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Systematic Review

Cushing's Syndrome and Topical Corticosteroids in Pediatrics: A Systematic Review

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Abstract

Introduction

Despite the increasing number of pediatric cases of iatrogenic Cushing's syndrome (CS) due to topical corticosteroids, systematic reviews are lacking to provide comprehensive insights into the disease. This study aims to provide a systematic overview of the disease.

Methods

Relevant literature was identified using Google Scholar and PubMed. The search strategy was restricted to studies on human published in English. The inclusion criteria encompassed confirmed pediatric cases of iatrogenic CS induced by topical corticosteroids.

Results

The mean age of the cases was 38.8 months, with a female gender predominance (57.1%). Abnormalities in growth patterns were observed in approximately 75% of the cases. The most common clinical presentation was a "moon face" appearance (74.6%), followed by weight gain (55.5%). Clobetasol propionate was the most frequently used topical steroid (54%), followed by betamethasone types (35%). The mean duration of steroid use was 25.4 weeks. The primary indications for steroid use were dermatitis (47.6%), psoriasis (17.5%), and scabies (15.9%). Laboratory tests for adrenocorticotropic hormone and cortisol levels revealed low levels in 73% and 78% of cases, respectively. All cases had their initial steroid discontinued. Oral hydrocortisone was the primary replacement therapy (39.7%), followed by sulfur cream (12.7%). Fifty-one cases (81%) recovered from the disease. Partial recovery was observed in 2 cases (3.2%), while four cases (6.3%) did not survive.

Conclusion

A specialist should supervise topical corticosteroid administration, and parents need to be fully informed about the proper usage and potential side effects to avoid iatrogenic CS and other complications.

1. Introduction

Cushing syndrome (CS) is a reversible endocrinological disorder characterized by elevated levels of cortisol or other glucocorticoids in the bloodstream. It can arise from either endogenous factors, such as excessive steroid secretion due to adrenal or pituitary tumors, or exogenous factors, such as prolonged use of corticosteroid medications, leading to iatrogenic CS [1]. While topical corticosteroids are extensively prescribed, they are less commonly reported as a cause of iatrogenic CS [2,3]. Although CS is exceptionally rare in the pediatric population, with an annual incidence of only five cases per million, children are at a higher risk of developing iatrogenic CS. This increased risk is likely attributed to the high prevalence of diseases requiring chronic corticosteroids, like dermatological diseases, and increased absorption of these steroids due to the thinness of children's skin [4]. The systemic side effects of topical corticosteroids are influenced by the specific corticosteroid used and the individual's absorption conditions [5]. Clinically, patients with CS present with facial plethora and edema, resulting in a "moon face" appearance. They may also exhibit fat accumulation in the supraclavicular area and upper trunk, leading to a "buffalo hump" appearance. Additional features include purple striae, particularly on the abdomen, arms, and upper thighs, and hirsutism, skin bruising, ecchymoses, delayed wound healing, muscle weakness, and impaired growth. Moreover, the patients may develop tertiary adrenal insufficiency following the reduction or discontinuation of corticosteroids [4]. Despite the increasing number of reported cases of iatrogenic CS in pediatrics, there is no systematic review providing comprehensive insights into the disease. This study aims to provide a systematic overview of the disease.

2. Methods

2.1 Literature search

The study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Relevant literature published up to July 14, 2024, was identified using Google Scholar and PubMed. The search strategy employed the keywords: (Cushing OR Cushing's OR hypercortisolism OR cushingoid AND topical) and was restricted to studies on humans published in English.

2.2 Eligibility criteria

The inclusion criteria encompassed confirmed pediatric cases of iatrogenic CS induced by topical steroids. Studies were excluded if they involved iatrogenic CS due to non-topical steroids, adult patients, or were published in journals listed on warning lists [6].

2.3 Study selection

One author conducted a literature search and reviewed the titles and abstracts of the identified studies, followed by full-text screening based on eligibility criteria. A second author verified this work to correct errors and add missing data. In cases of disagreement or uncertainty, both authors resolved them through re-checking and discussion.

2.4 Data extraction

The collected data included various parameters, such as the first author's name, patient demographics, disease presentation, characteristics of the steroid used, regularity of use, administration site, purpose of use, frequency of use, laboratory findings, adrenal status, replacement therapy, and outcomes.

2.5 Statistical Analysis

The extracted data was compiled into an Excel sheet (2019) and subsequently analyzed for qualitative synthesis (descriptive) using the Statistical Package for the Social Sciences (SPSS, v. 27, IBM Co.). The findings were presented as frequencies, percentages, means, and medians with quartile ranges.

3. Results

3.1 Study identification

The systematic search identified 116 studies. After eliminating duplicates (5) and non-English articles (11), the titles and abstracts of 100 articles were screened. Of these, 13 studies were excluded for being irrelevant. Full-text screening of the remaining 87 articles led to the exclusion of 35 more. Six studies were also excluded from the eligibility assessment due to publishing in warning-listed journals. Ultimately, 46 eligible articles comprising 63 cases of iatrogenic CS were included (Tables 1 and 2). A PRISMA flow chart of the identification process is provided in Figure 1.

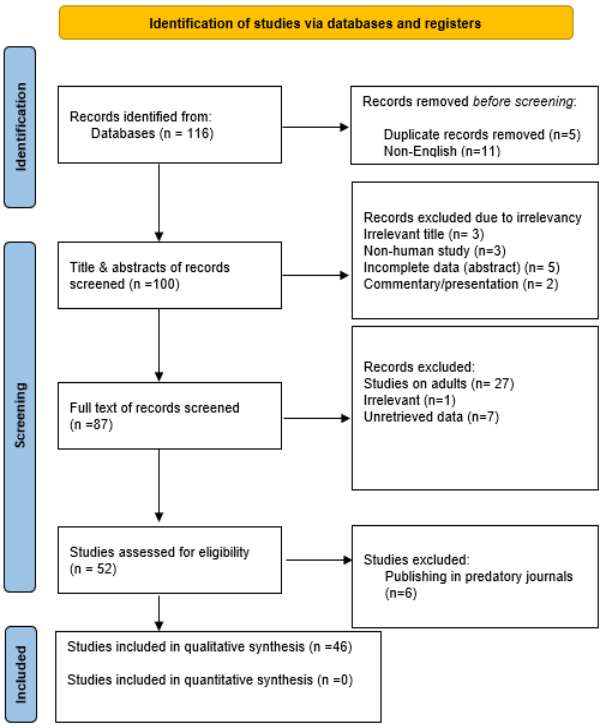

Figure 1. Study selection PRISMA flow chart.

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Table 1. Patient demographics, presentation, and characteristics of used corticosteroids in each study.

