

# Clinical Indications and Abuse of Corticosteroids: A Narrative Review

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## ABSTRACT

Corticosteroids are lifesaving drugs; however, their abuse has been noted in general population. The objectives of the review were to highlight the adverse effects after prolonged use and abuse of corticosteroids. The review covers the period of 2000-2023. After extracting information from over 76 articles and evaluating their quality, data was presented as PRISMA diagram. The main adverse effects appear after abuse or prolonged use of corticosteroids are immune suppression, osteoporosis, weight gain, stunted growth in children, glucose intolerance, hypertrichosis, acne, telangiectiasis, hypertension, mood disorder, rosacea, peri-oral dermatitis, fibrosis of renal, cardiac and vascular cells, hormonal-disturbances, cataract, glaucoma and prolong use in COVID-19 patients enhanced the mortality. Mostly corticosteroids were used as a fairness cream for a long time without medical supervision. Despite corticosteroids' clinical benefits, their abuse as fairness cream is not justified. Therefore, the general public has to be educated about the adverse effects associated with corticosteroid prolongation and abuse. A coordinated strategy is required among patients, physicians and pharmacists to stop the mistreatment of topical corticosteroids.

**Keywords:** Corticosteroids, abuse, adverse effects, awareness, legitimate indication.

## INTRODUCTION

Corticosteroid drugs are often inexpensive and their prolonged use has been noted in the general population with various adverse effects [1]. Long-term usage of corticosteroids has resulted in weight gain, osteoporosis, hypertension, diabetes mellitus, cataracts, dyspepsia, and mental health issues [2, 3]. In general; patients hardly know about prescription medications [4]. The majority of patients are ignorant of the drug's recommended use, adverse effects, and caution [4]. The causes of abuse and prolonged use of corticosteroids can be divided into three categories: systemic (the hospital doesn't have any pharmacists), patient-related (patient illiteracy, lack of specific labeling on medications for patients who cannot read), and health management related (increased workload, inadequate time and attention provided by authentic professionals to patients); these factors significantly contributed in patients' understanding and awareness of drugs [4].

Most organ systems e.g. musculoskeletal, gastrointestinal, cardiovascular, endocrine, neuropsychiatric, dermatologic, ophthalmic, and immunologic are affected by abuse and prolonged use of corticosteroids [5]. Outcomes of abuse and prolonged use included hypertension and dyslipidemia [6]. It is also recommended that during the first two to three days of treatment with a medium-high dose of glucocorticoids; glycemic levels should be assessed in the morning,

lunch postprandial or dinner pre-prandial [7]. If the patient has a risk factor of type II diabetes; glycemic levels should be assessed even in cases when low doses of corticosteroids are prescribed [7]. Unexpected hyperglycemia appears as a result of the start of glucocorticoids, which frequently results in hospital admissions and/or extended hospital stays, elevated infection risks, and diminished graft function in recipients of solid organ transplanted patients [8]. According to one reference, serious complications associated with hyperglycemia due to prolonged use of corticosteroids might lead to hospitalization, extended hospital stays, or recurrent ER visits [9]. Glucocorticoids increase hepatic gluconeogenesis and decrease the absorption of glucose by peripheral tissues like muscle cells and adipocytes might result in hyperglycemia [10, 11].

Abuse of mineralocorticoids also results in promoting peritoneal, cardiac, vascular, and renal fibrosis [12]. Corticosteroids can be given orally, topically, and IV; as compared to topical or inhaled corticosteroids, oral and IV corticosteroids are more likely to have side effects since they are absorbed systemically [13]. It is thought that prolonged abuse of steroids will result in more side effects; oral prednisolone prescriptions exceeding 5 mg are classified as high doses and longer treatment periods exceed one month [13]. Their abuse potential is high because they offer quick symptom alleviation in dermatoses [14] occasionally used as a depigmenting agent in cosmetic procedures [1] some general practitioners prescribe topical steroids for all skin rashes with extended periods, which exacerbates the adverse effects of these medications [1]. Topical Corticosteroids (TC) abuse in patients with facial dermatoses is also

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quite common [15]. TC use as a fairness cream is also the most common abuse [14]. Serious negative repercussions associated with prolonged use of topical corticosteroids are rebound erythema, burning, and scaling [16]. This disorder has been called “topical steroid-dependent face” (TSDf) [16]. Orthopedic surgeons and primary care physicians frequently use intra-articular corticosteroid injections to alleviate knee discomfort related to osteoarthritis (OA) [17]. Meta-analyses have indicated that intra-articular use only provides relief for up to six weeks [15].

