

## Physicians Perception towards Corticosteroids as Therapeutic Agent: A Survey

Hemakshi E. Chaudhari<sup>1</sup>, Hiren R. Panchmiya<sup>1</sup>, Sameer N. Goyal<sup>2</sup>, \*Chandragouda R. Patil<sup>2</sup>

1. Department of Clinical Pharmacy, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule, Maharashtra, India.

2. Department of Pharmacology, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule, Maharashtra, India.

### ABSTRACT

We surveyed 224 physicians including allopaths, surgeons and physician trained in complementary and alternative therapies (Ayurveda and Homeopathy) to systematically explore their perceptions about the corticosteroids as therapeutic agents by administering a questionnaire to allopaths and physician of complementary and alternative medicines to appraise their understanding about indications for corticosteroids, alternate day therapy, tapering of doses after prolonged use, need of concurrent calcium supplements and advice to be given to the patients while on corticosteroids. This survey reveals that 80% alternative therapeutics prescribe corticosteroids as compared to the allopathic physicians which are about 27.67%. About 24.53% of allopathic physicians showed concern to reporting adverse reactions as compared to about 13.8% the alternative physician. About 22.05% of the allopathic physicians who are post-graduated only could arrange the steroids in right order of potency, whereas only 33.87% of allopathic physicians and a meager 35.29% of alternative therapeutics could do this. The corticosteroid preferred for respiratory diseases were prednisolone, budesonide a dexamethasone by post-graduated allopaths, post-graduate allopathic pediatricians and alternative therapeutics respectively. On an average, 63% of the physicians advocated tapering of steroid therapy upon prolonged use. There were inconsistencies in the suggested indications for corticosteroids. The perceptions of physicians as revealed in this survey highlight the need of a handy reference about the clinical data on corticosteroids that may enable the physicians to rationally use corticosteroids. Personal interviews with the physicians and their replies to this survey have generated important data on the physician's perceptions of steroid use.

**Keywords:** Advice to patients, alternate day therapy, corticosteroids, handy reference, potency, prescribing pattern, tapering of doses

Received 07 Oct 2014

Received in revised form 28 Jan 2015

Accepted 09 Feb 2015

### \*Address for correspondence:

**Dr. Chandragouda R. Patil,**

Professor and HOD,

Department of Pharmacology, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Dhule, Maharashtra, India.

E-mail: pchandragouda@yahoo.com

### INTRODUCTION

Corticosteroids are commonly prescribed by medical practitioners in many specialties for the treatment of autoimmune and chronic inflammatory conditions ranging from common cold to cancer [1, 2]. Owing to striking and apparently curative effects of steroids, physicians tend to routinely prescribe them to attract patients to their clinics [3]. This generally involves irrational use of corticosteroids in non-indicated disease conditions. During prolonged use of corticosteroids in pulmonary disease, Septic shock, chronic skin diseases, toxic

epidermal necrolysis, and rheumatoid arthritis [4-9], there is a need of judicious selection of dosage regimen and tapering of doses while ceasing the treatment [10]. Steroid therapy is always associated with multiple drug interactions, adverse effects and super infections [11]. With the increasing number and types of corticosteroids available to clinicians, there is a need to better understand current prescribing practices. There is an alarming up rise in the prescription of steroids by

physicians trained in complementary and alternative therapies.

Jan SU conducted a study to observe the irrational use of steroids. Twenty-nine pharmacies were randomly selected in various areas of the Province and 321 prescriptions of those patients with complaints of arthritis or lower back pain were evaluated for use of steroids. A total of 103 out of 321 prescriptions (about 30 %) were containing corticosteroids and the patients were using these steroids mostly in an irrational manner. These prescriptions were prescribed by medical practitioners of all specialties including orthopedics. A small number of non medical doctors (about 2%) were also responsible for the steroids prescriptions. He concluded that developing countries has a need for strict regulations for steroid prescriptions [4]. Nash et al analyzed the medical malpractice of corticosteroids and concluded that the most common conditions for which steroids were prescribed were pain (23%), asthma or another pulmonary condition (20%), a dermatologic condition (18%), a no dermatologic autoimmune condition (17%), and allergies (6%). Allegation of negligent use was the most common reason for a suit being filed (65%), followed by lack of proper informed consent (36%), failure to diagnose or misdiagnosis (22%), multiple allegations (25%), and wrongful death (4%) [12].

Searing et al. found that vitamin D level decreases due to increased corticosteroid use in children's with asthma [13]. An educational campaign for physicians is warranted to improve the practice for the prevention of this treatable complication. Several studies indicate educating patients about prescription drug therapy is becoming an increasingly important aspect of health care [14]. Physician adherence to standard guidelines is critical in translating recommendations into improved outcomes. However, numerous obstacles in prescription guidelines are physician's attitude, lack of agreement, self-efficacy, outcome expectancy, inertia of previous practice and external barriers [15]. Ungprasert et al. conducted a study to determine the awareness of prescribers in therapeutic use of corticosteroids. The total

no of patients receiving corticosteroids is 499 and specialties of physicians that prescribed corticosteroid treatment is 449. It was concluded that the physicians were less concerned about the osteoporosis induced by the corticosteroids [16].

Hence, present survey aimed to explore the perceptions of allopaths and therapists of complementary and alternative medicines regarding the therapeutic use of corticosteroids. The survey targeted to decide whether there is a need of quick reference guide for the physicians to rational use of corticosteroids and to determine the trends in therapeutic use of glucocorticoids, possibilities of overdosing, adverse events and unreasonable use of glucocorticoids. In this study, fact sheet is planned to prepare regarding clinical use of glucocorticoids that can be used by physicians as a bench top reference while prescribing glucocorticoids.

#### **METHODOLOGY**

In present study, information on physicians' perception on therapeutic use of corticosteroids was collected through direct interview with individual physicians in their clinics followed by filling up of a questionnaire. Care was taken to note physician's expectations from the clinical pharmacists, supportive staff, and patients regarding proper use of corticosteroids. The questionnaire was designed in such a way that one could fill in the information through marking the options given below each question and could also write elaborative details if needed. For convenience of comparison of trends, the physicians were divided into different groups depending upon their qualifications and specializations as post-graduates in allopathic Medicine (MD-medicine), post-graduates in allopathic pediatric medicines (MD- pediatricians), post-graduates in allopathic medicine and surgery (MS), graduates in allopathic medicines and surgery (general practitioners) and physicians of alternative therapies (mainly Ayurveda referred as alternate therapists). Total 350 physicians from the Dhule and Nashik districts of Maharashtra State were contacted for this survey out of which 224 responded. During its preparation, the questionnaire was scrutinized by selected

physicians for its suitability and scientific relevance. The questions which retrieved important information were highlighted in the questionnaire using different font colors so as to emphasize the importance of answering them. The finalized pamphlet questionnaire included those points on physician's perceptions and understanding on therapeutic use of corticosteroids which could expose patients to irrational prescriptions of corticosteroids and their adverse effects.