Author (year) reference	Sex	Age (months)	BMI/Growth	Presentation	Type of steroid	Potency	Regularity of use	Site of administration	Purpose of use	Usage duration (weeks)	Frequency of use (time/day)
Rai et al. (2023) [7]	F	168	Abnormal	Weight gain, moon face, muscle weakness, growth delay	Clobetasol propionate	Ultrahigh	Intermittent	Whole body	Psoriasis	48	3 to 4
Tan (2023) [8]	F	82	Abnormal	Weight gain, stunted growth, striae	Betamethasone dipropionate	High	Continuous	Whole body	Psoriasis	48	2
Kuikel et al. (2022) [9]	N/A	15	Abnormal	Hair growth, moon face, weight gain	Clobetasol propionate	Ultrahigh	N/A	N/A	Scabies	N/A	N/A
Matejek et al. (2022) [5]	M	6	Abnormal	Moon face, striae	Clobetasol propionate	Ultrahigh	Continuous	Whole body	Scabies	4	2
	F	24	Abnormal	Stunted growth	Dexamethasone eye drops	Low	Continuous	Eyes	Congenital glaucoma (after surgery)	2	1
Takaiwa et al. (2022) [10]	F	132	Abnormal	Stunted growth, moon face, striae, hair growth	Betamethasone butyrate propionate	High	Continuous	Whole body	Dermatitis	N/A	N/A
Ahmed et al. (2021) [1]	F	4	Normal	Moon face	Clotrimazole and Betamethasone	High	Continuous	Diaper area	Diaper dermatitis	12	5 to 8
Ghirardo et al. (2021) [11]	M	132	Abnormal	Buffalo humps, moon face, hair growth, striae, weight gain	Clobetasol propionate	Ultrahigh	Continuous	Oral	Oral mucositis	N/A	1
Katsura et al. (2021) [12]	F	48	Abnormal	Moon face	Clobetasol propionate	Ultrahigh	Continuous	Buttocks	Pruritic scar after grafting	13	N/A
Sachdeva et al. (2020) [13]	F	132	Abnormal	Fever, chills, rigor, striae, moon face, hypertrichosis, buffalo hump	N/A	N/A	Continuous	Whole body	Psoriasis	N/A	N/A
Taylor et al. (2020) [14]	F	5	Abnormal	Weight gain, stunted growth, moon face	Triamcinolone cream	Moderate	Continuous	Diaper area	Diaper dermatitis	12	4 to 5
Alkhuder et al. (2019) [4]	F	14	N/A	Moon face, edema	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	5 to 8
Sardesai et al. (2019) [15]	M	3	N/A	Body swelling, moon face, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Face, scalp, trunk	Skin rashes	8	N/A
Ali et al. (2018) [2]	M	11	Abnormal	Appetite loss, moon face, weight gain, lethargy	Triamcinolone cream	Moderate	N/A	Whole body	Seborrheic dermatitis	12	N/A
Çömlek et al. (2018) [16]	F	2.5	Abnormal	Weight gain, buffalo hump, moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	2 to 3
Estrada-Chávez et al. (2018) [17]	F	5	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	4	4
	F	6	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Intermittent	Whole body	Scabies	20	1 to 2
	M	7	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	12	2
	M	7	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Intermittent	Whole body	Scabies	8	2 to 3
	M	8	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	32	1
	F	9	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	4	3
	M	16	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	20	1
	F	17	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Intermittent	Whole body	Scabies	16	1 to 2

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Table 1. Continued…

Rai et al. (2023) [7]	F	168	Abnormal	Weight gain, moon face, muscle weakness, growth delay	Clobetasol propionate	Ultrahigh	Intermittent	Whole body	Psoriasis	48	3 to 4
Tan (2023) [8]	F	82	Abnormal	Weight gain, stunted growth, striae	Betamethasone dipropionate	High	Continuous	Whole body	Psoriasis	48	2
Kuikel et al. (2022) [9]	N/A	15	Abnormal	Hair growth, moon face, weight gain	Clobetasol propionate	Ultrahigh	N/A	N/A	Scabies	N/A	N/A
Matejek et al. (2022) [5]	M	6	Abnormal	Moon face, striae	Clobetasol propionate	Ultrahigh	Continuous	Whole body	Scabies	4	2
	F	24	Abnormal	Stunted growth	Dexamethasone eye drops	Low	Continuous	Eyes	Congenital glaucoma (after surgery)	2	1
Takaiwa et al. (2022) [10]	F	132	Abnormal	Stunted growth, moon face, striae, hair growth	Betamethasone butyrate propionate	High	Continuous	Whole body	Dermatitis	N/A	N/A
Ahmed et al. (2021) [1]	F	4	Normal	Moon face	Clotrimazole and Betamethasone	High	Continuous	Diaper area	Diaper dermatitis	12	5 to 8
Ghirardo et al. (2021) [11]	M	132	Abnormal	Buffalo humps, moon face, hair growth, striae, weight gain	Clobetasol propionate	Ultrahigh	Continuous	Oral	Oral mucositis	N/A	1
Katsura et al. (2021) [12]	F	48	Abnormal	Moon face	Clobetasol propionate	Ultrahigh	Continuous	Buttocks	Pruritic scar after grafting	13	N/A
Sachdeva et al. (2020) [13]	F	132	Abnormal	Fever, chills, rigor, striae, moon face, hypertrichosis, buffalo hump	N/A	N/A	Continuous	Whole body	Psoriasis	N/A	N/A
Taylor et al. (2020) [14]	F	5	Abnormal	Weight gain, stunted growth, moon face	Triamcinolone cream	Moderate	Continuous	Diaper area	Diaper dermatitis	12	4 to 5
Alkhuder et al. (2019) [4]	F	14	N/A	Moon face, edema	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	5 to 8
Sardesai et al. (2019) [15]	M	3	N/A	Body swelling, moon face, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Face, scalp, trunk	Skin rashes	8	N/A
Ali et al. (2018) [2]	M	11	Abnormal	Appetite loss, moon face, weight gain, lethargy	Triamcinolone cream	Moderate	N/A	Whole body	Seborrheic dermatitis	12	N/A
Çömlek et al. (2018) [16]	F	2.5	Abnormal	Weight gain, buffalo hump, moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	2 to 3
Estrada-Chávez et al. (2018) [17]	F	5	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	4	4
	F	6	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Intermittent	Whole body	Scabies	20	1 to 2
	M	7	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	12	2
	M	7	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Intermittent	Whole body	Scabies	8	2 to 3
	M	8	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	32	1
	F	9	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	4	3
	M	16	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Continuous	Whole body	Scabies	20	1
	F	17	Abnormal	Hair growth, weight gain, striae	Betamethasone	High	Intermittent	Whole body	Scabies	16	1 to 2