Corticosteroid therapy (CST) has been used mostly in acute respiratory conditions, which gives the same pathological features as COVID-19 diseases like Severe Acute Respiratory Syndrome (SARS-CoV), Middle East Respiratory Syndrome (MERS-CoV) and community-acquired pneumonia (CAP), as well as in H1N1 influenza [18]. Corticosteroids have been linked to delay in viral clearance, their use was not advised early in the COVID-19 pandemic except for concurrent conditions such as Acute respiratory distress syndrome (ARDS) and septic shock [19]. A large randomized trial found that treating patients with severe and critical COVID-19 with dexamethasone improves survival [18]. In a retrospective cohort analysis of hospitalized patients with positive SARS-CoV-2, it was demonstrated that more than 10 days usage of corticosteroids was associated with a higher risk of in-hospital death compared to 10 days of therapy [20].

Corticosteroids can cause a wide range of adverse psychological side effects (APSE), from moderate mood swings, emotional instability, and cognitive impairments to severe psychotic symptoms such as auditory hallucinations or persecution delusions [21]. Literature mentioned that depressive symptoms are typically induced by prolonged treatment [22]. The most frequent side effects of short-term corticosteroid medication are euphoria and hypomania, however, other potential consequences included are confusion, delirium, and even psychosis [22]. A significant portion of individuals take corticosteroids at night, which results in severe adrenal suppression [23]. Ayurvedic, homeopathic, and unknown or other category of drugs were found to have a different percentage of steroids; regarding which neither patient nor prescriber might be aware and unnecessarily patient is exposed to steroids [24].

Writing a review on the present subject is mainly aimed to highlight the adverse effects associated with abuse and prolonged use of corticosteroids in the general population, which can lead to a range of adverse outcomes. It's crucial to emphasize that Corticosteroids should only be used under the guidance and supervision of a healthcare professional and according to prescribed regimens. Many patients in Pakistani society still use steroids without medical consultation.

## METHODOLOGY

To write an in-depth review, literature was collected from the year 2000 to 2023. Collected articles were more than 50; articles focused on the reasons for using corticosteroids in the general population and knowledge about their adverse outcomes if used for a long time. The relevant literature was gathered from PubMed, Google Scholar, PakMediNet, the National Database of Indian Medical Journals, African Journals Online (AJOL), Science Direct, BMJ (British Medical Journals), Karger, Indian Journal of Clinical Biochemistry, The Academy of Psychosomatic Medicine, Europe PMC, National Library of Medicine, Dove Press, Research Gate, Journal of the National Medical Association, American Society of Regional Anesthesia and Pain Medicine, Journal of translational internal medicine. Keywords and truncation techniques were used for the collection of the literature. More than 70 publications about the uses and abuses of corticosteroids were obtained; they were selected based on appropriate information, quality, data, and presentation of the results. The whole process followed the PRISMA flow diagram (Fig. 1) [25]. The quality of literature is classified by the GRADE (Grading of Recommendation Assessment, Development, and Evaluation) criteria [26, 27].

### Inclusion Criteria

Literature was obtained for all those diseases where corticosteroids were clinically indicated particularly for chronic diseases, literature about awareness of corticosteroids adverse effects published from 2000 to 2023.

### Exclusion Criteria

Published literature before the year 2000. Corticosteroids were prescribed for acute conditions.

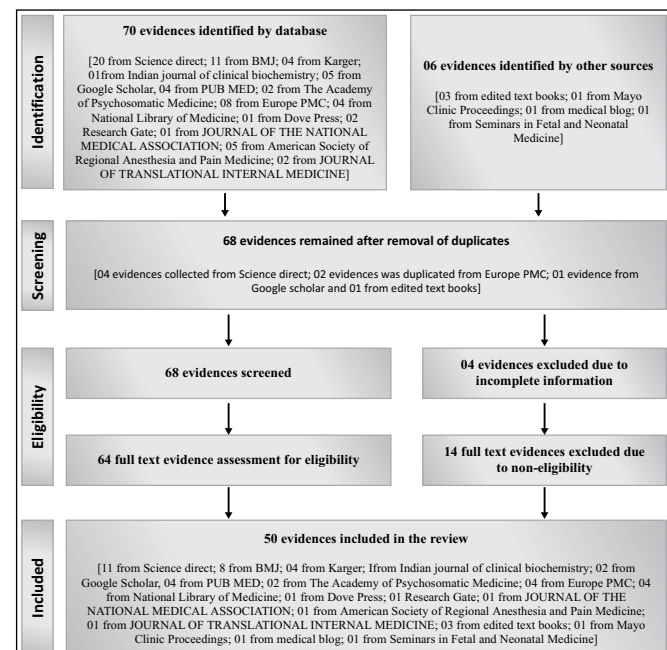


Fig. (1): PRISMA flow diagram.

