GC exposure and toxicity	• Monitor concurrent use for signs of GC overdose (fluid retention, hypertension, hyperglycemia) • Dose alteration of methylprednisolone and dexamethasone may be needed (prednisone and prednisolone not affected to a clinically relevant degree by this interaction)
Antivirals (e.g., atazanavir, indinavir, ritonavir, saquinavir)	• ↑ GC exposure and toxicity • Dexamethasone may ↑ levels of indinavir and saquinavir	• Monitor concurrent use for signs of GC overdose (fluid retention, hypertension, hyperglycemia) • Dose alteration of methylprednisolone and dexamethasone may be needed (prednisone and prednisolone not affected to a clinically relevant degree by this interaction) • Monitor antiviral efficacy of indinavir and saquinavir if patient is taking dexamethasone
Anti-infectives (e.g., efavirenz, nevirapine, rifampin)	• ↓ GC exposure and efficacy; may persist for weeks following discontinuation of anti-infective	• Closely monitor outcomes, especially in transplant recipients • ↑ GC dose accordingly
Diuretics, potassium wasting (e.g., furosemide, HCTZ)	• GCs may ↑ kaliuretic effects of these diuretics	• Monitor potassium levels to determine whether alteration of diuretic therapy and/or potassium supplementation is needed
Live vaccines	• Immunization with live vaccines while taking immunosuppressive GC doses (40 mg/day of prednisolone [or equivalent] for > 7 days) may increase risk of both generalized and life-threatening infections	• Postpone live vaccines for at least 3 months after high-dose GC therapy is discontinued
NSAIDS	• May ↑ risk of GI ulcers when given concomitantly with corticosteroids	• Consider use of PPI if person is at risk of GI ulcers

GC glucocorticoid, *INR* international normalized ratio, *BG* blood glucose, *GI* gastrointestinal, *HCTZ* hydrochlorothiazide, *PPI* proton pump inhibitor, *NSAIDS* non-steroidal anti-inflammatory drugs.

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Severe Adverse Effects Associated With Corticosteroid Treatment in Patients With IgA Nephropathy

Qingqing Cai [1 2 3 4], Xinfang Xie [1 2 3 4], Jinwei Wang [1 2 3 4], Sufang Shi [1 2 3 4], Lijun Liu [1 2 3 4], Yuqing Chen [1 2 3 4], Jicheng Lv [1 2 3 4], Hong Zhang [1 2 3 4]

Affiliations + expand

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1034 IgAN patients were followed up from 2003 to 2014

369 patients (35.7%) received a single corticosteroid (n ¼ 150) or corticosteroids plus other immunosuppressive agents (n ¼ 219) for $3 months

The two groups were definitely different in terms of GFR, BP, proteinuria, CKD STAGING, and the disease was mor

SAEs
serious adverse events with clinical relevance

(i) all-cause mortality

(ii) severe infection necessitating hospitalization or fatal infection

(iii) osteonecrosis of the femoral head or bone fracture

(iv) gastrointestinal hemorrhage or gastrointestinal perforation

(v) newonset diabetes mellitus (DM); (vi) new-onset cataract

(vii) major cardiocerebral vascular disease (including fatal/nonfatal myocardial infarction, fatal/nonfatal stroke, and heart failure)

Table 1. Baseline characteristics and follow-up information of the corticosteroid user group and corticosteroid nonuser group

Baseline characteristic	Corticosteroid users (n = 369, 35.7%)	Corticosteroid nonusers (n = 665, 64.3%)	P value
Male (n [%])/female (n)	203 (55.0)/166	317 (47.7)/348	**0.024**
Age (yr)	34 ± 13	35 ± 11	0.082
Systolic BP (mm Hg)	125 ± 16	122 ± 16	**0.006**
Diastolic BP (mm Hg)	80 ± 12	78 ± 12	**0.019**
Serum creatinine (mmol/l)	106 (80–146)	87 (70–114)	**<0.001**
Proteinuria (g/24 h)	3.0 (1.7–5.2)	1.1 (0.6–1.9)	**<0.001**
eGFR (ml/min per 1.73 m^2)	73 ± 33	86 ± 29	**<0.001**
Uric acid (μmol/l)	387 ± 102	361 ± 101	**<0.001**
Hemoglobin (g/l)	133 ± 20	134 ± 18	0.289
Albumin (g/l)	34 ± 8	39 ± 5	**<0.001**
Triglyceride (mmol/l)	2.2 ± 1.6	1.9 ± 1.6	**0.005**
Total cholesterol (mmol/l)	5.9 ± 2.1	4.7 ± 1.1	**<0.001**
Follow-up (mo)	49 (25–84)	49 (28–85)	0.615
ESRD and death	55 (14.9)	51 (7.7)	**<0.001**
SAEs	46 (12.5)	18 (2.7)	**<0.001**
CKD stage			
1	116 (26.5)	321 (73.5)	**<0.001**
2	108 (34.4)	206 (65.6)	
3	116 (48.3)	124 (51.7)	
4/5	29 (67.4)	14 (32.6)	