Table 1. Continued…

Hansen et al. (2018) [18]	M	14	Abnormal	Moon face, weight gain, hypertrichosis	Betamethasone dipropionate	High	Continuous	Diaper area	Scalp and perineal dermatitis	40	N/A
Milana-Martinez et al. (2018) [19]	F	3	Normal	Fever, cough, moon face, hair growth	Clobetasol propionate	Ultrahigh	Continuous	Whole body	Neck and diaper area erythematous plaque	N/A	3
Notay et al. (2018) [20]	F	72	Normal	Moon face	Clobetasol propionate	Ultrahigh	Continuous	Vulva	Vulvar lichen sclerosus	8	2
Üstebay et al. (2018) [21]	F	8	Abnormal	Weight gain, moon face, hypertrichosis, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	24	3
Fukuhara et al. (2017) [22]	F	108	Abnormal	Striae, weight gain, buffalo hump, moon face	Betamethasone sodium phosphate	Moderate	Continuous	Eyes	Iridocyclitis	24	6
Mahe´ (2017) [23]	M	108	N/A	Moon face	Betamethasone dipropionate, clobetasol propionate	Ultrahigh	Continuous	Palms	Palmoplantar psoriasis	8	Every other day
	M	84	N/A	Moon face	Clobetasol propionate	Ultrahigh	Continuous	Palms	Palmoplantar psoriasis	1.3	N/A
Rainsbury et al. (2017) [24]	M	180	N/A	Moon face, weight gain	Dexamethasone eye drops	low	Continuous	Eyes	Vernal keratoconjunctivitis	N/A	2
Ciccone et al. (2016) [25]	M	6	Abnormal	Poor growth, appetite loss, hair growth, moon face	Betamethasone valerate	High	Continuous	Neck	Neck dermatitis	16	2 to 3
Jevalikar et al. (2016) [26]	F	8	Abnormal	Hair growth, moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Hypopigmentation in diaper area	12	N/A
Kotrulja et al. (2015) [27]	F	36	Abnormal	Moon face, weight gain, buffalo hump, striae	N/A	High	Continuous	Whole body	Netherton syndrome	24	N/A
Nantarakchaikul et al. (2015) [28]	F	5	Abnormal	Moon face, weight gain, hair growth, buffalo hump	Triamcinolone acetonide	Moderate	Continuous	Whole body	Diaper dermatitis	6	3 to 4
Sahana et al. (2015) [29]	M	180	Abnormal	Weight gain, striae, fatigue, hypertrichosis, muscle weakness	Clobetasol propionate	Ultrahigh	Continuous	Whole body	Psoriasis	N/A	N/A
Demirsoy et al. (2014) [30]	F	156	Abnormal	Moon face, buffalo hump, striae	Clobetasol propionate	Ultrahigh	Continuous	Whole body	Psoriasis	240	N/A
Buluş et al. (2014) [31]	M	3	Abnormal	Weight gain, moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	6	2 to 3
	F	5	Abnormal	Weight gain, moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	6	3
	F	3.5	Abnormal	Moon face	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	4	2
Ozdemir et al. (2014) [3]	M	7	Abnormal	Cough, fever, moon face, hair growth, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	16	3 to 4
Rustowska et al. (2013) [32]	F	48	Abnormal	Moon face, hair growth, growth retardation, buffalo hump	Mometasone	Moderate	Continuous	Whole body	Dermatitis	N/A	N/A
Tiwari et al. (2013) [33]	F	5	N/A	Fever, cough, tachypnea, body swelling	Betamethasone	High	Continuous	Whole body	Seborrheic dermatitis	N/A	N/A
Tempark et al. (2010) [34]	F	8	Abnormal	Weight gain, moon face, hair growth, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	8 to 9
Tütüncüler et al. (2010) [35]	M	3	Abnormal	Weight gain, appearance change, moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	4	2 to 3
Al-Khenaizan et al. (2008) [36]	M	11	Normal	Moon face, hypertrichosis	Clobetasol propionate	Ultrahigh	Intermittent	Diaper area	Diaper psoriasis	28	N/A

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Table 1. Continued…

Rahmayunita et al. (2008) [38]	M	90	Abnormal	Moon face, striae, buffalo hump	Mometasone furoate, fluocinolone acetonide	Moderate	Continuous	Whole body	Psoriasis	168	3
Semiz et al. (2008) [39]	F	6	Abnormal	Weight gain, hypertrichosis, moon face	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	4 to 5
	F	5	Abnormal	Weight gain, moon face	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	18	3 to 4
Atabek et al. (2007) [40]	F	9	Abnormal	Weight gain, moon face, changes in appearance	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	24	3 to 4
	F	4	Normal	Weight gain, moon face, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	10	N/A
	M	8	Normal	Weight gain, moon face, buffalo hump	Diflucortolone valerate	Moderate	Continuous	Diaper area	Diaper dermatitis	16	4 to 5
Güven et al. (2007) [41]	M	3	Normal	Weight gain, moon face, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	6	N/A
	F	7	Normal	Weight gain, moon face, hypertrichosis, buffalo hump	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	N/A
	F	6	Abnormal	Appetite loss, edema	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	N/A
Simson et al. (2006) [42]	M	204	Abnormal	Dizziness, nausea, moon face, striae	Clobetasol and halobetasol propionate	Ultrahigh	Continuous	Scalp	Psoriasis	144	N/A
Güven et al. (2005) [43]	F	3	Abnormal	Discomfort, moon face, hypertrichosis, edema	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	8	5 to 6
Şiklar et al. (2004) [44]	F	9	Normal	Moon face, striae	Clobetasol propionate	Ultrahigh	Continuous	Diaper area	Diaper dermatitis	12	4 to 5
Joe (2003) [45]	M	11	N/A	Skin changes, weight gain, striae	Halobetasol propionate and betamethasone dipropionate	Ultrahigh	Continuous	Whole body	Psoriasis	N/A	N/A
Ruiz-Maldonado et al. (1982) [46]	M	28	Abnormal	Moon face, hypertrichosis, striae	Betamethasone valerate	High	Continuous	Neck, arm, pectoral area	Accidental burn	68	Once a week
Borzyskowski et al. (1976) [47]	M	3	Abnormal	Moon face	Betamethasone valerate	High	Continuous	Whole body	Eczema	12	2
	F	120	Abnormal	Moon face, striae, weight gain	Fluocinolone acetonide, betamethasone valerate	High	Continuous	Whole body	Non-bullous ichthyosiform erythroderma	> 24	1

N/A: non-available

Table 2. Laboratory findings, treatment, and outcome in each study.