**Table 1:** Studies pertaining to the use and abuse of corticosteroids and their outcomes.

S. No.	Types of Corticosteroids & Routes of Administration	Study Year	Study Design	Sample Size	Aim of Study	Outcomes	Quality of Evidence
1	Topical corticosteroids	2014	Cross-sectional study	6723	Examination of abuse and adverse effects of corticosteroids	Telangiectasia and acne were the main adverse effects reported due to misuse of topical corticosteroids [1].	High
		2006	Cross-sectional study	414	Evaluation of complications associated with topical steroids use.	Main complications reported with the use of 9 years median duration were hypertrichosis (13.9%), mycosis (40.4%), acne (45.3%), telangiectasis (21.3%), diabetes mellitus (2.1%) and facial hyperpigmentation (37.2%) [14].	Moderate
2	Oral corticosteroids in children	2011	Prospective multicenter Cross-sectional study	2926	Study the clinical features of topical corticosteroid abuse on the face.	Misuse reported as fairness cream (29%), acne (24%), 90.5% of individuals had adverse effects such as exacerbation of acne, telangiectasis, rosacea, hirsutism, hypopigmentation, perioral dermatitis and Tinea incognita [16].	High
3	Dexamethasone IV	2016	Systematic review of 22 RCTs	3200	Identify the risks of adverse effects	Reported adverse effects of the abuse of corticosteroids were vomiting, increased blood pressure, weight gain, behavioral changes, sleep disturbance and hypothalamic pituitary adrenal axis suppression [2].	Moderate
4	Dexamethasone	2011	Double-blind, randomized, and dose response trial	98	Investigation of efficacy, dose response and safety of dexamethasone in radicular pain.	Efficacy and safety were found satisfactory of all doses of dexamethasone; however, statistically non-significant adverse outcomes were weight gain, behavioral changes, hyperglycemia and edema [28].	High
5	Glucocorticoids	2008	Case series study	271	Corticosteroid-induced Diabetes occurrence in COPD patients.	Corticosteroids (methylprednisolone) can cause hyperglycemia in the chronic use of COPD patients; therefore, it's important to strike a balance between the risks and the benefits [11].	Moderate
6	Glucocorticoids	2008	Multicenter Cross-sectional study	400	Investigations of occurrence of hypertension due to medium-dose glucocorticoid therapy over an extended period in patients of rheumatoid arthritis.	Hypertension was significantly (p=0.028) prevalent in 85.7% of patients exposed to glucocorticoids for extended periods [29].	High
7	Mineralocorticoid	2023	Case-crossover study	508	Flare-up risk of rheumatoid arthritis while tapering the dose of glucocorticoid.	It was noted that there was a high chance of a flare-up while tapering to dosages of less than 2.5 mg/day [30].	Moderate
8	Prednisolone or Dexamethasone	2014	Review article	74	Investigation of SGK-1 Sensitive Inflammation and Tissue Fibrosis after use of mineralocorticoids.	Mineralocorticoids may enhance the fibrosis of renal, cardiac, peritoneal and vascular muscles. It also fosters inflammation [12].	Low
9	Intra-articular corticosteroids (IACs)	2016	Review article	373	Investigations of anti-inflammatory responses in cancer patients.	Dexamethasone may be frequently used for cancer pain management due to its high potency; however, it may suppress the immune system and individuals are prone to infections rapidly [31].	Low
10	Prolonged corticosteroids (methylprednisolone) use	2019	Randomized control trials	684	Evaluation of knee osteoarthritis after IACs use.	Continuous use of IACs may raise the probability of knee radiographic osteoarthritis advancement [15].	High
11	Intra-articular corticosteroids (IACs)	2021	Randomized Trials	4313	Determination of the link between corticosteroid use and mortality in Covid-19 infection	Corticosteroids may perform well and reduce mortality if used seven days after admission to the hospital of COVID-19 positive patient; however, more than seven days use may enhance mortality [32].	Moderate
12	Prolonged corticosteroids (methylprednisolone) use	2023	Retrospective cohort study	1539	Investigate the differences between COVID-19 patients treated with short-term and long-term corticosteroid treatment.	In hospitalized COVID-19 patients, a longer corticosteroid treatment regimen was linked to increased death. The higher risk of death is associated with prolonged use of steroids i.e. 30 days [20].	High
13	Corticosteroids alternative medicine	2000	Original report	120	Determination of the proportion of steroid positive in homeopathic, ayurvedic, and other medicinal products.	38.32% of alternative medicines contained corticosteroids used for the treatment of arthritis and asthma. Ayurvedic preparation was found to have 41.70% steroids, 18.30% homeopathic and 31.70% in other unknown category of drugs [24].	Low