#### **Questions included in the Pamphlet**

The pamphlet included questions of various aspects of steroid use such as;

- Frequency per day of prescriptions including corticosteroids.
- Indications for which corticosteroids are prescribed by individual practitioner.
- Treatment duration after which tapering of steroids dose should be considered to avoid withdrawal symptoms?
- Potency of corticosteroids and their relevance to activity or adverse effects.
- Frequently encountered adverse effect during corticosteroids use by patients treated by individual prescriber.
- Justification of alternate day therapy during chronic corticosteroids use
- Need of concurrent calcium supplement for patients on long term steroid therapy
- Advice to be given to the patients while prescribing corticosteroids.
- Need of 'steroid cards' for patients on steroid therapy.
- Expectation from clinical pharmacists during therapeutic use of corticosteroids

Information related to prescription pattern, irrational use and frequency of prescription of particular drug was also collected with respect to above points. The question regarding frequency of prescription of corticosteroids in daily practices is introduced to determine the usage of corticosteroids in daily practices by number of physicians belonging to different specialties. To analyze irrational prescription of corticosteroids, we enlisted some non-indicated conditions the questionnaire to determine the percentage of physicians who may tend to prescribe steroids in such conditions. The reason is to

determine whether the corticosteroids are used in indicated disease condition or not. Most of the physicians do not consider the potency of the corticosteroids while prescribing them. Hence, we included a list of corticosteroids and requested physicians to state the rank of each drug in a descending order of potency. Need of tapering in corticosteroid therapy is to reduce the relapse of disease and to avoid rebound disturbance in the HPA axis [16]. We intended to determine whether physicians consider tapering of steroid therapy properly as per standard guidelines [17]. Advice to the patient in corticosteroids prescription is essential to reduce adverse effects, misuse of corticosteroids, and compliance of patient. The question is asked to determine the commonly given advices to the patient by the physicians while prescribing corticosteroids and to compare these advices with standard guidelines about prescribing corticosteroid [18]. The personal interviews with physicians were to inform them about the aims and objectives of study. The opinions collected were analyzed and are presented in graphical format as percent frequency of responses by physicians.

#### **RESULT**

On the basis of clinical survey related to use of corticosteroid it was observed that all the physicians irrespective of their speciality, prescribed corticosteroids at least to one patient in a day. The extent of corticosteroids to be prescribed by the physicians is shown in (Fig. 1).

The most interesting finding was that the physicians trained in alternative therapies, mainly in Ayurveda (who were contacted in this study) prescribed the corticosteroids most frequently that (>3 prescriptions/day) as compared to the physicians trained as allopath (<2 prescription/day). The average number of prescriptions per day in case of alternative therapists was more than three. In the next part of the study, we collected the opinion of number of physicians towards precautions while administering the corticosteroid. The data regarding this fact was given in (Fig. 2).