Author (year) reference	**ACTH**	**Cortisol**	**NA$^+$/K$^+$**	**Adrenal gland status**	**Replacement therapy**	**Dose**	**Usage duration (Weeks)**	**Follow up**
Rai et al. (2023) [7]	Low	Low	Normal	Suppression	Prednisolone	7.5 mg	N/A	Recovery after 8 months
Tan (2023) [8]	Low	Low	N/A	N/A	Steroid-sparing UV phototherapy, Oral hydrocortisone	6 mg/m^2	N/A	Recovery after 6 months
Kuikel et al. (2022) [9]	N/A	Low	N/A	N/A	Permethrin lotion, prednisolone syrup	N/A,15 mg	6	Recovery after 3 months
Matejek et al. (2022) [5]	Low	UDB	Normal	Suppression	Oral hydrocortisone	9 mg/m^2	N/A	Recovery
	Low	UDB	N/A	Suppression	Decreasing the steroid dose	0.15 mg	4	Recovery after 2 months
Takaiwa et al. (2022) [10]	Normal	Low	Normal	Normal	Steroid (unknown type)	N/A	N/A	Recovery after 24 months
Ahmed et al. (2021) [1]	Low	Low	Normal	Normal	Oral hydrocortisone	10 mg/m^2	4	Recovery after 7 months
Ghirardo et al. (2021) [11]	Low	Low	N/A	Suppression	Only steroid discontinuation	N/A	N/A	Recovery
Katsura et al. (2021) [12]	Low	Low	N/A	Suppression	Only steroid discontinuation	N/A	N/A	Recovery after 3 months
Sachdeva et al. (2020) [13]	Normal	Low	N/A	N/A	Acitretin	50 mg	N/A	Recovery
Taylor et al. (2020) [14]	UDB	UDB	Normal	Suppression	Systemic fluconazole and topical clotrimazole cream, zinc oxide paste	N/A	N/A	Recovery after 5 months
Alkhuder et al. (2019) [4]	Low	Normal	N/A	Normal	Oral hydrocortisone	12 mg/m^2	6	Recovery
Sardesai et al. (2019) [15]	N/A	High	N/A	N/A	Oral hydrocortisone, beclomethasone dipropionate	N/A	N/A	Recovery
Ali et al. (2018) [2]	N/A	Normal	(+/-)	N/A	Selenium sulphide 2.5% with ketoconazole gel and ciclopirox	N/A	N/A	Recovery after 3 months
Çömlek et al. (2018) [16]	Normal	Normal	N/A	Normal	Zinc oxide	N/A	N/A	Recovery after 1 week
Estrada-Chávez et al. (2018) [17]	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
	N/A	N/A	N/A	N/A	Sulfur cream (4%)	N/A	N/A	Recovery
Hansen et al. (2018) [18]	N/A	N/A	N/A	N/A	Oral hydrocortisone	13 mg/m^2	24	Recovery after 12 months
Milana-Martinez et al. (2018) [19]	N/A	High	N/A	N/A	Fluid replacement and antibiotics	N/A	N/A	Died due to sepsis
Notay et al. (2018) [20]	N/A	N/A	N/A	Normal	Triamcinolone, Desonide, Pimecrolimus	N/A	8	Recovery
Üstebay et al. (2018) [21]	Low	Low	N/A	N/A	Oral hydrocortisone	10 mg/m^2	N/A	Recovery
Fukuhara et al. (2017) [22]	UDB	UDB	N/A	N/A	Methotrexate	N/A	24	Recovery after 6 months
Mahe´ (2017) [23]	N/A	N/A	N/A	N/A	Only steroid discontinuation	N/A	N/A	Recovery after 2 months
	N/A	N/A	N/A	N/A	Betamethasone dipropionate and calcipotriol	N/A	N/A	Recovery
Rainsbury et al. (2017) [24]	N/A	Low	N/A	N/A	Tacrolimus 0.1%	N/A	N/A	Recovery after 12 months
Ciccone et al. (2016) [25]	Low	Low	(-/+)	Suppression	Oral hydrocortisone	10 mg/m^2	8	Recovery after 3 months
Jevalikar et al. (2016) [26]	Low	Low	N/A	N/A	Oral hydrocortisone	6 mg/m^2	12	Recovery after 3 months

Table 2. Continued…

Nantarakchaikul et al. (2015) [28]	N/A	Low	Normal	Suppression	Steroid (unknown type)	N/A	N/A	N/A
Sahana et al. (2015) [29]	Low	Low	N/A	Suppression	N/A	N/A	N/A	N/A
Demirsoy et al. (2014) [30]	High	Low	N/A	Normal	Methotrexate and hydrocortisone acetate	7.5 and 8 mg/m^2	N/A	Recovery after two weeks
	Low	Low	Normal	N/A	Oral hydrocortisone	10 mcg/m^2	24	Recovery after 6 months
Buluş et al. (2014) [31]	Low	Low	Normal	N/A	Oral hydrocortisone	12 mg/m^2	N/A	N/A
	Normal	Low	N/A	Normal	Oral hydrocortisone	20 mg/m^2	N/A	Recovery after 2 months
Ozdemir et al. (2014) [3]	Normal	Low	N/A	Suppression	Oral hydrocortisone	7 mg/m^2	16	Recovery after 6 months
Rustowska et al. (2013) [32]	N/A	Low	Normal	Suppression	Oral hydrocortisone	8.5	12	Recovery
Tiwari et al. (2013) [33]	N/A	High	N/A	N/A	N/A	N/A	N/A	Died
Tempark et al. (2010) [34]	Low	Low	Normal	Suppression	Oral hydrocortisone	50 mg/m^2	<1	Recovery
Tütüncüler et al. (2010) [35]	Low	Low	N/A	N/A	Only steroid discontinuation	N/A	N/A	Recovery after 1 month
Al-Khenaizan et al. (2008) [36]	N/A	UDB	N/A	N/A	Topical 1% hydrocortisone and micon azole combination cream (Daktacort) and Pimecrolimus (Elidel)	N/A	N/A	Recovery after 8 months
Coureau et al. (2008) [37]	N/A	Low	N/A	N/A	Betamethasone dipropionate, mometasone furoate in combination with desonide, oral hydrocortisone	N/A	N/A	Recovery after 6 months
Rahmayunita et al. (2008) [38]	N/A	Normal	Normal	N/A	Acitretin	25 mg	5	Recovery after 8 months
	Low	Low	N/A	Suppression	N/A	N/A	N/A	Recovery
Semiz et al. (2008) [39]	Low	Low	N/A	Suppression	Hydrocortisone	N/A	N/A	Died due to disseminated CMV infection
Atabek et al. (2007) [40]	UDB	Low	Normal	Suppression	Oral hydrocortisone	N/A	N/A	Recovery after 7 months
	Low	Low	N/A	N/A	Oral hydrocortisone	15 mg/m^2	12	Recovery after 6 months
	Normal	Normal	N/A	N/A	Only steroid discontinuation	N/A	N/A	Partial recovery
Güven et al. (2007) [41]	Low	Low	N/A	N/A	Oral hydrocortisone	15 mg/m^2	N/A	Recovery after 3 months
	Low	Low	N/A	N/A	Oral hydrocortisone	30 mg/m^2	8	Partial recovery after 3 months
	Normal	Normal	N/A	N/A	Oral hydrocortisone	15 mg/m^2	N/A	N/A
Simson et al. (2006) [42]	Low	Low	N/A	Suppression	Oral hydrocortisone	N/A	N/A	N/A
Güven et al. (2005) [43]	Normal	Normal	Normal	Normal	Oral hydrocortisone	15 mg/m^2	N/A	Died due to disseminated CMV infection
Şiklar et al. (2004) [44]	Normal	Low	N/A	Suppression	N/A	N/A	N/A	N/A
Joe (2003) [45]	N/A	Low	N/A	N/A	Calcipotriene, ketoconazole, adapalene, tazarotene	N/A	N/A	Recovery
Ruiz-Maldonado et al. (1982) [46]	N/A	N/A	N/A	N/A	Proteolytic enzyme ointment, corticotropin	N/A	N/A	Recovery after 3 months
Borzyskowski et al. (1976) [47]	N/A	Normal	N/A	N/A	Topical hydrocortisone %1, emulsifying ointment	N/A	<1	Recovery after 2 months
	Low	Low	N/A	Suppression	Emulsifying ointment, cortisone acetate	25 mg	16	Recovery after 4 months