## FINDINGS AND RESULTS OF REVIEW

The class of corticosteroids, route of administration, study design, objective of study, outcomes, and quality of study are mentioned in Table 1.

## DISCUSSION

It is now a bleak reality that corticosteroids can have adverse consequences that are dose- and time-dependent [33]. In the physiological state; adrenal glands cortex produce corticosteroids [34]. Adrenal cortex produces two different forms of naturally occurring corticosteroids: mineralocorticoids and glucocorticoids [28]. All steroids in the body are produced from a cholesterol moiety by a strictly controlled enzymatic biosynthesis process [35]. In numerous body tissues and organs including liver, skin epidermis, brain, and prostate, additional alterations in the steroid structure and its consequent activity may transpire [36].

On the other hand, the chronic low-to-moderate dosage of a glucocorticoid may also result in several significant adverse effects such as osteoporotic fracture in up to 40% of patients [34]. Mineralocorticoids also enhance the renal excretion of potassium, calcium, and phosphate in replacement of sodium, so they can cause fluid retention, edema, weight gain, hypertension, and arrhythmias [12]. Since arthritis is a prevalent chronic autoimmune illness, it requires long-term care with steroid-based medications, therefore adverse effects are inevitable [37]. Corticosteroids are used for a variety of diseases, which are frequently referred to the terms dermatoses and steroid-responsive disorders [34]. Although corticosteroids are considered life-saving medication; however, it is also recognized that their abuse or prolonged use may also produce major adverse effects [34]. These adverse effects included skeletal muscular atrophy, fluid retention, mental disorders, insulin resistance, myopathy, osteonecrosis, hypertension, glaucoma, and gastric ulcer disease [3].

Psychotic or mixed emotional states, mania, sadness, cognitive impairments, and mild psychiatric problems (anxiety, sleeplessness, irritability, and mood swings) are prevalent mental disorders caused by corticosteroids [38]. These psychiatric issues frequently show up as behavioral modifications in youths [22]. Due to this reason, it is recommended that when the patient is on long-term corticosteroid therapy; must be kept at an effective dose of SSRIs (Selective Serotonin Reuptake Inhibitors) [22]. Corticosteroid use in the short and long term has been associated with cognitive impairments [22]. Short-term treatments are associated with reversible diminution of hippocampus neurons and are suggestive of hippocampal dysfunction [22]. Risk evaluation and mitigation (REM) should be applied to individuals who experience mental health issues while taking corticosteroids because of their risk of suicide ideation [39]. REM is also necessary because mental relapses from psychosocial stresses are not uncommon

and preventive measures are necessary [40]. Since younger patients are more prone to experience psychotic features and recurrences of corticosteroid-induced mood disorders, hence more care should be given [38]. Psychiatrists ought to counsel other medical practitioner [40] on corticosteroid treatment regimens, particularly the effects of prolonged use of steroid pulse therapy [40].

Corticosteroids can induce chronic issues in COVID-19 patients, although they minimize immediate symptoms of COVID-19 [41, 42]. Findings of the current review in COVID-19 patients regarding prolonged use of corticosteroid treatments were linked to a higher probability of mortality, hence it is advisable for hospitalized COVID-19 patients to receive corticosteroid therapy for the shorter period until randomized controlled trial results fill the gap of this knowledge [20]. Furthermore, its usage is restricted due to potential adverse effects, such as the appearance of black fungus in India among steroid-treated COVID patients [42]. In this study, it is recommended that severely sick COVID-19 patients receive low doses of corticosteroids under the care of knowledgeable medical professionals [42].

