Assessment of Adverse Drug Events in Patients with Steroid Treatment in an Indian Tertiary Care Hospital

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ABSTRACT: The study aimed to assess the adverse drug events in patients with steroids treatment in an Indian tertiary care hospital. The data collected from whole information about the objectives as from patient medication chart, patient case reports notes, nurse's reports and notes, doctor's daily reports and notes and laboratory reports of patients admitted in BBH. Therefore all collected data filled in a prepared form. Data collected from patients those used steroids for more than 5 days, because the minimum days we need for find out of the adverse effects is 5 days. Therefore the adverse drug reaction recorded in the study evaluated for their percentages per patients and drugs; also they are evaluated based on the probability and severity. It is prospective observational study on 141 patients in BBH hospital, where 87 of patients were man and 57 patients were women. The hypertension, diabetes mellitus infection diseases and respiratory diseases were the most popular diseases among patients in the study. 187 steroid drugs are used, therefore the average of the corticosteroid drugs used per patients are 1.32; totally 59 adverse drug reactions achieved most of them includes oral candidiasis (22.03%), hyperglycemia (18.64%); 59.32% of total ADRs were for budesonide and 30.5% of total ADRs for hydrocortisone. 18 adverse drug reactions were severe (30.5%), 29 adverse drug reactions were moderate (45.76%) and 12 adverse drug reactions were mild (20.33%).20.33% were defined in concerned to drug caused adverse effect, also 45.76% and 33.89% respectively were related to the probable and possible in concern to steroid drugs caused adverse effects. Based on this study males were the most exposure to steroids and mostly in ages more than 66 years olds. The most popular diseases evaluated among patients are respiratory diseases, infection diseases, diabetes mellitus and hypertension. Most steroids used among patients were budesonide and hydrocortisone, the average of steroids used is 1.32 per patients. Most adverse drug reactions achieved in this study are oral candidiasis, hyperglycemia and hypokalemia. Most of adverse drug reactions were moderate in their severity and probable in their relation to steroids. According to this study steroids are well known among prescribers especially on their adverse drug reactions. The range of steroids use in our hospital could be in high level especially on budesonide and hydrocortisone. Based on the adverse drug reactions of the steroids we achieved in this study, monitoring and reporting of steroids ADRs are not much good or it is not care in some of ADRs like oral candidiasis.

KEYWORDS: Adverse drug reaction, Steriod use, Budesonide, Hydrocortisone.

I.   INTRODUCTION

Corticosteroids are potent medications that have been extensively used to treat many inflammatory and autoimmune conditions. They have been used in a variety of life threatening and disabling conditions and have saved or improved many lives[7].

Corticosteroids are commonly prescribed by practitioners in many medical specialties for the treatment of chronic inflammatory conditions. The use of corticosteroids in the treatment of chronic diseases like chronic obstructive disease, arthritis conditions and rhino sinusitis is well described and based on their anti-inflammatory effects. The duration of corticosteroid therapy in these conditions is often less than 1 month, in contrast to the treatment of chronic respiratory diseases (i.e., asthma, chronic obstructive pulmonary disease) or autoimmune disorders (i.e., rheumatoid arthritis, systemic lupus erythematous, Crohn disease, and ulcerative colitis), which can last for years [1,]
 Systemic corticosteroids (SCS) are commonly prescribed to treat patients with respiratory

conditions such as asthma and to treat or reduce the risk of fare-ups of inflammatory conditions, such as rheumatologic and autoimmune diseases, allergic reactions, and inflammatory bowel disease. [1, 2, 5] A dose-response relationship with SCS exposure has been documented for many of adverse events [6, 9].

Even short-term use of oral corticosteroids (OCS) in a large population-based study has been associated with increased rates of sepsis, thromboembolism, and fracture within 30 days of OCS initiation.[5, 10] decreases in serum cortisol and markers of bone formation, and changes in white blood cell counts, are evident within hours of oral prednisone administration to healthy subjects [5]. There are many steroids drugs which could be classified based on the mechanism of actions or company name and based on the targets, mostly corticosteroids are classified based on the their biological half-life and duration of effects; therefore they classified as short acting (between 8 to 12 hours), intermediate acting (12-36 hours) and long acting (between 36 to 72hours).