N/A: Non-available, ACTH: Adrenocorticotropic hormone, UDB: Undetectable, (+/-): (high/low), CMV: Cytomegalovirus

Main Findings

The mean age of the cases was 38.8 months, with quartile ranges from 5 to 48 months. There was a gender preference towards females (57.1%). Abnormalities in growth patterns were observed in approximately 75% of the cases. The most common clinical presentation was a "moon face" appearance in 74.6% of the cases, followed by weight gain (55.5%), striae (36.5%), facial or body hair growth (28.6%), and buffalo hump (27%). Clobetasol propionate, an ultrahigh potency steroid, was the most frequently used topical steroid, accounting for 54% of cases, while betamethasone, of moderate to high potency, was used in 35% of cases. The steroid was administered continuously in 88.9% of cases, with 39.7% applying it more than twice daily. The mean and median duration of steroid use was 25.4 and 12 weeks, respectively. The primary indication for steroid use was dermatitis (47.6%), followed by psoriasis (17.5%) and scabies (15.9%). The most common administration sites were the whole body (41.3%) and the diaper area (38.1%) (Table 3). Laboratory tests for adrenocorticotropic hormone (ACTH) and cortisol levels revealed low levels or undetected in 73% and 78% of cases, respectively. Among the 27 cases with defined adrenal status, 19 (70.4%) were found to have suppressed adrenal function. All cases had their initial steroid discontinued. Replacement therapy varied according to individual conditions, with oral hydrocortisone being the most common treatment (39.7%), followed by sulfur cream (12.7%). In five cases (7.9%), no replacement therapy was administered. Fifty-one cases (81%) recovered from the disease. Partial recovery was observed in 2 cases (3.2%), while four cases (6.3%) did not survive. The causes of death included disseminated cytomegalovirus (CMV) infection in two cases, sepsis in one case, and an unknown reason in the fourth case (Table 4).

Table 3. Summary of the patient demography, disease presentation and characteristics of the medication

Variables	Frequency / Percentage
Patient demography	
Age, months (mean, median [Q1-Q3])	38.8, 9 [5 - 48]
Sex	
Male	26 (41.3%)
Female	36 (57.1%)
N/A	1 (1.6%)
BMI/growth status	
Normal	9 (14.3%)
Abnormal	47 (74.6%)
N/A	7 (11.1%)
Symptoms/Presentation*	
Moon face	47 (74.6%)
Weight gain	35 (55.5%)
Striae	23 (36.5%)
Hair growth	18 (28.6%)
Buffalo hump	17 (27.0%)
Hypertrichosis	14 (22.2%)
Growth defect	8 (12.7%)
Body swelling/edema	5 (7.9%)
Fever	4 (6.3%)
Loss of appetite	3 (4.8%)
Cough	3 (4.8%)
Others	12 (19.0%)
Type of steroid/potency*	
Clobetasol propionate/ Ultrahigh	34 (54.0%)
Betamethasone/ Moderate to high	22 (35.0%)
Triamcinolone/ Moderate	3 (4.8%)
Mometasone/ Moderate	3 (4.8%)
Dexamethasone eye drops /Low	2 (3.2%)
Fluocinolone acetonide/ Moderate	2 (3.2%)
Halobetasol propionate/ Ultrahigh	2 (3.2%)
Others/ Low to moderate	4 (6.3%)
N/A	2 (3.2%)
Site of administration	
Whole body	26 (41.3%)
Diaper area	24 (38.1%)
Eyes	3 (4.7%)
Others	9 (14.3%)
N/A	1 (1.6%)
Purpose of use	
Dermatitis	30 (47.6%)
Psoriasis	11 (17.5%)
Scabies	10 (15.9%)
Others	12 (19.0%)
Regularity of use	
Continuous	56 (88.9%)
Intermittent	5 (7.9%)
N/A	2 (3.2%)
Usage duration, weeks (mean, median [Q1-Q3])	25.4, 12 [8 - 24]
Frequency of use, time/day	
Once a week	1 (1.6%)
Every other day	1 (1.6%)
Once	5 (7.9%)
Twice	9 (14.3%)
More than twice	25 (39.7%)
N/A	22 (34.9%)

Q1: First quartile, Q3: Third quartile, N/A; non-available, BMI: Body mass index
** For each case, multiple options may be present.*

4. Discussion

This condition is an endocrine disorder characterized by elevated levels of glucocorticoids in the bloodstream. It is classified into ACTH-dependent CS, which results from pituitary tumors or excessive ACTH administration, and ACTH-independent CS, which is due to adrenal tumors or excessive glucocorticoid intake. Typically, the pituitary gland releases ACTH, which stimulates cortisol production in the adrenal glands. However, prolonged use of exogenous corticosteroids can cause several adverse effects, such as suppression of the hypothalamic-pituitary-adrenal (HPA) axis, iatrogenic CS, severe infections, and growth failure [1,2]. The symptoms of iatrogenic adrenal insufficiency are often nonspecific and difficult to distinguish from other underlying conditions. As a result, clinicians and healthcare practitioners may not recognize these symptoms and might overlook them in their differential diagnoses. It is, therefore, essential to consider iatrogenic adrenal insufficiency in patients receiving any form of steroid treatment, particularly those presenting with iatrogenic CS [4]. While iatrogenic CS frequently arises from prolonged oral or parenteral corticosteroid use, it is rarely associated with topical corticosteroids [1,2]. The present systematic review revealed that only 63 cases of iatrogenic CS in pediatrics caused by topical corticosteroids have been published in legitimate

Table 4. Summary of the laboratory findings, treatment and outcome.