Unless otherwise indicated values are n (%), means ± SDs, or median (25th–75th centiles). Bold values are statistically significant.
BP, blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; SAEs, severe adverse effects.

Table 3. Prevalence of SAEs associated with corticosteroids in the corticosteroid user group and corticosteroid nonuser group, and median time from initial use of corticosteroids to SAE occurrence

SAEs	Corticosteroid users, n (%)	Time, median (range) (mo)	Corticosteroid nonusers, n (%)
Diabetes mellitus	19 (5.1)	3.5 (0.5–55.4)	3 (16.7)
Severe infection	18 (4.9)	3.8 (1.1–14.4)	10 (55.5)
Death	7 (1.9)	12.4 (2.3–64.8)	0
Osteonecrosis of femoral head or bone fracture	6 (1.6)	22.4 (1.3–57.2)	2 (11.1)
Cardiocerebral vascular disease	4 (1.1)	7.2 (2.0–31.1)	2 (11.1)
Cataract	3 (0.8)	11.4 (5.6–17.1)	0
Gastrointestinal hemorrhage	1 (0.3)	3	1 (5.6)
Total	58	4.9 (0.5–64.8)	18

SAEs, severe adverse effects.

58 from 396

18 from 665

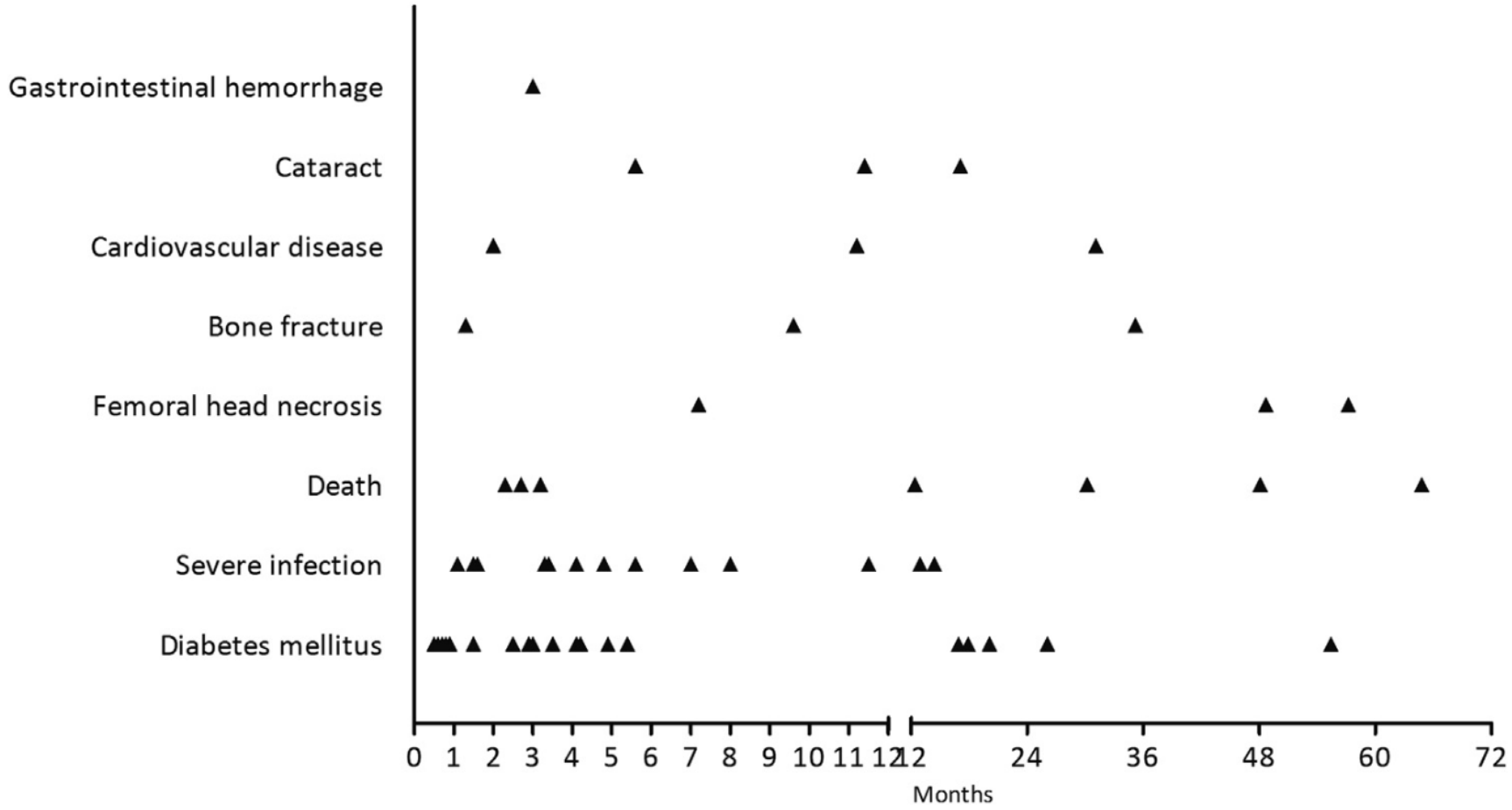
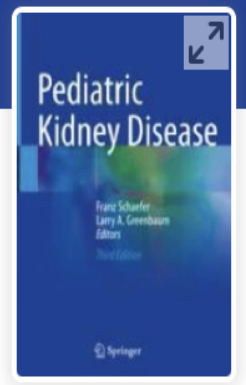