• Clinical Pharmacists in organized health care systems should develop comprehensive, ongoing programs for monitoring and reporting adverse drug reactions (ADRs).It is the pharmacist's responsibility and professional obligation to report any suspected ADRs. ADR-monitoring and reporting programs encourage ADR surveillance, facilitate ADR documentation, promote the reporting of ADRs, provide a mechanism for monitoring the safety of drug use in high-risk patient populations, and stimulate the education of health professionals regarding potential ADRs. A comprehensive, ongoing ADR program should include mechanisms for monitoring, detecting, evaluating, documenting, and reporting ADRs as well as intervening and providing educational feedback to prescribers, other health care professionals, and patients. Additionally, ADR programs should focus on identifying problems leading to ADRs, planning for positive changes, and measuring the results of these changes. Positive outcomes resulting from an ADR program should be emphasized to support program growth and development[4]

OBJECTIVE
Primary objective:
• Evaluation and assessment of steroids adverse drug reactions among patients with steroids treatment.
Secondary objective:

• Demographic calculation of age and sex of patients treated with steroids.
• Demographic calculation of general disease variability in patients treated with steroids.
• Evaluation of average use of steroids per patients.

II. METHODOLOGY
Study design:
• It is a prospective observational study at a teaching tertiary care hospital.

Source of data and Materials:
• Inpatient prescription
• Medication chart
• Medication history chart
• Medicine strips
• Medication history interview

Inclusive Criteria:
• Age ≥ 18 years
• Both female and male
• Patients prescribed with Minimum of five drugs

Exclusion Criteria:
• Patient with non-steroids medication prescription
• Age below 18 years old
• pediatric wards patients
• pregnancy women patients
• Patient in ambulatory care

Sample Size:
Candidates or patient are selected based on steroids used in their treatment chart during hospitalizations, totally data are collected from 141 patients in this study.

Method of collection of data:
The data collected from whole information about the objectives as from patient medication chart, patient case reports notes, nurse's reports and notes, doctor's daily reports and notes and laboratory reports of patients admitted in BBH. Therefore all collected data filled in a prepared form. Data collected from patients those used steroids for more than 5 days, because the minimum days we need for find out of the adverse effects is 5 days.

Study procedure:

All medically relevant information use to be noted in a predefined data collection form. Alternatively, The demographic data and the detailed history of patient regarding past, present, family, personal and drug history (especially in steroids) conducted to be record. The other details like the present diagnosis, reason for the present admission is also noted with during 6 month. Patients of both genders who are admitted into the inpatient wards in the Hospital, in age greater than 18 years are include in the study.

And at the end of collection data, all of detail used as to calculate the result of study in suitable excel form. Therefore the adverse drug reaction recorded in the study evaluated for their percentages per patients and drugs; also they are evaluated based on the probability and severity.

A professional form prepared with all of details about ADRs, to study about the steroids in case of patients prescribed for steroids; therefore to prove the ADRs we are using NARANJO scale to see the probability of ADRs in percentages [table 2]. And also with help of Medscape and Micromedex scales about severity of ADRs considered to study.

Table 1-NARNAJO SCALE

NARANJO SCALE Score												
NO	Questions	RATE			DRUG 1:			DRUG 2:			DRUG 3:		
		yes	no	Don't know	ADR1	ADR2	ADR3	ADR1	ADR2	ADR3	ADR1	ADR2	ADR3
01	Are there previous conclusive reports on this reaction?	+1	0	0									
02	Did the ADR appear after the suspected drug was administered?	+2	-1	0									
03	Did the ADR improve when the drug was discontinued?	+1	0	0									
04	Did the ADR appear with re-administration?	+2	-1	0									
05	Are there												

	alternative causes for the ADR?	-1	+2	0			
06	Did the reaction appear when the placebo was given?	-1	+1	0			
07	Was the drug detected in blood at toxic levels?	+1	0	0			
08	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0			
09	Did the patient have a similar reaction to the same or similar drug in any previous exposure?	+1	0	0			
10	Was the ADR confirmed by any objective evidence?	+1	0	0			
11	Total SCORE						