Topical corticosteroids are used to treat chronic inflammatory skin diseases; however, their efficacy, safety, tolerability, and adverse effects vary according to several factors, including potency, the preparation type, organic dilute solutions, quantity used, size of the addressed body surface, frequency of implementation, the location, patient age, applied technique, and state of the skin barrier [43]. The emergence of an unexpected dermatosis may not only be a medical but also a social issue because of the development of steroid dermatitis as a result of the self-application of local steroids as cosmetic cream [44]. In children with moderate chronic asthma when present with an acute exacerbation of their condition, it is advised to use an oral corticosteroid dosage of 1mg/kg daily; however, benefits are equivalent to side effects and are unpleasant [45]. Fortunately, an interview of parents of the children, who took corticosteroids mentioned that after cessation of oral steroid medication, behavior issues disappeared [45].

Hepatomegaly is another adverse effect observed in children receiving 2-4 mg/kg of prednisone daily for whole one week [45]. Although the use of corticosteroids and their association with hepatotoxicity is weak, the mechanism and clinical implications are not fully understood [46]. Injury to the liver has been seen by several workers receiving large doses of methylprednisolone [46]. Steroidal medications might potentially cause oxidative stress and induce hepatotoxicity in human systems [47]. Many researches and investigations have demonstrated that patients, pharmacists, and practitioners themselves may abuse topical steroids [44]. In many countries including Pakistan, steroids are accessible easily to patients without medical prescription; e.g. despite being prohibited by the Federal Ministry of Health, topical

steroids are easily acquired without a prescription in the majority of African nations, including Nigeria [15]. This easy access by patients further increases the potential for abuse of corticosteroids.

In addition, it has been reported that due to the poor quality control systems, certain alternative medicines are available in the market for the treatment of acute and chronic diseases; however, their analysis revealed that these medications contained corticosteroids [24]. Roughly one-third of the population on corticosteroids suffer adrenal insufficiency; this condition is more common among patients who have been exposed to high doses and prolonged corticosteroid therapies [48]. Patients who get corticosteroid medication for 14 to 21 days typically do not experience hypothalamic-pituitary axis suppression, so there is no need for them to follow a tapering schedule when stopping treatment [30]. It is important to note that, there is no widely acknowledged ideal regimen; nonetheless, tapering is necessary if the therapy has been going on for longer than three weeks [34]. When prescribing glucocorticoid to patients with diabetes mellitus, it should be considered that it may cause hyperglycemia [49]. Therefore, when managing diabetic patients with corticosteroids; it is imperative to regularly check blood glucose levels throughout corticoid treatment [11]. In addition, hypoglycemia should be taken into consideration by the physician when reducing or stopping corticosteroids [9, 48].

### RECOMMENDATIONS

The general public has to be educated and aware of the adverse effects of prolonged corticosteroid use [50]. Controlling the OTC (Over-the-Counter) availability of topical corticoids is a solution [50]. A coordinated strategy is required among patients, physicians and pharmacists to stop abuse of topical corticosteroids [50]. Steroids must be used under medical supervision for legitimate indications. Due to strong potency, extended duration of action, and low mineralocorticoid impact; dexamethasone appears to be the most viable option for managing cancer pain [31]. Crohn's and Colitis Foundation of America views steroid-free remission as an ideal outcome for treatment [32]. Prolonged corticosteroid use increases hospital-acquired infections and also lengthens the duration of antibiotics needed [20].

### CONCLUSION

Corticosteroids have many clinical benefits; however, their abuse and prolonged use may result in adverse effects. In many clinical conditions, the use of corticosteroids is not recommended, however, their abuse by patients may produce adverse effects, e.g. as a fairness cream. Clinicians should also take precautions and monitor the patients while on corticosteroids because of their potential for causing hepatotoxicity, hyperglycemia, hypertrichosis, psychosis, depression, osteonecrosis, osteoporosis, muscular atrophy, hypertension, glaucoma and peptic ulcer disease.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