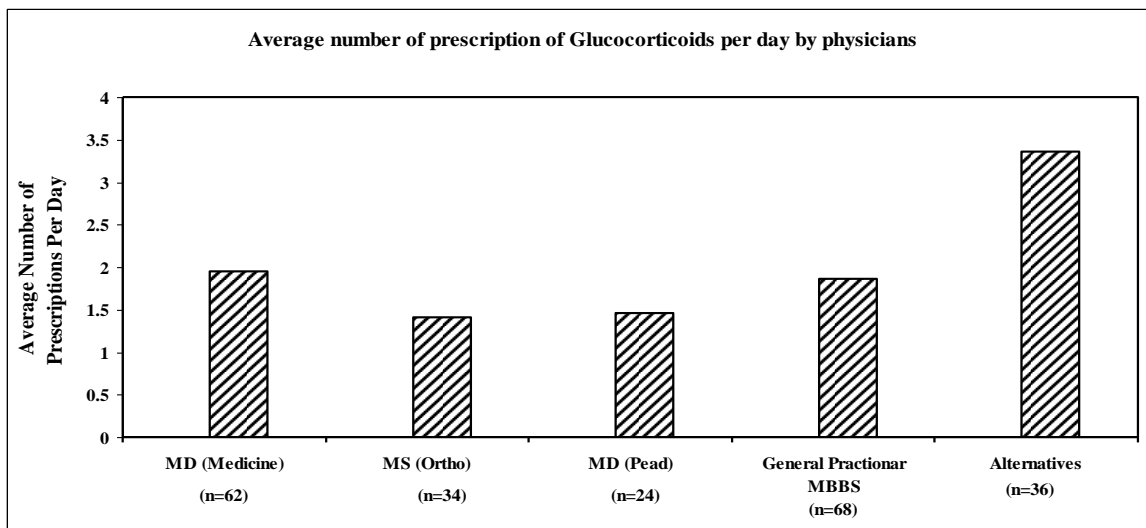


Figure 1: Average prescription corticosteroids in daily practice

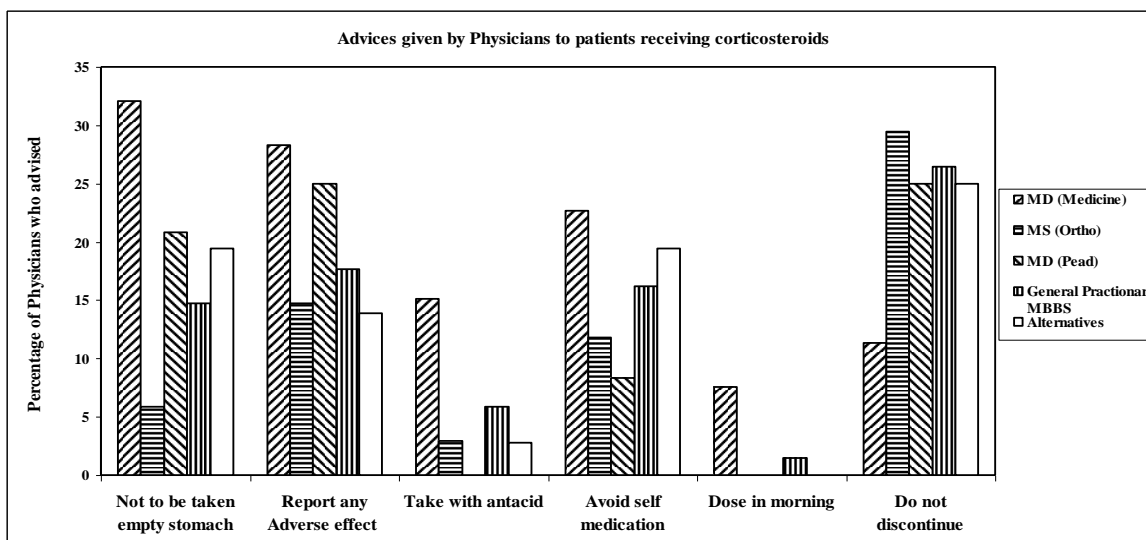


Figure 2: Advice to patient while prescribing corticosteroids in prescription

(Fig. 2) explained that physicians qualified as MD medicine shown more concern about reporting of adverse reactions and appeared to be educating their patients regarding the administration, adverse effect and precaution to be taken by the patients while on corticosteroids all physicians opined that self-medication by the patients must be avoided as far as corticosteroids are concerned. In comparison with other physicians, about 15% of physicians trained as MD medicine given advice to patients to take antacid along with corticosteroids. Actual information on the potency of the different corticosteroid drugs is necessary while prescribing the same. Considering this need we tried to estimate the percentage of doctors who could correctly

arrange different corticosteroids in the descending order of their potency. The data regarding this was given in (Fig. 3). It was observed that majority of the alternative physicians (35.29%) arranged drugs according to their potency in correct manner. This percentage decreased from alternative physician to 33.87% physicians trained as MD Medicine, 33.33% MD Pediatrics, 22.05% MD general practitioner and 11.76% MD (Orthopedics) could arrange the corticosteroid according to its potency. The next part of our study was common ADR due to use of corticosteroids. The ADR data regarding use of corticosteroids was presented in (Fig. 4).

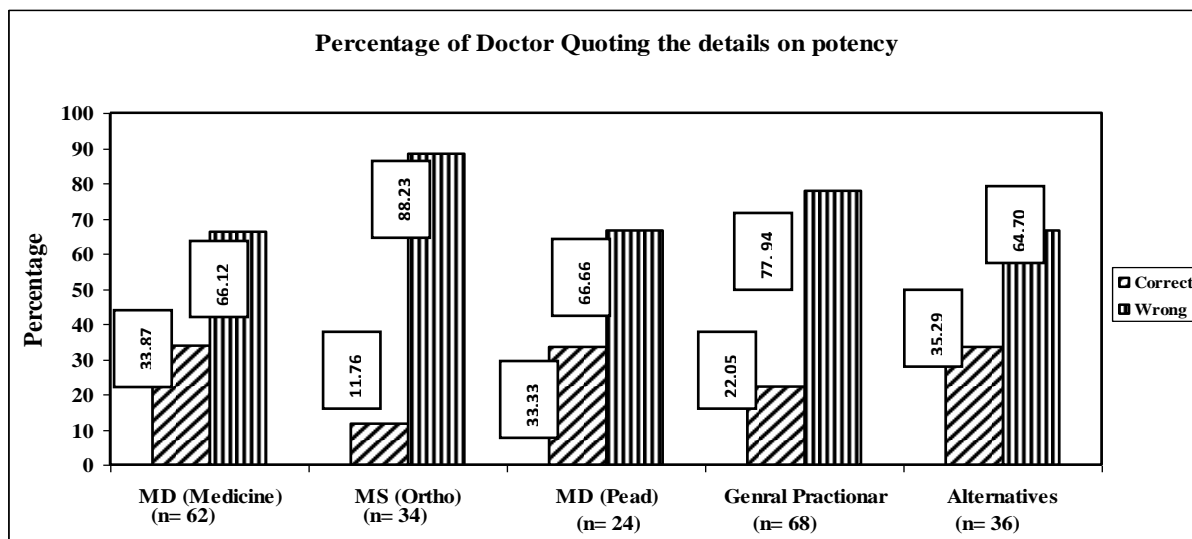


Figure 3: Percentage of doctors recognizing the correct potency of corticosteroids

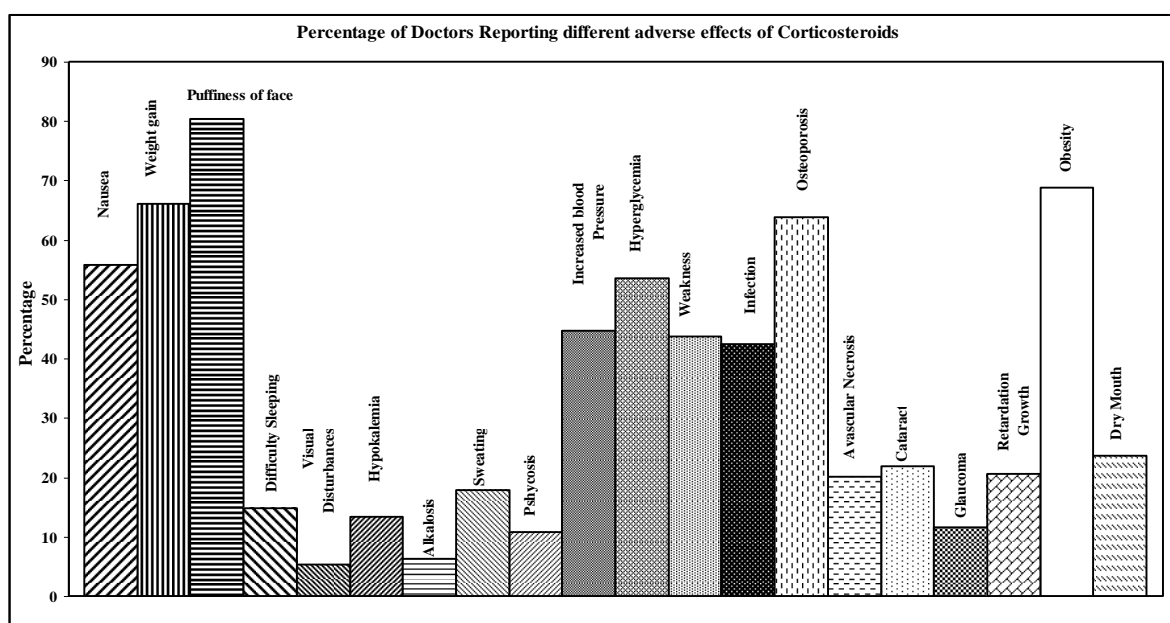


Figure 4: Frequently encountered adverse effects of corticosteroid

The most common ADR to be reported puffiness of face by 85% physicians, obesity by 70% Physicians, weight gain and osteoporosis by 68% physicians, nausea by 60%.