*Defined = >8, probable= 5 to 8, possible = 1to 4, doubtful=<1

Along with above details we also consider to study and evaluate the populations of patients used steroids based on the genders, age groups and population of diseases which is recorded as paste history and diagnosis.
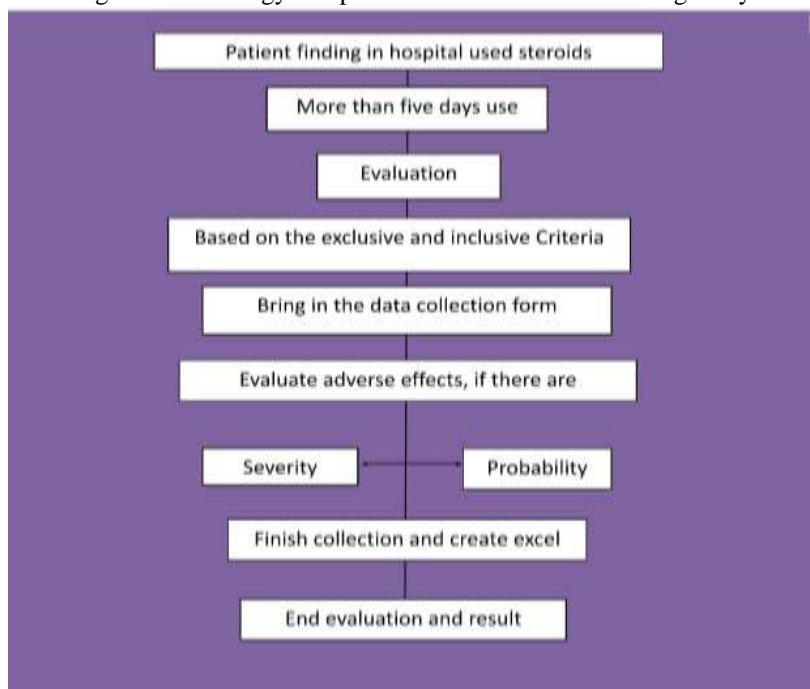
Study period:
- The study and data collection carried out for a period of 6 month (24 weeks)

Study site:
- The study is done in the inpatient department of Bangalore Baptist Hospital in Bangalore, Karnataka, India.

Fig 2- Methodology and process of data collection during study


III. OBSERVATION

It is prospective observational study on 141 patients in BBH hospital, where 87 of patients were man and 57 patients were women, therefore the most popular patients are mans; also patients are classified based on their ages and the most popular ages used in study were 66 years old and above (47.51%) more from males [table 3] [fig 4].

Table 3- Classification of patients based on the age and sex

GENDER STATUS	TOTAL		AGE STATUS							
			18-30		31-50		51-65		66 and above	
	NO	%	no	%	no	%	no	%	no	%
MAN	87	61.7%	5	3.54%	9	6.38%	26	18.43%	47	33.33%
WOMEN	54	38.29%	6	4.25%	9	6.38%	19	13.47%	20	14.18%
TOTAL	141		11	7.8%	18	12.76%	45	31.91%	67	47.51%