Variables	Frequency / Percentage
ACTH status[#]	
Normal	9 (24.3%)
Low	24 (64.9%)
Undetectable	3 (8.1%)
High	1 (2.7%)
Cortisol[#]	
Normal	8 (16.0%)
Low	34 (68.0%)
Undetectable	5 (10.0%)
High	3 (6.0%)
NA^+/ K^+[#]	
Normal	14 (87.5%)
Low	1 (6.3%)
High	1 (6.3%)
Adrenal gland status[#]	
Normal	8 (29.6%)
Suppressed	19 (70.4%)
Replacement therapy[*]	
Oral hydrocortisone	25 (39.7%)
Sulfur cream	8 (12.7%)
Only steroid discontinuation	5 (7.9%)
Topical hydrocortisone	3 (4.8%)
Pimecrolimus	2 (3.2%)
Desonide	2 (3.2%)
Zinc oxide	2 (3.2%)
Acitretin	2 (3.2%)
Prednisolone	2 (3.2%)
Steroid (unknown type)	2 (3.2%)
Methotrexate	2 (3.2%)
Betamethasone dipropionate	2 (3.2%)
Emulsifying ointment	2 (3.2%)
Others	16 (25.4%)
Follow up	
Recovery within a month	3 (4.8%)
Recovery within three months	11 (17.5%)
Recovery within six months	8 (12.7%)
Recovery within 12 months	9 (14.3%)
Recovery (unknown period)	20 (31.7%)
Partial recovery	2 (3.2%)
Died	4 (6.3%)
N/A	6 (9.5%)

ACTH: Adrenocorticotropic hormone
** For each case, multiple options may be present.*
 # The data is only for cases with available finding for the test

journals [1-5,7-47]. The first reported case dates back to 1972, with the most recent case published in August 2023 [7,47].

Infants under six months are particularly susceptible to iatrogenic CS from topical corticosteroids [4]. Most cases have been reported in infants with diaper dermatitis [1-4,10,14,16,18,21,25,28,31-35,39-41,43,44]. The likely reasons include greater body surface area, underdeveloped skin barrier, the occlusive environment of the diaper area, the naturally high absorption capacity of perineal skin, the atrophy of local skin caused by steroids, and increased absorption due to skin inflammation [4,14,31]. Additional factors that can raise the risk of developing the condition include the corticosteroid's potency and the quantity, frequency, and period of application [4,18,25].

The risk of adrenal suppression correlates with the dosage and duration of treatment. Similarly, the recovery period for adrenal axis functionality is proportional to the duration and severity of suppression and may take weeks or months [18]. Even small doses of a super potent topical steroid can reduce morning cortisol levels (due to HPA axis suppression) after only a few days of use, even on healthy skin. Therefore, potent and super-potent topical steroids should be avoided in patients under 12 years of age [25]. Topical steroid creams are categorized into seven classes, with Class 1 being the most potent and Class 7 the least potent [2]. Clobetasol is the corticosteroid most commonly used for treating diaper dermatitis and other conditions, followed by betamethasone. The average application duration needed to suppress cortisol and ACTH levels has been reported to be 2.75 months, ranging from 1 to 17 months [1]. Clobetasol propionate is 600 to 1,000 times more potent than hydrocortisone. Even relatively low doses (2g/day for two weeks) can lead to adrenal gland suppression [7]. Tempark et al., on reviewing 23 cases of iatrogenic CS caused by topical steroids in children, reported that most affected children were infants (86%), with clobetasol (82%) or betamethasone (18%) applied for an average of 2.75 months [34]. In the current study, the mean age of the reviewed cases was 38.8 months, with a quartile range of 5 to 48 months. The female gender was slightly more prevalent (57.1%), which may be attributed to a higher likelihood of dermatological issues in females [48]. Clobetasol propionate was the causative agent in 54% of the cases, followed by betamethasone types in 35%. Interestingly, in two cases, even low-potency topical corticosteroids, such as dexamethasone eye drops, caused the condition. This indicates that low-potency topical corticosteroids may also induce the disorder if misused. Almost 88.9% of the cases involved continuous steroid use, with 39.7% applying the medication more than twice a day. The mean duration of drug use was 6.4 months, indicating heavy exposure to the medication. These findings support the assumption that the frequency and duration of application play a vital role in developing the disease. The primary reason for topical corticosteroid administration was dermatitis (47.6%), followed by psoriasis (17.5%) and scabies (15.9%). The main application sites were the whole body (41.3%) and diaper area (38.1%), which enhanced steroid absorption.

The disease is typically manifested with moon face (facial puffiness), hirsutism, generalized body edema, weight gain, hypertension, buffalo hump, purple striae, and skin fragility [1]. Parents may overlook rapid weight gain as a symptom of developing a health issue in their infant because of the widespread notion that "a chubby baby is a healthy baby." This belief often results in reassuring and positive remarks from friends and family about the infant's appearance [17]. The primary disease manifestation in the reviewed cases was moon face appearance (74.6%), followed by weight gain (55.5%) and body striae (36.5%). The growth pattern or BMI was abnormal in nearly 75% of the cases.

Moreover, intensive use of topical corticosteroids can cause hypercortisolism, leading to immune system suppression. This immunosuppression increases the risk of opportunistic and bacterial infections [39]. Semiz et al. and Guven et al. reported two infant cases with fatal disseminated CMV infection associated with CS due to abuse of the clobetasol propionate

[39,43]. Hypercortisolism also adversely affects wound healing, potentially leading to recurrent or non-healing dermatitis and creating a persistent cycle of inflammation and impaired recovery [31].

There are no specific and definitive diagnostic methods for iatrogenic CS. However, the prolonged use of exogenous glucocorticoids can suppress ACTH secretion, reducing the body's need for endogenous cortisol production. Consequently, most cases of iatrogenic CS present with low levels of both ACTH and cortisol, which can facilitate diagnosis [4,16]. Management begins with discontinuing the corticosteroid causing the issue and administering physiological hydrocortisone [1]. Before starting steroid therapy, a low-dose ACTH stimulation test (1 μg/m²) may be used to evaluate adrenal suppression, as it offers greater sensitivity than the standard dose test (250 μg/m²) [31].