We tried to estimate the percentage of physicians who justified the alternate day therapy for corticosteroids and correctly stated the reason for the same. Awareness of Physicians on alternate day therapy of corticosteroids was shown in (Fig. 5). Largest percentage (47.2 %) of the alternate therapists appeared to be non-supportive to alternate day therapy and could not state

the reason for accepting the alternate day regime.

As per the comments entered in the questionnaire, the major role of clinical pharmacist as expected by the physicians was to inform the patients about adverse effects of the corticosteroids and provide additional counseling to the patients on corticosteroids. Apart from this physicians expected from clinical pharmacists to prepare the dosing charts suggesting proper use of corticosteroids. This is depicted in (Fig. 6).

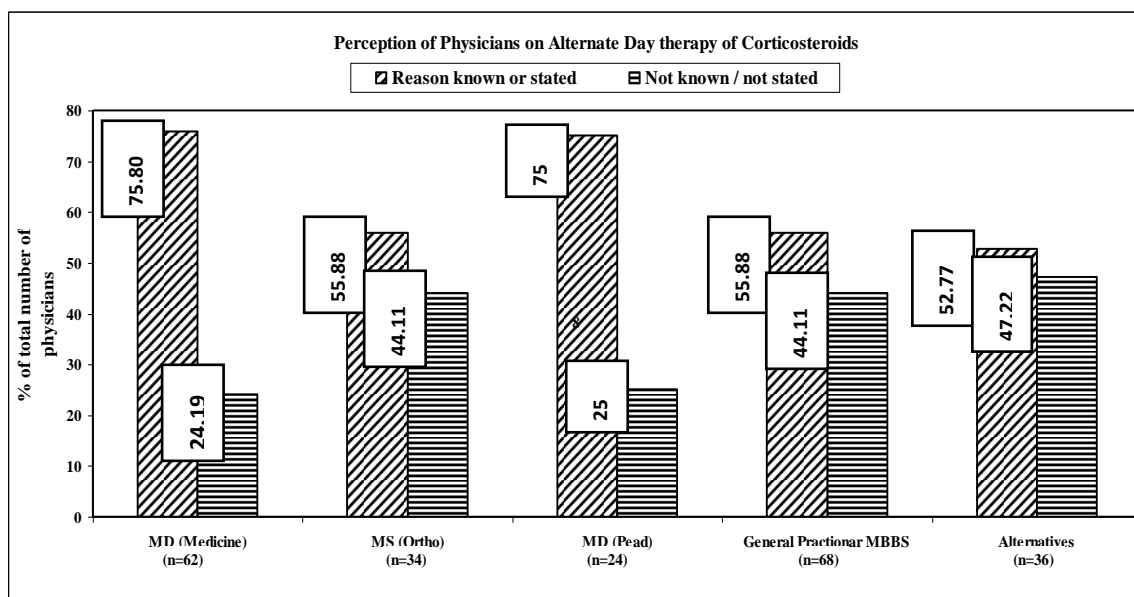


Figure 5: Awareness of Physicians on alternate day therapy of corticosteroids

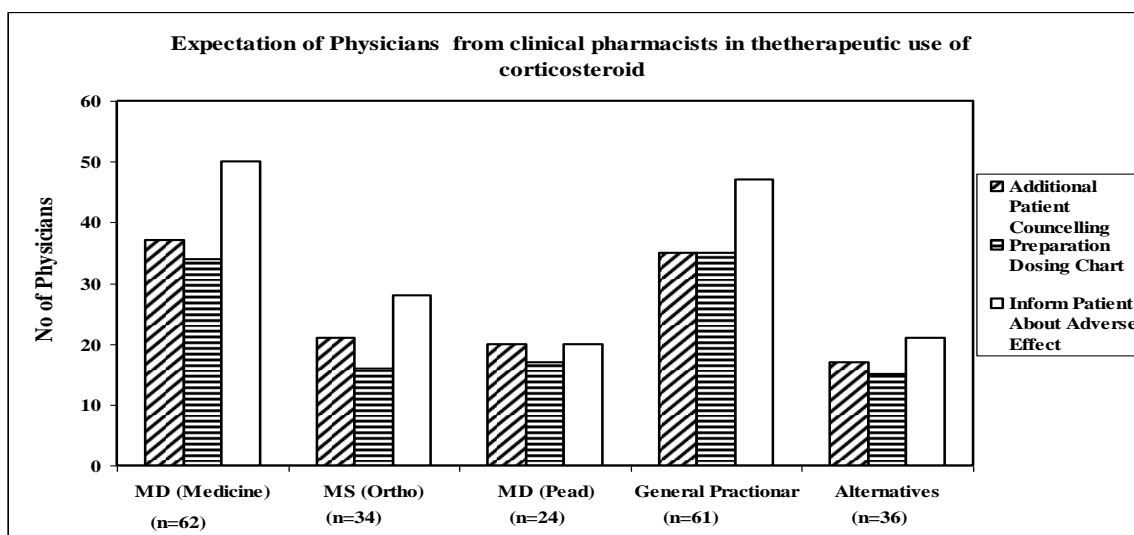


Figure 6: Expectation from clinical pharmacist in corticosteroids prescription

The practice of prescribing corticosteroids in non-indicated conditions like fever, cough, common cold, viral infection and

viral fever was also studied in this survey. This data was given in (Fig. 7).