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### REFERENCES

1. Dey VK. Misuse of topical corticosteroids: A clinical study of adverse effects. *Indian Dermatol Online J* 2014; 5(4): 436-40. DOI: <https://doi.org/10.4103/2229-5178.142486>
2. Aljebab F, Choonara I, Conroy S. Systematic review of the toxicity of short-course oral corticosteroids in children. *Arch Dis Child* 2016; 101(4): 365-70. DOI: <https://doi.org/10.1136/archdischild-2015-309522>
3. Van Raalte D, Diamant M. Steroid diabetes: from mechanism to treatment. *Neth J Med* 2014; 72(2): 62-72.
4. Shetty YC, Vinchurkar P, More S, Siddiqui A, Tilak S, Ginodia S, et al. Knowledge and awareness regarding corticosteroids and effectiveness of a novel steroid educational module among people visiting general OPD of a tertiary care hospital. *Indian J Pharmacy Practice* 2022; 15(1): 40-45. DOI: <http://dx.doi.org/10.5530/ijopp.15.1.8>
5. Oray M, Abu Samra K, Ebrahimiadib N, Meese H, Foster CS. Long-term side effects of glucocorticoids. *Expert Opin Drug Saf* 2016; 15(4): 457-65. DOI: <https://doi.org/10.1517/14740338.2016.1140743>
6. Sholter DE, Armstrong PW. Adverse effects of corticosteroids on the cardiovascular system. *Can J Cardiol* 2000; 16(4): 505-11.
7. Perez A, Jansen-Chaparro S, Saigi I, Bernal-Lopez MR, Miñambres I, Gomez-Huelgas R. Glucocorticoid-induced hyperglycemia. *J Diabetes* 2014; 6(1): 9-20. DOI: <https://doi.org/10.1111/1753-0407.12090>
8. Hwang JL, Weiss RE. Steroid-induced diabetes: a clinical and molecular approach to understanding and treatment. *Diabetes Metab Res Rev* 2014; 30(2): 96-102. DOI: <https://doi.org/10.1002/dmrr.2486>
9. Panthakalam S, Bhatnagar D, Kliemiuk P. The prevalence and management of hyperglycaemia in patients with rheumatoid arthritis on corticosteroid therapy. *Scott Med J* 2004; 49(4): 139-41. DOI: <https://doi.org/10.1177/003693300404900407>
10. Clore JN, Thurby-Hay L. Glucocorticoid-induced hyperglycemia. *Endocr Pract* 2009; 15(5): 469-74. DOI: <https://doi.org/10.4158/EP08331.RAR>
11. Tryfon S, Papanas N. Corticosteroid-induced diabetes in patients with chronic obstructive pulmonary disease: brief review. *Clin Pulm Med* 2008; 15(3): 127-31. DOI: <https://doi.org/10.1097/CPM.0b013e318170f82e>
12. Artunc F, Lang F. Mineralocorticoid and SGK1-sensitive inflammation and tissue fibrosis. *Nephron Physiol* 2014; 128(1-2): 35-9. DOI: <https://doi.org/10.1159/000368267>
13. Mundell L, Lindemann R, Douglas J. Monitoring long-term oral corticosteroids. *BMJ Open Qual* 2017; 6(2): 01-9. DOI: <https://doi.org/10.1136/bmjopen-2017-000209>
14. Nnoruka E, Okoye O. Topical steroid abuse: its use as a depigmenting agent. *J Natl Med Assoc* 2006; 98(6): 934.
15. Zeng C, Lane N, Hunter D, Wei J, Choi H, McAlindon T, et al. Intra-articular corticosteroids and the risk of knee osteoarthritis progression: results from the Osteoarthritis Initiative. *Osteoarthr Cartil* 2019; 27(6): 855-62. DOI: <https://doi.org/10.1016/j.joca.2019.01.007>
16. Saraswat A, Lahiri K, Chatterjee M, Barua S, Coondoo A, Mittal A, et al. Topical corticosteroid abuse on the face: A prospective, multicenter study of dermatology outpatients. *Indian J Dermatol*