Topical corticosteroids have been an effective treatment for many mucocutaneous disorders for decades. In pediatrics, they and emollients continue to be the primary approach for managing eczema. It is crucial to avoid "corticophobia," a reluctance to use corticosteroids by some healthcare practitioners and patients, as it can lead to increased side effects, poor adherence to treatment, and suboptimal outcomes [25]. To prevent the onset of iatrogenic CS, clinicians should avoid prescribing high-potency corticosteroids for treating infantile dermatological disorders. Instead, they should opt for low-potency topical steroids. Parents should also be advised to avoid overusing these medications and apply only a thin layer to the affected areas [1]. Cortisol and ACTH were decreased or undetectable in 78% and 73% of the reviewed cases, respectively, and the adrenal gland function was suppressed in 70.4%. In all cases, the topical corticosteroids were discontinued. Oral hydrocortisone was used as replacement therapy in 39.7% of the cases, followed by sulfur cream in 12.7%. Only four patients died: two from disseminated CMV infection, one from sepsis, and one from an unknown cause.

5. Conclusion

Although topical corticosteroids effectively treat various dermatological diseases in pediatric patients, they can lead to unsatisfactory outcomes or side effects if not used properly. A specialist should supervise the drug administration, and parents need to be fully informed about the proper usage and potential side effects to avoid iatrogenic CS and other complications.

Declarations

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References

1. Ahmed SM, Ahmed SF, Othman S, Abdulla BA, Mohammed SH, Salih AM, et al. Topical corticosteroid-induced iatrogenic Cushing syndrome in an infant; a case report with literature review. Annals of Medicine and Surgery. 2021;71: 102978. doi:10.1016/j.amsu.2021.102978.
2. Zil-E-Ali A, Janjua OH, Latif A, Aadil M. Case of Iatrogenic Cushing's syndrome by Topical Triamcinolone. Journal of Ayub Medical College Abbottabad. 2018;30(1):121-3. doi: N/A.
3. Ozdemir A, Bas VN. Iatrogenic Cushing's syndrome due to overuse of topical steroid in the diaper area. Journal of Tropical Pediatrics. 2014;60(5):404-6. doi:10.1093/tropej/fmu036.
4. Alkhuder L, Mawlawi H. Infantile iatrogenic Cushing syndrome due to topical steroids. Case reports in pediatrics. 2019;2019(1):2652961. doi:10.1155/2019/2652961.
5. Matejek N, Hoos J, Holterhus PM, Bettendorf M, Choukair D. Topical glucocorticoid application causing iatrogenic Cushing's syndrome followed by secondary adrenal insufficiency in infants: two case reports. Journal of Medical Case Reports. 2022;16(1):455. doi:10.1186/s13256-022-03659-2.
6. Mohammed, K. K., Hama, J. I., & Kakamad, F. H. (2024). Beyond Beall's list: The need for contemporary evaluation tools in predatory publishing research. Learned Publishing, 37(2), 157-158. doi:10.1002/leap.1602
7. Rai A, Tamrakar R, Maskey R. Topical Corticosteroid-Induced Iatrogenic Cushing Syndrome in an Adolescent: A Case Report. Journal of Diabetes and Endocrinology Association of Nepal. 2023;7(1):33-8. doi:10.3126/jdean.v7i1.57458.
8. Tan TY. Case report: exogenous Cushing syndrome in a growing child following chronic topical steroids for familial psoriasis. Journal of the ASEAN Federation of Endocrine Societies. 2023 ;38(S2):86-7. doi: 10.15605/jafes.038.S2.135.
9. Kuikel S, Aryal S, Basnyat RS, Rimal S. Cushing Syndrome in a Pediatric Patient with Topical Steroid Overuse. Case Reports in Endocrinology. 2022;2022(1):8487737. doi: 10.1155/2022/8487737.
10. Takaiwa Y, Ichikawa G, Otsubo Y, Komori I, Ogawa M, Kano Y, et al. Iatrogenic Cushing Syndrome Caused by Long-term Use of High Potency Topical Steroid. Dokkyo Medical Journal. 2022;1(2):135-40. doi:10.51040/dkmj.1.2_135.
11. Ghirardo S, De Nardi L, Tommasini A, Barbi E, Tornese G. Topical clobetasol: an overlooked cause of Cushing syndrome. Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders). 2021;21(12):2300-2. doi:10.2174/1871530321666210426131423
12. Katsura M, Sato T, Morita K, Ishii T, Kishi K, Hasegawa T. Iatrogenic Cushing syndrome due to topical corticosteroids after skin graft surgery for giant nevus: A case report. Pediatric Dermatology. 2022;39(1):147-8. doi:10.1111/pde.14910.
13. Sachdeva S, Arora P, Kulhari A, Sardana K. Iatrogenic Cushing's syndrome due to topical steroid abuse in a child with Psoriasis presenting as septicaemia. Dermatologic therapy. 2020;33(4):e13514. doi:10.1111/dth.13514.
14. Taylor O, Mejia-Otero JD, Tannin GM, Gordon K. Topical triamcinolone induced Cushing syndrome: A case report. Pediatric dermatology. 2020;37(3):582-4. doi:10.1111/pde.14140.
15. Sardesai VR, Dhamale SS, Hegde SS. A case of iatrogenic Cushing syndrome secondary to application of topical corticosteroids. Indian Dermatology Online Journal. 2019;10(4):476-8. doi:10.4103/idoj.IDOJ_374_18