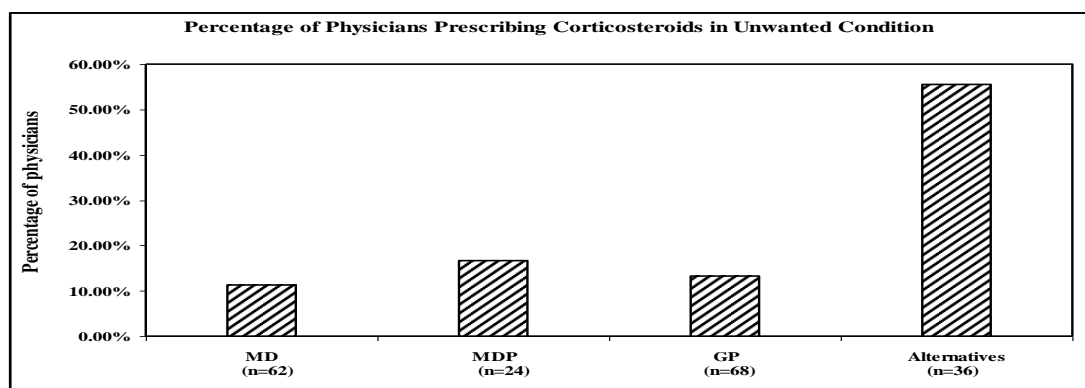
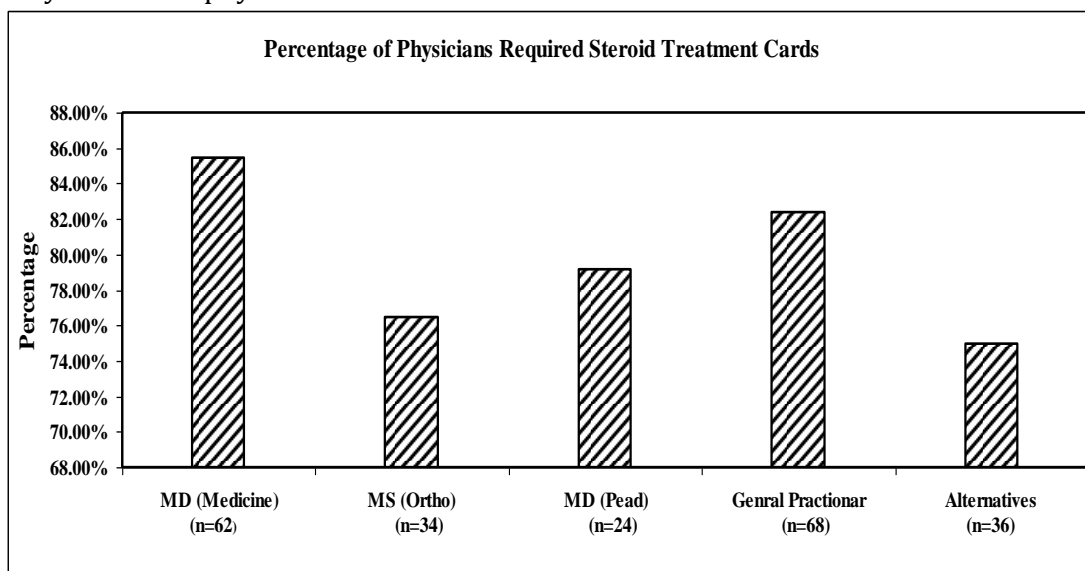


Figure 7: Prescription of corticosteroids in unwanted condition

It was found that about 55.55% and 15% of alternative therapists and physicians trained in allopathic medicines and surgery prescribed the corticosteroids in unwanted condition, respectively.

It was evident from our survey that majority of the physicians trained in

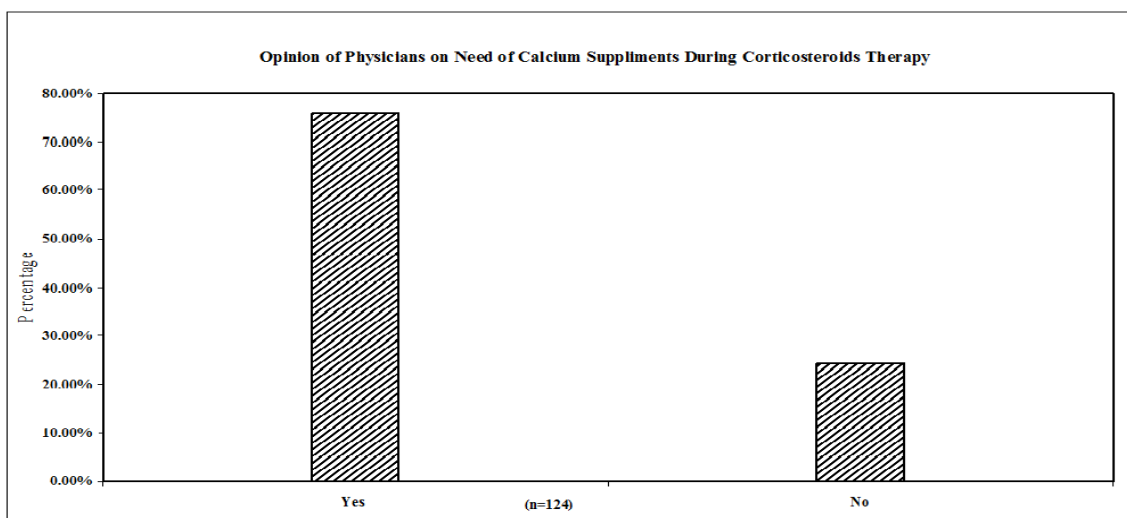
allopathy (75 – 85%) advocated the use of steroid cards whereas, the alternative therapists showed no concerns in this regard. The information regarding this fact was shown in (Fig. 8).



**Figure 8: Need for steroid treatment card in corticosteroids therapy**

In the next part of the survey, we studied the calcium supplement while prescription

of corticosteroid therapy. The data regarding this fact was given in (Fig. 9).