- Venereol Leprol 2011; 77(2): 160-6.  
DOI: <https://doi.org/10.4103/0378-6323.77455>
17. Law TY, Nguyen C, Frank RM, Rosas S, McCormick F. Current concepts on the use of corticosteroid injections for knee osteoarthritis. *Phys Sportsmed* 2015; 43(3): 269-73.  
DOI: <https://doi.org/10.1080/00913847.2015.1017440>
  18. Tlayjeh H, Mhish OH, Enani MA, Alruwaili A, Tleyjeh R, Thalib L, *et al.* Association of corticosteroids use and outcomes in COVID-19 patients: a systematic review and meta-analysis. *J Infect Public Health* 2020; 13(11): 1652-63.  
DOI: <https://doi.org/10.1016/j.jiph.2020.09.008>
  19. Johns M, George S, Taburyanskaya M, Poon YK. A review of the evidence for corticosteroids in COVID-19. *J Pharm Pract* 2022; 35(4): 626-37.  
DOI: <https://doi.org/10.1177/0897190021998502>
  20. Viana MV, Pellegrini JAS, Perez AV, Schwarz P, da Silva D, Teixeira C, *et al.* Association between prolonged corticosteroids use in COVID-19 and increased mortality in hospitalized patients: a retrospective study with inverse probability of treatment weighting analysis. *Crit Care* 2023; 27(1): 01-9.  
DOI: <https://doi.org/10.1186/s13054-023-04434-5>
  21. Munjampalli SKJ, Davis DE. Medicinal-Induced Behavior Disorders. *Neurol Clin* 2016; 34(1): 133-69.  
DOI: <https://doi.org/10.1016/j.ncl.2015.08.006>
  22. Warrington TP, Bostwick JM, editors. Psychiatric adverse effects of corticosteroids. *Mayo Clin Proc* 2006; 81(10): 1361-7.  
DOI: <https://doi.org/10.4065/81.10.1361>
  23. Dyer O. Iraqi healthcare system still crippled five years after invasion, says report. *BMJ* 2008; 1-12.  
DOI: <https://doi.org/10.1136/bmj.39461.651921.4E>
  24. Gupta S, Kaleekal T, Joshi S. Misuse of corticosteroids in some of the drugs dispensed as preparations from alternative systems of medicine in India. *Pharmacoepidemiol Drug Saf* 2000; 9(7): 599-602.  
DOI: <https://doi.org/10.1002/pds.553>
  25. Lindsey WT, Olin BR, Hansen RA. Systematic review and meta-analysis. In: *Principles of Research Design and Drug Literature Evaluation*. 2nd ed. Aparasu RR, Bentley JP, Eds. USA: McGraw-Hill Education 2020; pp.151-60.  
DOI: <https://doi.org/10.1111.98074578/PRS>
  26. Alonso-Coello P, Schünemann HJ, Moher J, Brignardello-Petersen R, Akl EA, Davoli M, *et al.* GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. *BMJ* 2016; 353(1): 1-10.  
DOI: <https://doi.org/10.1136/bmj.i2016>
  27. Schwingshackl L, Rüschemeyer G, Meerpohl J. How to interpret the certainty of evidence based on GRADE (Grading of Recommendations, Assessment, Development and Evaluation). *Urologe A* 2021; 60(1): 444-54.  
DOI: <https://doi.org/10.1007/s00120-021-01471-2>
  28. Ahadian FM, McGreevy K, Schulteis G. Lumbar transforaminal epidural dexamethasone: a prospective, randomized, double-blind, dose-response trial. *Reg Anesth Pain Med* 2011; 36(6): 572-8.  
DOI: <https://doi.org/10.1097/AAP.0b013e318232e843>
  29. Panoulas VF, Douglas KM, Stavropoulos-Kalinoglou A, Metsios GS, Nightingale P, Kita M, *et al.* Long-term exposure to medium-dose glucocorticoid therapy associates with hypertension in patients with rheumatoid arthritis. *Rheumatology* 2008; 47(1): 72-5.  
DOI: <https://doi.org/10.1093/rheumatology/kem311>
  30. Adami G, Fassio A, Rossini M, Bertelle D, Pistillo F, Benini C, *et al.* Tapering glucocorticoids and risk of flare in rheumatoid arthritis on biological disease-modifying antirheumatic drugs (bDMARDs). *RMD Open* 2023; 9(1): 1-5.  
DOI: <https://doi.org/10.1136/rmdopen-2022-002792>
  31. Lossignol D. A little help from steroids in oncology. *J Transl Intern Med* 2016; 4(1): 52-4.  
DOI: <https://doi.org/10.1515/jtim-2016-0011>
  32. Ho KS, Narasimhan B, Difabrizio L, Rogers L, Bose S, Li L, *et al.* Impact of corticosteroids in hospitalised COVID-19 patients. *BMJ Open Respir Res* 2021; 8(1): 1-8.  