Fig 4- Age classification based on the sex
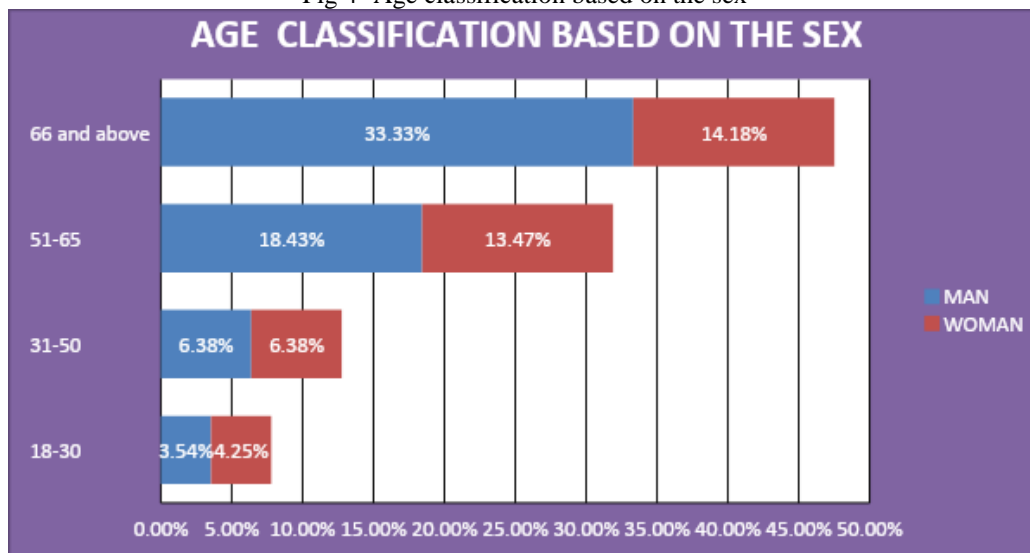
For the evaluation of past history from the 141 patients data collected for the study, 104 patients had hypertension (73.75%), 109 patients had diabetic mellitus (77.30%), 14 patients had thyroid disease (9.93%), 97 patients had respiratory disease (68.79%), 34 patients had cerebrovascular conditions (24.11%), 12 patients had accident situations (8.51%), 21 pain and fever (14.9%), 32 heart diseases (22.7%), 19 gastrointestinal disease (13.47%), 21 renal diseases and about 17 patients had different rare conditions which are not included from above categorizes [table 4]. the hypertension, diabetes mellitus and respiratory diseases were the most popular past history among patients in the study.

Table 4- Classification of past history diseases obtained among patients

PAST HISTORY STATUS	NUMBER	PERCENTAGE
Hypertension	104	73.75%
Diabetes Mellitus	109	77.30%
Thyroid Disease	14	9.93%
Respiratory Disease	97	68.79%
Cerebrovascular	34	24.11%
Accident	12	8.51%
Pain And Fever	21	14.9%
Heart Disease	32	22.7%
Gastrointestinal Disease	19	13.47%
Renal Diseases	21	14.9%
Rare Cases	17	12.05%

According to complains and diagnoses of diseases recorded among patients, from 141 patients 121 patients had respiratory diseases (85.81%), 31 patients had heart and vascular diseases (21.98%), 28 patients had fever and pain (19.85%), 8 patients had allergy reactions (5.67%), 22 patients brain disorders (15.6%), 54 patients infection diseases (38.3%), 22 patients gastrointestinal diseases (15.6%), 18 patients renal diseases (12.76%),6 patients had poisoning (4.25%) and there are 9.93% of rare cases which are not included from above categorizes or they were not able to classify [table 5].

Table 5- Classification of complained and diagnosed diseases obtained among patients

PRESENT DIAGNOSIS	NUMBER	PERCENTAGE
Respiratory Disease	121	85.81%
Heart And Vascular Disease	31	21.98%
Fever And Pain	28	19.85%
Allergic Reactions	8	5.67%
Brain Disorders	22	15.6%
Infection Disease	54	38.3%
Gastrointestinal Disease	22	15.6%
Renal Diseases	18	12.76%
Poisoning	6	4.25%
Rare Cases	14	9.93%

Among 141 patients in this study 187 steroid drugs are used, therefore the average of the corticosteroid drugs used per patients are 1.32; this drugs are includes Hydrocortisone (37.58% of patients), Dexamethasone (5.67% of patients), Budesonide (79.43% of patients), Fludrocortisone (1.42% of patients), Prednisolone (6.38% of patients), and Methyl Prednisolone (0.7% of patients) [table 6] [fig 5].