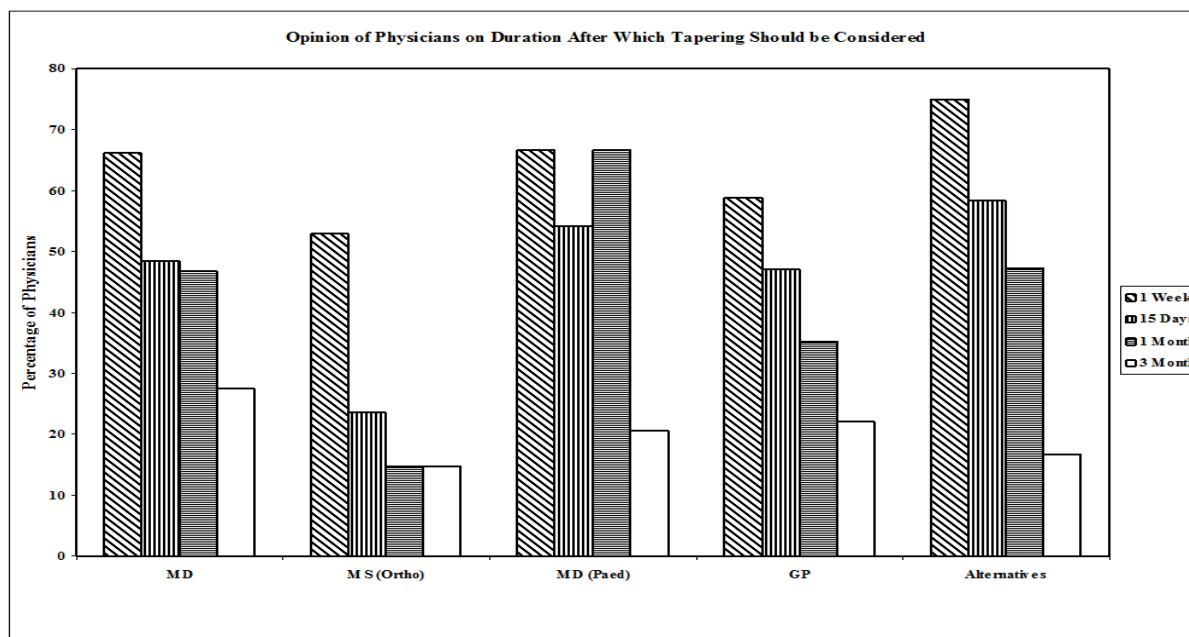


**Figure 9: Calcium supplement prescription in corticosteroid therapy**

About 78.26% of the physicians supported concurrent administration of calcium supplements while chronically using corticosteroids in order to minimize the consequences of osteoporosis.

After chronic use of corticosteroids, there is a need to gradually taper the doses of

corticosteroids to avoid the reversals of the patients and also induction of endocrinal symptoms. However, there is a wide variation in the opinion about the time after which such tapering of dose is to be considered.



**Figure 10: Opinion of physician on duration after which tapering should be considered**

(Fig. 10) indicated that about 66.12 % of MD (physicians), 52.94% of MS (ortho), 58.82% of GP and 75% of Alternative practitioner believe that the tapering of steroid therapy is essential after one week, 66.66% of MD (paediatric) believes that the tapering of steroid therapy is essential either after one week or after one month.

#### DISCUSSION

Corticosteroids are widely used in treatment of various disease conditions such as asthma, skin diseases, and rheumatoid arthritis [19-21]. Prolonged use of corticosteroids is associated with a wide range of adverse effect like sleep disturbances, lipodystrophy, adrenal suppression, metabolic syndrome, weight gain, and hypertension, vertebral fractures, Psychiatric disorders [22-23]. Corticosteroids affect bone metabolism, bone growth and bone density [24]. Abrupt discontinuation of corticosteroids after a prolonged use may precipitate disturbing withdrawal symptoms like fever, anorexia, psychosis, mood swings, generalized body aching, and weight loss [25]. Management of steroid withdrawal syndrome includes a temporary increase in the dose of glucocorticoids, followed by slow tapering to a maintenance dose [26]. In present study, a survey through direct interview with the physicians followed by filling of a questionnaire was performed to collect

information on individual physician's opinions and perceptions about therapeutic use of corticosteroids. All the points in the pamphlet were filled by the physicians during our personal visits to them. Reason behind these personal meetings was to inform the physicians about the objectives of the study and to give the detailed information about the proforma containing questionnaire so it could be easier for physicians to fill the proforma in a short period of time and provide us more insight into their perceptions on corticosteroid use. Physicians having different educational background and practicing different pathies were included so that major trends in utilization of this class of drugs could be covered in the survey. As per present survey, around 30 percent of the physician's advice their patients to take corticosteroids never on empty stomach. Corticosteroids are available in the market as different chemical entities, having different potencies (in terms of their effects on electrolyte distribution metabolism and immune response). Hence, there is a need that physicians get a chance to clearly analyze what potencies of the corticosteroids indicating and how they determine the dose, duration and mode of effects [27]. Very few physicians could arrange the list of corticosteroids in the descending order of their potencies. Hence, fact sheet contain



clear details on the concept of the potency of corticosteroids and its significance in daily practice. Study by Moghadam-Kia suggested that the duration of glucocorticoid therapy and the glucocorticoid dose should be as low as possible, because even low-dose glucocorticoid replacement therapy can decrease bone mineral density [28]. Alternative therapy with other medications is recommended [29]. Even after presence of such a vast data on alternate day therapy, many physicians included in present survey informed us that they do not practice this regimen for corticosteroids routinely and few did not state the basis of using alternate day therapy. If properly communicated regarding these details, there is a possibility that the alternate day therapy will be considered by physicians when they are prescribing corticosteroids for longer duration. In dispensing of corticosteroids, pharmacists can play an important role by giving information about use of corticosteroids, preparation of dosing charts and informing the patients about possible disadvantage of taking steroids without physician's permission.

The observation by Dana et al shows that physicians really expect pharmacists to take the responsibility of patient counseling and to inform the patients about risks involved in the improper use of steroids [31]. Community pharmacists are ideally placed to provide information so as to aid in patient compliance. Saini et al concluded from her study that community pharmacist's perceived three-dimensional role in asthma care with regional pharmacists more likely to embrace a broader role in asthma management compared to metropolitan counterparts. Clinical pharmacist can assist for the provision of the all the essential information while dispensing corticosteroids in order to minimize misuse of corticosteroids. Moreover, only clinical pharmacist is sufficiently equipped with knowledge of this class of medicines that can be presented by him to the prescribers from time to time and can be easily accessed by them for updating their skills [31]. Present data reveals that MD (Physicians) and general practitioner prefer

prednisolone as a first drug of choice in respiratory disorders, MD (Pediatrics) appeared to prefer budesonide.

Weldon David has justified that the corticosteroids have multiple effects on bones metabolism while it disturbs bone growth and affect bone density [24]. Searing et al analyzed 25-hydroxyvitamin D serum levels in 100 asthmatic children to investigate relationships between 25-hydroxyvitamin D levels and patients characteristics. He determined Vitamin D's effects on dexamethasone (DEX) induction of mitogen-activated protein kinase phosphatase 1 and IL-10 in PBMCs. Finally it is concluded that vitamin D level decreases in children with asthma due to corticosteroid use [13]. The use of such concurrent therapy depends upon the doctor's discretion and experiences in his practice. Still this point of concurrent calcium supplementation has been emphasized in the pamphlets prepared for this study.