Figure 1. Occurrence time of severe adverse effects (SAEs). Scatter diagram of time when SAEs occurred.



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Steroid Sensitive Nephrotic Syndrome

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KI REPORTS
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MEETING REPORT

2017 Kidney Disease: Improving Global Outcomes (KDIGO) Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD) Guideline Update Implementation: Asia Summit Conference Report

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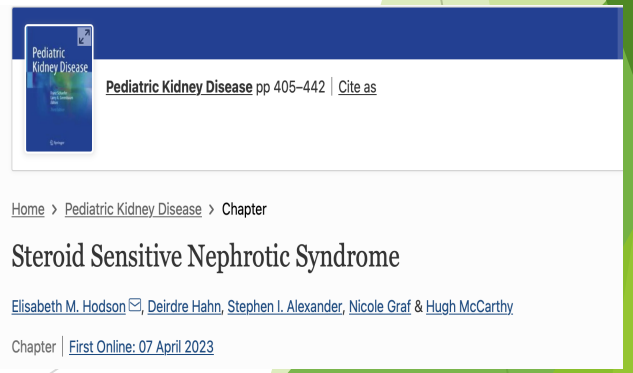
The Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on Chronic Kidney Disease–Mineral and Bone Disorder (CKD–MBD) 2009 provided recommendations on the detection, evaluation, and treatment of CKD-MBD in patients CKD who are and are not undergoing dialysis. Because of the accumulation of evidence since this initial publication, the CKD-MBD Guideline underwent a selective update in 2017. In April 2018, KDIGO convened a CKD-MBD Guideline Implementation Summit in Japan with the key objective to discuss various barriers to the uptake and implementation of the CKD-MBD Guideline in 8 Asian countries/regions. These countries/regions were comparable according to their high-to-middle economic ranking assigned by the World Bank. The discussion took into account the availability of CKD-MBD medication therapies and government health policies that may influence reimbursement and practice patterns in the region. Most importantly, Summit participants developed a framework of multifaceted strategies aimed at overcoming barriers to guideline implementation. The Summit attendees suggested a shared decision-making approach between clinicians and patients in CKD-MBD management, as well as individualized care based on the treatment risk-benefit ratio. The Summit participants also discussed how KDIGO, as a guideline development organization, may work in partnership with local and national nephrology societies to provide education and facilitate implementation of the guideline by clinicians. The conclusions drawn from this Summit in Asia may serve as an important guide for other regions to follow.