Table 6- Classification of corticosteroids used for patients during study

DRUG NAME	NUMBER OF PATIENTS	PERCENTAGE
Total Drugs	187	-
Hydrocortisone	53	37.58%
Dexamethasone	9	6.38%
Budesonide	112	79.43%
Fludrocortisone	2	1.42%
Prednisolone	10	7.1%
Methyl Prednisolone	1	0.7%

*a patient may use more than one steroid drug.

Fig 5- Number of Patients Used Steroids on their treatment chart
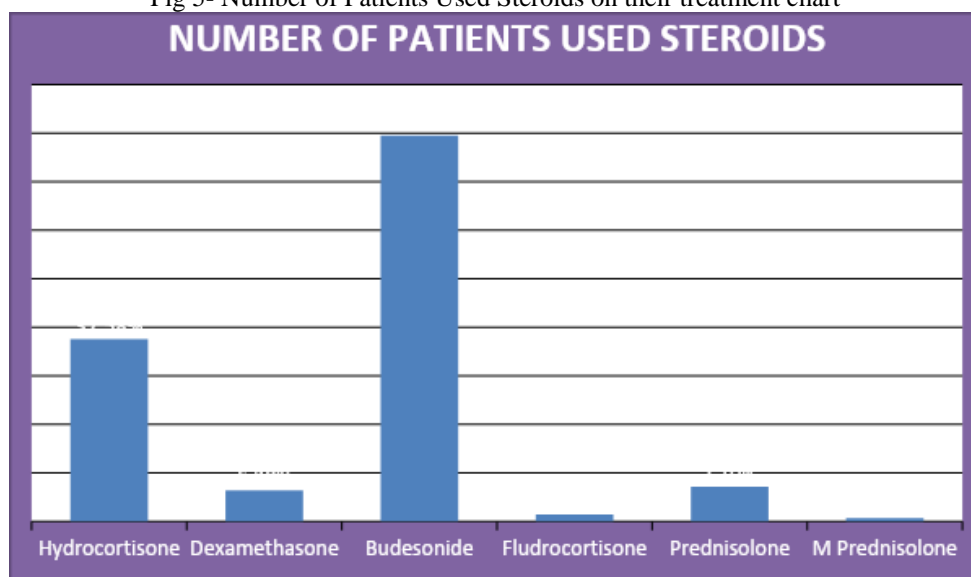
According to data in this study, totally 59 adverse drug reactions achieved among 141 patients [table 7] where they are includes oral candidiasis (22.03%), hyperglycemia (18.64%), respiratory infection (8.47%), hypokalemic alkalosis (20.33%), angioedema (1.69%), tachycardia (1.69%), otitis media (10.16%), gastroenteritis (1.69%),glucose tolerance (1.69%),increased appetite (1.69%),diabetes mellitus (8.47%), insomnia (1.69%) and osteoporosis (1.69%)among patients during study [fig 6].

Table 7- Evaluation of adverse drug reaction achieved among patients

ADR NAME	NUMBER	PERCENTAGE
Total Adverse Drug Reactions	59	*
Oral Candidiasis	13	22.03%
Hyperglycemia	11	18.64%
Respiratory Infection	5	8.47%
Hypokalemic Alkalosis	12	20.33%
Angioedema	1	1.69%
Tachycardia	1	1.69%
Otitis Media	6	10.16%
Gastroenteritis	1	1.69%
Glucose Tolerance	1	1.69%
Increased Appetite	1	1.69%
Diabetes Mellitus	5	8.47%
Insomnia	1	1.69%
Osteoporosis	1	1.69%