Even after presence of such a vast data on tapering of steroid therapy, many physicians included in this survey informed that they taper the corticosteroids regimen after one week in various disease conditions and few of them reported that tapering is considered after one month. Physicians prescribing corticosteroids reconsider their opinions on tapering of steroid. There is necessity for further surveillance and studies to determine the probable duration for individual corticosteroids after which tapering should be considered. Even though such finalization of duration difficult, at least certain biomarkers may be determined that can hint regarding the tapering if discontinuation is to be considered. Details in this regard have been included in the handouts prepared for this study. Many times physicians are compelled to prescribe corticosteroids due to their palliative effects and can attract the patients to their clinics in subsequent visits. This always leads to irrational prescription of this class of drugs. Some physicians start prescribing these drugs in undiagnosed conditions where steroid therapy is either ineffective or even can cause worsening of disease conditions. Nash et al analyzed the malpractice of

corticosteroids litigation trends related to the administration of corticosteroids and the reported complications [12]. The study conducted in this regard shows that there is considerable misuse of corticosteroids in non-indicated conditions like cough, obstructive lung disease inhaled and systemic corticosteroids are associated with diabetes, hypertension, infection, pneumonia, glaucoma, adrenal insufficiency, thrush, dysphonia, myopathy, and cardiovascular events [33]. The study by Jan SU investigate the irrational prescription habit of steroids by medical practitioners in patients with arthritis and lower back pain, this type of irrational practice is the reflection of state and regulatory affairs in the country and this is a warning for all developing countries which need strict regulations for steroid prescriptions [4]. In present study, some of the physicians agreed that they are using corticosteroids in unwanted conditions like cough, viral fever and general febrile conditions. This trend is more seen in the practitioners trained in alternative therapies. To such irrational use of corticosteroids, there appears to be a need of more popularization of standard guidelines and inclusion of the list of conditions where corticosteroids are either ineffective or harmful. In India steroid treatment card is not still utilized due to lack of awareness and drive for such practice. The present survey reveals that, physicians widely accept the significance of steroid treatment card' and agree that this practice can reduce adverse effects & avoid misuse of corticosteroids by the patients. The card is needed because treatment with systemic corticosteroids suppresses the adrenal and immune responses. This has a number of potentially serious consequences including adrenal crisis if steroid treatment is stopped abruptly or there is some other physiological stress. The steroid treatment card gives guidance to the patient on minimizing risks and provides details of the prescriber, the drug, dosage and duration of treatment etc. It also carries a series of instructions for the patient and informs the health professionals to whom the patient shows this card that they are receiving systemic corticosteroid treatment. As per

standard guidelines, pharmacists dispensing systemic corticosteroids or high doses of inhaled steroids can check that the patient has been given a steroid treatment card and, if not, issue one if they consider it appropriate [34].

The fact-sheet clearly states regarding these conditions. In current practice the use of corticosteroids is enormous and duration of corticosteroids is longer in treatment of asthma and rheumatoid arthritis. Such long term exposure of the patients to glucocorticoids can cause severe and life threatening adverse effects. The patients need to be well informed regarding the cautions to be observed while using corticosteroids for longer terms. Further, they must be encouraged to carry the steroid cards so as to the complications which may arise during their subsequent hospital visits, change of the physicians or to trace the causes of their discomfort in the prolonged use of steroids. All the physicians, irrespective of their qualifications and specializations prescribe corticosteroids for one or the other disease condition. There is great variation in the way different physicians use these classes of agents in their practice. In country like India, the problem of indiscriminate use of drugs is still severe because along with the physicians trained in modern medicines, physicians of alternative medical faculties also prescribe corticosteroids. The use of corticosteroids also depends upon the experiences of the physicians in their routine practice. Hence, there is a need to reconsider the way corticosteroids are used and to provide the prescribers with the pocket reference if they wish to prescribe corticosteroids. Hence, present survey aimed to explore the perceptions of allopaths and therapists of complementary and alternative medicines regarding the therapeutic use of corticosteroids. The survey targeted to decide whether there is a need of quick reference guide for the physicians to rationally use corticosteroids.

Due to round the clock schedules and work pressure, physicians need some educational aids that will update their knowledge in lucid manner. To achieve this in case of corticosteroids, we further prepared a

handout that could inform physicians regarding recent developments and standard guidelines related to therapeutic use of corticosteroids [30, 35]

### CONCLUSION

Purpose of present study was introduced in short to physicians by highlighting the critical points in different colors so as to get significant information about potency, indication, adverse effects, tapering, alternate day therapy and calcium supplement in corticosteroid therapy. After this physician were requested to fill in the questionnaire. The collected information was analyzed and the scientific information expected in this regard was included in the handouts to be gives the current trends in prescription of corticosteroids by various physicians.

The pamphlet consists of those points on physician's perceptions and understanding on therapeutic use of corticosteroids which may affect the irrational exposure of patients to corticosteroids and their adverse effects. The purpose of preparing the handout was to provide the physicians with easy access to present knowledge on corticosteroids regarding standard guidelines for prescribing pattern of corticosteroids and to rationalize and optimize the exposure of patients to corticosteroids. These interviews have generated several potential solutions that we plan to investigate in future phases of this research program.

### ACKNOWLEDGMENT

We are heartily thankful to all physicians who supported us to give their opinion regarding corticosteroids by filling questionnaire and direct interview.