DOI: <https://doi.org/10.1136/bmjresp-2020-000766>
  33. Huscher D, Thiele K, Gromnica-Ihle E, Hein G, Demary W, Dreher R, *et al.* Dose-related patterns of glucocorticoid-induced side effects. *Ann Rheum Dis* 2009; 68(7): 1119-24.  
DOI: <https://doi.org/10.1136/ard.2008.092163>
  34. Yasir M, Goyal A, Sonthalia S. *Corticosteroid Adverse Effects*. Treasure Island (FL): StatPearls Publishing 2022.
  35. Katzung BG, Masters SB, Trevor AJ. *Basic and Clinical Pharmacology*. 16th Ed. USA: McGraw-Hill Education 2009.
  36. Cole TJ, Short KL, Hooper SB, Eds. *The science of steroids*. *Semin Fetal Neonatal Med* 2019; 24(3): 170-75.  
DOI: <https://doi.org/10.1016/j.siny.2019.05.005>
  37. Mateen S, Moin S, Zafar A, Khan AQ. Redox signaling in rheumatoid arthritis and the preventive role of polyphenols. *Clin Chim Acta* 2016; 463(1): 4-10.  
DOI: <https://doi.org/10.1016/j.cca.2016.10.007>
  38. Bolanos SH, Khan DA, Hanczyc M, Bauer MS, Dhanani N, Brown ES. Assessment of mood states in patients receiving long-term corticosteroid therapy and in controls with patient-rated and clinician-rated scales. *Ann Allergy Asthma Immunol* 2004; 92(5): 500-5.  
DOI: [https://doi.org/10.1016/S1081-1206\(10\)61756-5](https://doi.org/10.1016/S1081-1206(10)61756-5)
  39. Halper J. Corticosteroids and behavioral disturbances. In: *Principles of Corticosteroid Therapy*. Lin AN, Paget SA, Eds. London: Arnold 2002; pp. 174-201.
  40. Wada K, Yamada N, Sato T, Suzuki H, Miki M, Lee Y, *et al.* Corticosteroid-Induced psychotic and mood disorders: diagnosis defined by DSM-IV and clinical pictures. *Psychosomatics* 2001; 42(6): 461-6.  
DOI: <https://doi.org/10.1176/appi.psy.42.6.461>
  41. Langarizadeh MA, Tavakoli MR, Abiri A, Ghasempour A, Rezaei M, Ameri A. A review on function and side effects of systemic corticosteroids used in high-grade COVID-19 to prevent cytokine storms. *EXCLI J* 2021; 20(2): 339-65.  
DOI: <https://doi.org/10.17179/excli2020-3196>
  42. Akter F, Araf Y, Hosen MJ. Corticosteroids for COVID-19: Worth it or not? *Mol Biol Rep* 2022; 49(1): 567-76.  
DOI: <https://doi.org/10.1007/s11033-021-06793-0>
  43. Böckle BC, Jara D, Nindl W, Aberer W, Sepp NT. Adrenal insufficiency as a result of long-term misuse of topical corticosteroids. *Dermatology* 2014; 228(4): 289-93.  
DOI: <https://doi.org/10.1159/000358427>
  44. Rathi S. Abuse of topical steroid as cosmetic cream: a social background of steroid dermatitis. *Indian J Dermatol* 2006; 51(2): 154-5.  
DOI: <https://doi.org/10.4103/0019-5154.26949>
  45. Kayani S, Shannon DC. Adverse behavioral effects of treatment for acute exacerbation of asthma in children: a comparison of two doses of oral steroids. *Chest* 2002; 122(2): 624-8.  
DOI: <https://doi.org/10.1378/chest.122.2.624>
  46. Reuß R, Retzlaff K, Vogel S, Franke F, Oschmann P. Autoimmune hepatitis after high-dose intravenous methylprednisolone pulse in RR-MS. *Open Med* 2007; 2(3): 356-9.  
DOI: <https://doi.org/10.2478/s11536-007-0025-3>
  47. Tiwari P, Singh N, Sharma B. Long term treatment of corticosteroids may cause hepatotoxicity and oxidative damage: a case controlled study. *Ind J Clin Biochem* 2023; 39(1): 179-87.  
DOI: <https://doi.org/10.1007/s12291-023-01127-2>
  48. Nicolaides NC, Pavlaki AN, Maria Alexandra MA, Chrousos GP. *Glucocorticoid Therapy and Adrenal Suppression*. South Dartmouth (MA): MDText.com, Inc. 2000.
  49. Liu X-x, Zhu X-m, Miao Q, Ye H-y, Zhang Z-y, Li Y-m. Hyperglycemia induced by glucocorticoids in nondiabetic patients: a meta-analysis. *Ann Nutr Metab* 2014; 65(4): 324-32.  
DOI: <https://doi.org/10.1159/000365892>
  50. Kumar S, Goyal A, Gupta YK. Abuse of topical corticosteroids in India: Concerns and the way forward. *J Pharmacol Pharmacother* 2016; 7(1): 1-5.  
DOI: <https://doi.org/10.4103/0976-500X.179364>