Fig 6- Evaluation of adverse drug reaction achieved among patients
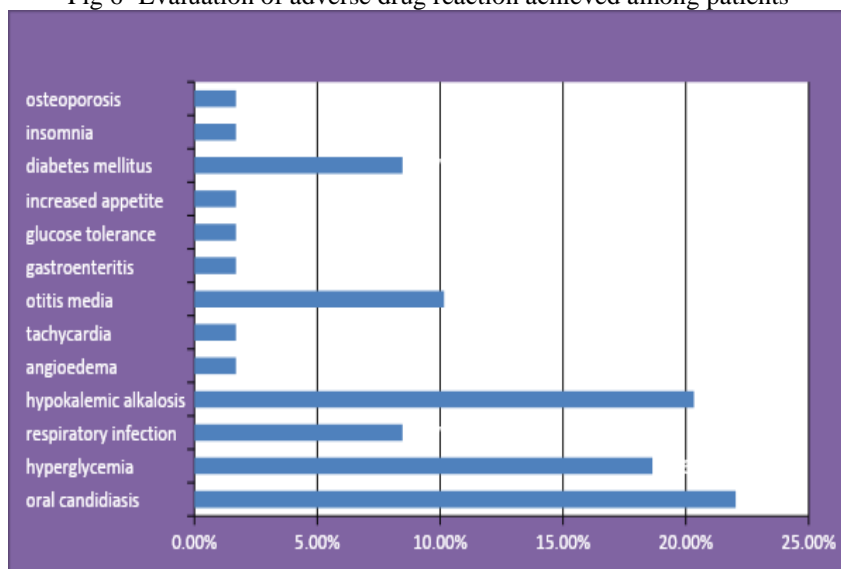
Among 187 drug used for 141 patients 59 adverse drug reactions are achieved [table 8]; where 3 adverse effects were related to prednisolone (5.08% of total ADRs), 18 adverse effects were related to hydrocortisone (30.5%of total ADRs), 35 adverse effects were related to the budesonide (59.32% of total ADRs), 1 adverse effect was related to fludrocortisone (1.69% of total ADRs) and 2 adverse effects were related to the dexamethasone (3.38% of total ADRs) [fig7].

Table 8- Evaluation of steroids drugs caused adverse drug reactions

DRUG NAME	NO OF ADRS	PERCENTAGE
Prednisolone	3	5.08%
Hydrocortisone	18	30.5%
Budesonide	35	59.32%
Fludrocortisone	1	1.69%
Dexamethasone	2	3.38%

*Total ADRs are 59

Fig 7- Evaluation of steroids drugs caused adverse drug reactions
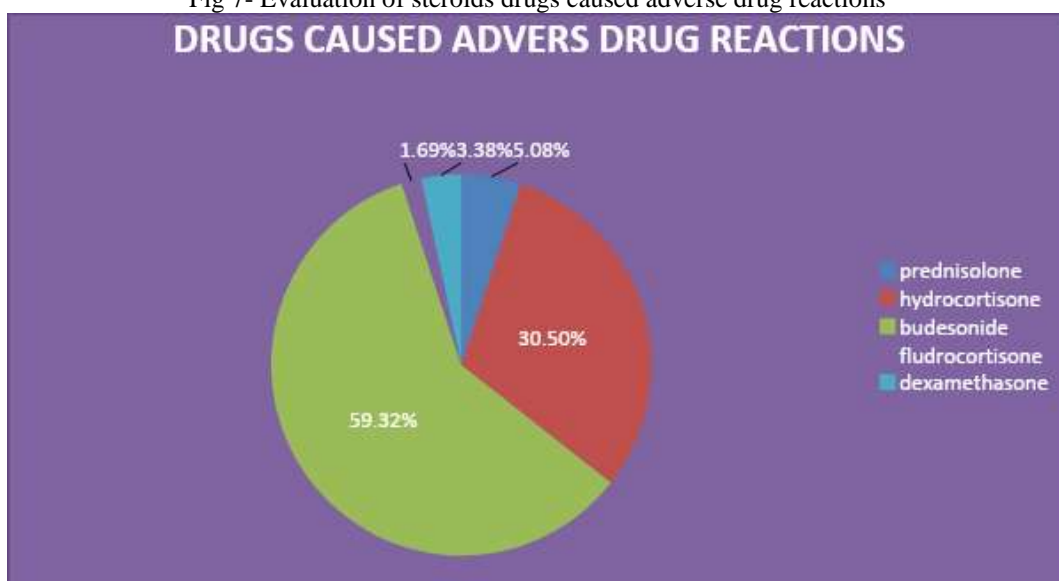
From the 59 adverse drug reactions achieved in the study, 18 adverse drug reactions were severe (30.5%), 29 adverse drug reactions were moderate (45.76%) and 12 adverse drug reactions were mild (20.33%) in types [table9] [fig8].