### REFERENCES

- Poetker DM, Reh DD. A Comprehensive Review of the Adverse Effects of Systemic Corticosteroids. *Otolaryngol Clin N Am* 2010; 43:753-768.
- Hayward G, Thompson MJ, Perera R, Del Mar CB, Glasziou PP, Heneghan CJ. Corticosteroids for the common cold. *Cochrane Database Syst Rev* 2012; 15: CD008116. doi: 10.1002/14651858.CD008116.pub2
- Murr AH, Smith TL, Hwang PH, Bhattacharyya N, Lanier BJ, Stambaugh BS, James W, Mugglin, AS. Safety and efficacy of a novel bioabsorbable, steroid-eluting sinus stent. *International Forum of Allergy & Rhinology*. 2012; 1:23-32.
- Quetta, Balochistan. Irrational use of steroids: a warning for the health care system. *Irrational use of steroids: a warning for the health care system. Value in Health* 2012;15:A602-A681.
- Welsh EJ, Cates CJ, Poole P. Combination inhaled steroid and long-acting beta2-agonist versus tiotropium for chronic obstructive pulmonary disease. *The Cochrane Library* 2013; 5: 1-26.
- Bruno JJ, Dee BM, Anderegg BA, Hernandez M, Pravinkumar SE. US practitioner opinions and prescribing practices regarding corticosteroid therapy for severe sepsis and septic shock. *Journal of Critical Care* 2012; 27: 351-361.
- Hannen RF, Michael AE, Jaulim A, Bhogal R, Burrin JM, Philpott MP. Steroid synthesis by primary human keratinocytes; implications for skin disease. *Biochemical and Biophysical Research Communications* 2011; 404:62-67.
- Kim HI, Kim SW, Park GY, Kwon EG, Kim HH, Jeong JY, Chang HH, Lee JM, and Kim NS. Causes and Treatment Outcomes of Stevens Johnson Syndrome and Toxic Epidermal Necrolysis in 82 Adult Patients. *Korean J Intern Med* 2012; 27:203-210.
- Gorter SL, Bijlsma JW, Cutolo M, Gomez-Reino J, Kouloumas M, and Smolen JS, Landewé R. Current evidence for the management of rheumatoid arthritis with glucocorticoids: a systematic literature review informing the EULAR recommendations for the management of rheumatoid arthritis. *Ann Rheum Dis*. 2010; 69: 1010-4.
- Minnecci P. C. Deans J, Eichacker PQ, Natanson C. The effects of steroids during sepsis depend on dose and severity of illness: an updated meta-analysis. *Clin Microbiol Infect* 2009; 15: 308-318.
- Patel GP, And Robert A. Balk Systemic Steroids in Severe Sepsis and Septic Shock. *Is J Respir Crit Care Med* 2012; 185: 133-139.
- Nash JJ, Nash AG, Leach ME, Poetker DM. Medical Malpractice and Corticosteroid Use. *Otorhinolaryngology* 2010; 1:26-29.
- Searing Daniel A, Zhang Yong, A. Murphy James R,B,C Pia J. Hauk,A,D Elena Goleva, A And Donald Y. M. Leung. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. *J Allergy ClinImmunol* 2010; 125:995-1000.
- Dunne S, Shannon B, Hannigan A, Dunne C, Cullen W. Physician and pharmacist perceptions of generic medicines what they think and how they differ. *Health Policy* 2014; 116: 214-223.

15. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PA, Rubin HR. Why Don't Physicians Follow Clinical Practice Guidelines? *JAMA* 1999; 282: 1458-1465.
16. LaRoche GE, LaRoche AG, Ratner RE, Borenstein DG. Recovery of the hypothalamic-pituitary-adrenal (HPA) axis in patients with rheumatic diseases receiving low-dose prednisone. *The American Journal of Medicine* 1993; 95: 258-264.
17. Fuhlbrigge AL, Lemanske RF Jr, Rasouliyan L, Sorkness CA, Fish JE. Practice patterns for oral corticosteroid burst therapy in the outpatient management of acute asthma exacerbations. *Allergy & Asthma Proceedings* 2012; 33: 82-89.
18. Brozek JL, Bousquet C, Jean E, Baena C, Bonini SE, Canonica GW et al. Allergic Rhinitis and Its Impact on Asthma (ARIA) Guidelines. *J Allergy Clin Immunol* 2010; 126: 466-475.
19. Massingham K, Fox S. Asthma Therapy in Pediatric Patients: A Systematic Review of Treatment with Montelukast versus Inhaled Corticosteroids. *Journal of Pediatric Health Care* 2013; 28:51-62.
20. Frew JW, Dédée MF. Corticosteroid Use in Autoimmune Blistering Diseases. *Dermatol Clin* 2011; 29: 535-544.
21. Sayah A, Joseph C. Rheumatoid arthritis: A review of the cutaneous manifestations. *J Am Acad Dermatol* 2004; 53: 193-209.
22. Shah M, Chaudhari S, McLaughlin TP, Shayan KH, Ferguson K, Singh HK et al. Cumulative Burden of Oral Corticosteroid Adverse Effects and the Economic Implications of Corticosteroid Use in Patients with Systemic Lupus Erythematosus. *Clinical Therapeutics* 2013; 35: 486-497.
23. Drozdowicz LB, Bostwick MJ. Psychiatric Adverse Effects of Pediatric Corticosteroid Use. *Mayo Clin Proc* 2014; 89:817-834.
24. Weldon D. The effects of corticosteroids on bone growth and bone density. *Ann Allergy Asthm Immunol* 2009; 103:3-11.
25. Mercadante S, Villari P, Intravaia G. Withdrawal acute psychosis after corticosteroid discontinuation. *J Pain Symptom Manage* 2007; 34: 118-119.
26. Bhattacharyya A, Kaushal K, Tymms DJ, and Davis. Steroid withdrawal syndrome after successful treatment of Cushing's syndrome: a reminder. *European Journal of Endocrinology* 2005; 153: 207-210.
27. Sketris SI, Kephart G, Cooke Ca, Skedgel DC. Use of Physician Profiles To Influence Prescribing Of Topical Corticosteroids. *J Clin Pharmacol* 2005; 12: e186-e197.
28. Moghadam-Kia S, Werth VP. Prevention and treatment of systemic glucocorticoid side effects. *International Journal of Dermatology* 2010; 49: 239.
29. Debbie SG, Susan F, Massengill LY, Shashi N, William E, Smoyer JD et al. Management of childhood onset nephrotic Syndrome. *Pediatrics* 2009; 124: 747-758.
30. Saeki H, Furue M, Furukawa F, Michihiro H, Mamitaro IK, Sasaki R, Suto H. Guidelines for management of atopic dermatitis. *Journal of Dermatology* 2009; 36: 563-577.
31. Ahmad DS, Wazaify MM, Younes A. Clinical Pharmacist in the Identification and Management of Corticophobia - An Interventional Study. *Tropical Journal of Pharmaceutical Research* 2014; 13: 445-453.
32. Saini B, LeMay K, Emmerton L, Krass I, Smith L, Bosnic-Anticevich S, Stewart K, Burton D, Armour C. Asthma disease management—Australian pharmacists' interventions improve patients' asthma knowledge and this is sustained. *Patient Education and Counseling* 2011; 83: 295-302.
33. Spyridon F, Joseph K, Manuel DA, Maria P, Armand W, Yaw AA. Perseverant, non-indicated treatment of obese patients for obstructive lung disease. *BMC Pulmonary Medicine* 2013; 10: 13-68.
34. [http://www.sehd.scot.nhs.uk/cmo/CMO\(2006\)10.pdf](http://www.sehd.scot.nhs.uk/cmo/CMO(2006)10.pdf)
35. Hussain S, Malik F, Hameed A, Ghazala P, Fahadya Y R, Humayun R et al. Pharmacoepidemiological studies of prescribing practices of health care providers of Pakistan: A cross sectional survey. *African Journal of Pharmacy and Pharmacology* 2011;5:1484-1493.