16. Özgüç Çömlek F, Örüm S, Aydın S, Tütüncüler F. Exogenous Cushing syndrome due to misuse of potent topical steroid. Pediatric dermatology. 2018;35(2):e121-3. doi:10.1111/pde.13409.
17. Estrada-Chávez G, Estrada R, Engelman D, Molina J, Chávez-López G. Cushing syndrome due to inappropriate corticosteroid topical treatment of undiagnosed scabies. Tropical Medicine and Infectious Disease. 2018;3(3):82. doi:10.3390/tropicalmed3030082.
18. Hansen SJ, Lacourt RP. Iatrogenic Cushing's syndrome in a infant due to prolonged use of topical corticosteroids. Case report. Revista chilena de pediatria. 2018;89(3):368-72. doi:10.4067/s0370-41062018005000302.
19. Milana-Martinez JK, Coo ER, Zabala DA, Tangtatco JA, Lacuesta-Gutierrez MP. A fatal case of staphylococcal scalded skin syndrome associated with iatrogenic Cushing syndrome due to potent topical steroid application in a 3-month-old female: A case report. Journal of the Philippine Dermatological Society. 2018;27(2):70-3. doi:N/A.
20. Notay M, Fazel N, Awasthi S. Cushing syndrome induced by topical corticosteroids for the treatment of lichen sclerosus. Journal of pediatric and adolescent gynecology. 2019;32(1):83-5. doi:10.1016/j.jpag.2018.09.004.
21. Üstebay S, Üstebay DÜ. Cushing's syndrome caused by topical steroid for treatment of diaper dermatitis: case report. Kafkas Journal of Medical Sciences. 2018;8(1):91-4. doi:10.5505/kjms.2017.64935.
22. Fukuhara D, Takiura T, Keino H, Okada AA, Yan K. Iatrogenic Cushing's syndrome due to topical ocular glucocorticoid treatment. Pediatrics. 2017;139(2): e20161233. doi:10.1542/peds.2016-1233.
23. Mahe´ E. Cushing's syndrome induced by high-potency topical corticosteroids in two children with palmoplantar psoriasis taking acitretin. Pediatric Dermatology. 2017 Mar;34(2):219-20. doi:N/A.
24. Rainsbury PG, Sharp J, Tappin A, Hussey M, Lenko A, Foster C. Ritonavir and topical ocular corticosteroid induced Cushing's syndrome in an adolescent with HIV-1 infection. The Pediatric Infectious Disease Journal. 2017;36(5):502-3. doi:10.1097/INF.0000000000001534.
25. Ciccone S, Marini R, Bizzarri C, El Hachem M, Cappa M. Cushing's syndrome in a 6-month-old boy: a rare side-effect due to inadequate use of topical corticosteroids. Acta Derm Venereol. 2016;96(1):138-9. doi:10.2340/00015555-2151.
26. Jevalikar G. Exogenous Cushing Syndrome due to Topical Clobetasone use for diaper rash. Indian Pediatrics. 2016; 53: 76. doi:N/A.
27. Kotrulja L, Bulić SO, Zakanj Z, Sabolić LL. Iatrogenic Cushing syndrome and adrenocortical insufficiency from topical steroids in a girl with Netherton syndrome-case report. Paediatrics Today. 2015;11(2):186-7. doi:10.5457/p2005-114.127.
28. Nantarakchaikul P, Nimdet K. An infantile exogenous Cushing syndrome caused by topical steroid. International Journal of Pediatric Endocrinology. 2015;2015(Suppl 1): 45. doi:10.1186/1687-9856-2015-S1-P45.
29. Sahana PK, Sarma N, Sengupta N, Somani PS. A florid case of iatrogenic Cushing's syndrome induced by topical steroid with osteoporosis and hypogonadism. Indian Journal of Dermatology. 2015;60(4):420. doi:10.4103/0019-5154.160514.
30. Demirsoy EO, Bilen N, Aktürk AS, Kocaoğlu Ö, Mutlu GY. Cushing's syndrome induced by high-potency topical corticosteroids. International Journal of Dermatology. 2014;53(1):1-79. doi:N/A.
31. Buluş AD, Andıran N, Koçak M. Cushing's syndrome: hidden risk in usage of topical corticosteroids. Journal of Pediatric Endocrinology and Metabolism. 2014;27(9-10):977-81. doi:10.1515/jpem-2013-0262.
32. Rustowska A, Wilkowska A, Nowicki R. Iatrogenic Cushing syndrome due to topical glicocorticosteroid therapy. Dermatol Online J. 2013 Oct 1;4(4):503-5. doi:10.7241/ourd.20134.129.
33. Tiwari A, Goel M, Pal P, Gohiya P. Topical-steroid-induced iatrogenic Cushing syndrome in the pediatric age group: a rare case report. Indian journal of endocrinology and metabolism. 2013;17(Suppl1):S257-8. doi:N/A
34. Tempark T, Phatarakijnirund V, Chatproedprai S, Watcharasindhu S, Supornsilchai V, Wananukul S. Exogenous Cushing's syndrome due to topical corticosteroid application: case report and review literature. Endocrine. 2010; 38:328-34. doi:10.1007/s12020-010-9393-6.
35. Tütüncüler F, Tekin M, Balcı D, Şahaloğlu Ö. Iatrogenic Cushing syndrome due to topical steroid administration in an infant. Balkan Medical Journal. 2010;2010(2):95-7. doi:N/A.
36. Al-Khenaizan S, Al Alwan I. Topical steroid-induced Cushing syndrome. Annals of Saudi Medicine. 2008;28(4):300-2. doi:10.5144/0256-4947.2008.300.
37. Coureau B, Bussières JF, Tremblay S. Cushing's syndrome induced by misuse of moderate-to high-potency topical corticosteroids. Annals of Pharmacotherapy. 2008;42(12):1903-7. doi:10.1345/aph.1L067.
38. Rahmayunita G, Pulungan AB, Wiryadi BE, Wisesa TW, Sugito TL, Boediardja SA. Cushing's syndrome induced by misuse of topical corticosteroids in a child with psoriasis vulgaris. Medical Journal of Indonesia. 2008;17(4):281. doi:N/A.
39. Semiz S, Balcı YI, Ergin Ş, Candemir M, Polat A. Two Cases of Cushing's Syndrome Due to Overuse of Topical Steroid in the Diaper Area . Pediatric dermatology. 2008;25(5):544-7. doi:10.1111/j.1525-1470.2008.00735.x.
40. Atabek ME. Cushing's syndrome following topical administration in an infant: case report. Reactions. 2007; 1156:16. doi:10.2165/00128415-200711560-00035.
41. Güven A, Gülümser Ö, Özgen T. Cushing's syndrome and adrenocortical insufficiency caused by topical steroids: misuse or abuse?. Journal of Pediatric Endocrinology and Metabolism. 2007;20(11):1173-82. doi:10.1515/JPEM.2007.20.11.1173.
42. Simson GG, Kohn B, Axelrod FB. Cushing syndrome from topical foam steroid use in an adolescent male. Clinical pediatrics. 2006;45(1):97-100. doi:10.1177/000992280604500118.
43. Güven A, Karadeniz S, Aydin O, Akbalik M, Aydin M. Fatal disseminated cytomegalovirus infection in an infant with Cushing's syndrome caused by topical steroid. Hormone research. 2005;64(1):35-8. doi:10.1159/000087288.
44. Şiklar Z, Bostanci I, Atli Ö, Dallar Y. An infantile Cushing syndrome due to misuse of topical steroid. Pediatric dermatology. 2004;21(5):561-3. doi:10.1111/j.0736-8046.2004.21508.x.
45. Joe EK. Cushing syndrome secondary to topical glucocorticoids. Dermatology Online Journal. 2003;9(4):16. : N/A.
46. Ruiz-Maldonado RA, Zapata G, Tamayo L, Robles C. Cushing's syndrome after topical application of corticosteroids. American Journal of Diseases of Children. 1982;136(3):274-5. doi:10.1001/archpedi.1982.03970390088024.
47. Borzyskowski M, Grant DB, Wells RS. Cushing's syndrome induced by topical steroids used for the treatment of non-bullous ichthyosiform erythroderma. Clinical and experimental dermatology. 1976;1(4):337-42. doi:10.1111/j.1365-2230.1976.tb01440.x.
48. Andersen LK, Davis MD. Sex differences in the incidence of skin and skin-related diseases in Olmsted County, Minnesota, United States, and a comparison with other rates published worldwide. International journal of dermatology. 2016;55(9):939-55. doi:10.1111/ijd.13285.