Table 9- Comparing the side effects of drugs according to their severity

SEVERITY	NUMBER ADRS	PERCENTAGE
SEVERE ADRS	18	30.5%
MODERATE ADRS	29	49.15%
MILD ADRS	12	20.33%

Fig 8- Comparing the side effects of drugs according to their severity
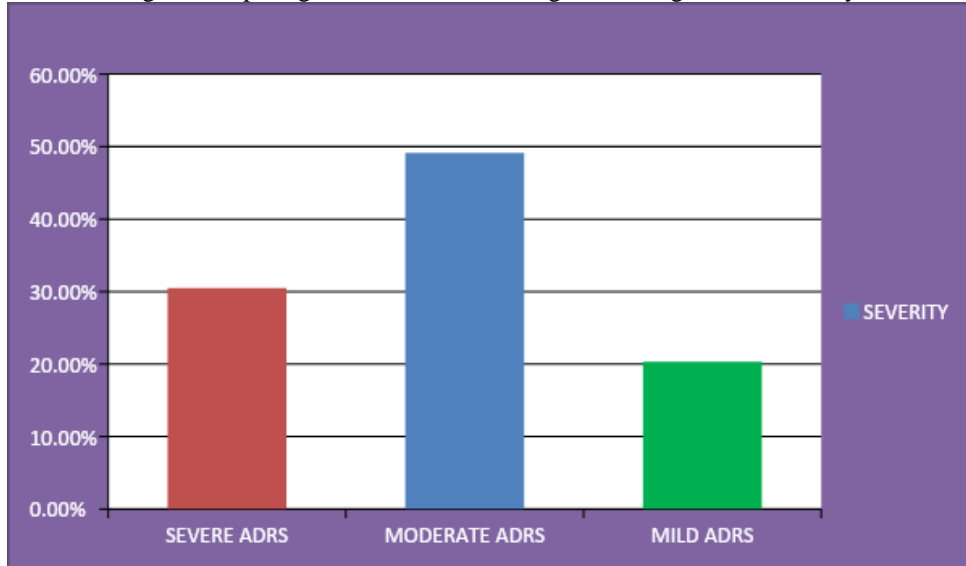
In other hands we consider to check out the adverse drug reactions probability concern to steroids drugs by use of scales, therefore from 59 adverse drug reactions 20.33% were defined in concerned to drug caused adverse effect, also 45.76% and 33.89% respectively were related to the probable and possible in concern to steroid drugs caused adverse effects [table 10] [fig9].