A cohort study (190)

- 884 patients (393 children) with primary proteinuric kidney disease, 534 received corticosteroids.
- At least one steroid associated adverse event was seen in 333 (62%)
- hypertension
- diabetes
- overweight and obesity
- infections
- short stature

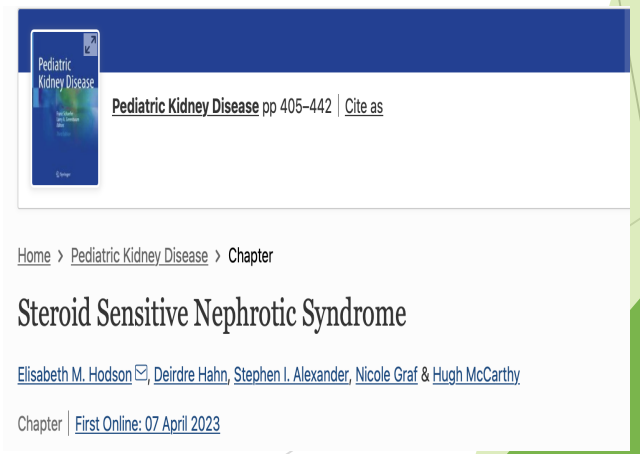
being the most common



- no difference in risk of steroid associated adverse effects between children and adults

The adjusted relative risk:

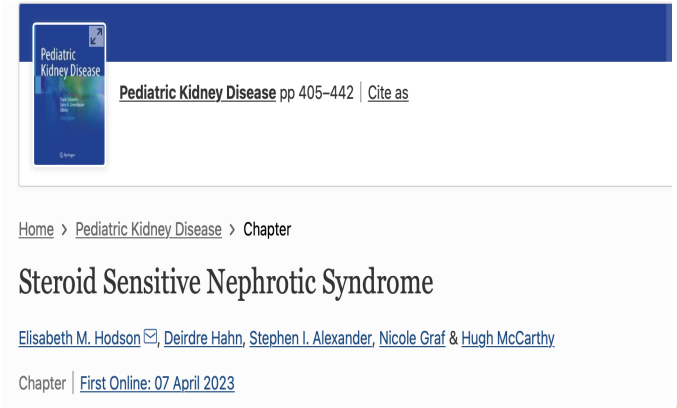
- increased overall 2.5- fold for each 1 mg/kg increase in corticosteroid dose
- hypertension increased 4.5 fold
- obesity increased 2.9 fold
- diabetes increased 1.9 fold

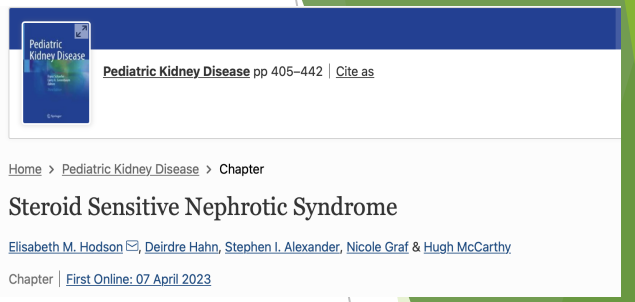


Behavioural changes are common(191-192)

Include:

- anxiety
- depression
- emotional lability
- aggressive behavior
- inattention
- hyperactivity
- sleep disturbance





that children given alternate day prednisone after RTx grew better than those given daily prednisone [195]

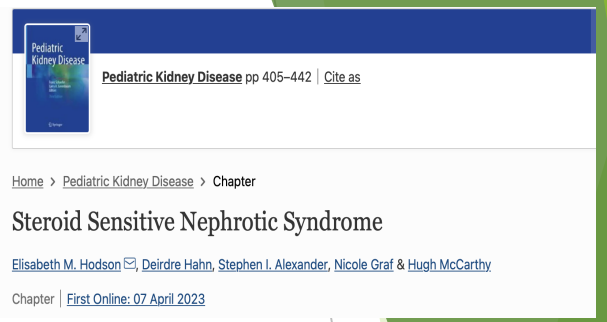
growth rates remained normal if prednisone doses were maintained below 1.5 mg/kg on alternate days in 41 prepubertal children [197]

A third study of 64 boys found that growth rates remained stable from diagnosis for 5 years and then deteriorated [198]

final height was signifcantly below target in children, who required prednisone during puberty [196, 198]

growth occurred in pubertal children permanently withdrawn from prednisone[196]

BMD



- Corticosteroid therapy is associated with osteopenia (decrease in quantity of bone tissue)
- osteoporosis (osteopenia with bone fragility)

- Trabecular bone is affected more severely than cortical bone

- DXA measures the mass of bone mineral per projection area [206]

Long term corticosteroid therapy

results in:

suppression of the hypothalamic-pituitary-adrenal (HPA) axis in 35–60% of children with nephrotic syndrome

particularly in younger children and children (215)

Interesting sights of Zanjan

Katlekhor Cave

Soltanieh Dome

Thanks for you attention