Table 10- Comparing the side effects of drugs according to their probability

PROBABILITY TYPE	NUMBER ADRS	PERCENTAGE
DEFINED	12	20.33%
PROBABLE	27	45.76%
POSSIBLE	20	33.89%

Fig 9- Comparing the side effects of drugs according to their probability
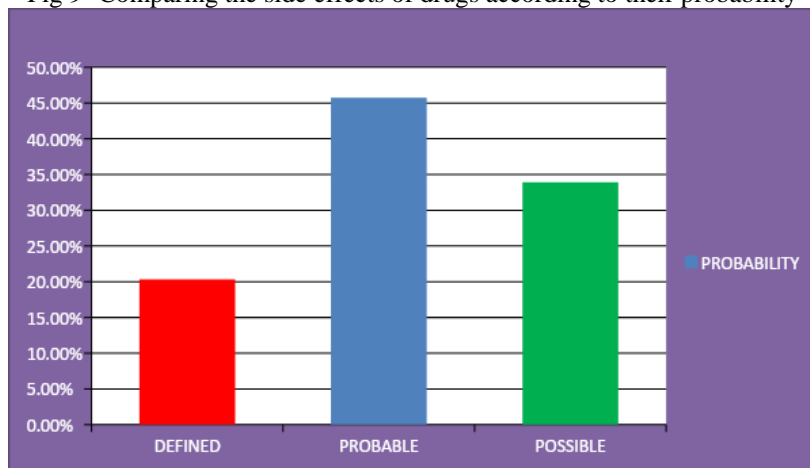
IV.   DISCUSSION

It is prospective observational study on 141 patients, 87 of patients were man and 57 patients were women; the most popular ages used in study were 66 years old and above (47.51%). While in the L Walsh study, total patients were 367 and 52% of patients were male, and the most popular ages were >50 years. Hypertension, diabetes mellitus and respiratory diseases were the most popular past history among patients in the

study. Respiratory disease and infection disease were the most popular disease of patients when they are admitted to hospital. While in the Tsung-Chieh Yao study most common indications (diseases) of corticosteroids were acute respiratory tract infections and allergic diseases. Among 141 patients in this study 187 steroid drugs are used, therefore the average of the corticosteroid drugs used per patients are 1.32; while in Tsung-Chieh Yao study, they mentioned that at last 1 corticosteroid used per patient.

Budesonide used among 79.43% of patients more than other steroids and after that hydrocortisone, which can be effective in the evaluation percentage of adverse drug reaction for all steroids in this study; which means that most ADRs could be recorded for budesonides in compare to other drugs.

Totally 59 adverse drug reactions achieved among 141 patients; where oral candidiasis and hypokalemic alkalosis were the most adverse effects among patient found with adverse drug reactions. Most of these adverse effects were related to the budesonide and hydrocortisone. But according to the number of these two drugs they are not much seems to include high level of ADRs. While in the Tsung-Chieh Yao study most adverse effects related to GI bleeding and pneumonia.

In evaluation of severity for adverse drug reactions, they are evaluated mostly for moderate ADRs and severe adverse effects were 30.5% of total ADRs. in compare to the THOMAS P. WARRINGTON study severe reactions occurred in nearly 6% of patients and most of adverse effects were moderate (mild to moderate reactions occurred in about 28% of patients). Also in Eric B. Suhler study most of adverse effects were categorized as mild and moderate. In evaluation of probability of adverse drug reactions, they are evaluated mostly as probable in relation to the steroid drugs. This means that these adverse drug reactions could be related to other drugs in medicine chart of patients during their treatment.

V. CONCLUSION
Based on this study males were the most exposure to steroids and mostly in ages more than 66 years old's. The most popular diseases evaluated among patients are respiratory diseases, infection diseases, diabetes mellitus and hypertension. Most steroids used among patients were budesonide and hydrocortisone, the average of steroids used is 1.32 per patients. Most adverse

drug reactions achieved in this study are oral candidiasis, hyperglycemia and hypokalemia. Most of adverse drug reactions were moderate in their severity and probable in their relation to steroids used.

According to this study steroids are well known among prescribers especially on their adverse drug reactions. The range of steroids use in our hospital could be in high level especially on budesonide and hydrocortisone. Based on the adverse drug reactions of the steroids we achieved in this study, the monitoring and reporting of steroids ADRs are not much good or it is not care in some of ADRs like oral candidiasis.

This study can form a basis for future studies with larger number of patients followed up for a longer duration of time and which will be reflective of a full population. This study can be improve and better done by doing it in other area and hospitals and comparing them to achieve a clear and broad result about prescribing patterns and evaluations of ADRs for steroid drugs in a large area. Adverse drug reactions are the main problem of many drugs especially steroids used among patients on their treatment, this adverse effect could keep patients in specific conditions because of their past history and habit of drug use, there we need to prove our information about steroids and their use.

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