RESEARCH PAPER

Oral Contraceptive Induced Anasarca in a Young Woman: A Rare Adverse Drug Reaction Case Report

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ABSTRACT

Oral contraceptives are commonly prescribed for prevention of pregnancy as well as gynecological disorders and are usually well-tolerated medications. However, in rare cases, these medications can lead to considerable fluid retention, resulting in generalized edema or anasarca. Drug-induced edema is often not recognized, and this can lead to a variety of clinical manifestations. Therefore, it is important to understand the causes, risk factors, and manifestations of hormonal contraceptive-induced edema. A case report of a female who was administered oral contraceptive medication and soon presented with bilateral lower limb swelling with generalized edema is discussed. Edema due to medications can resolve within a short span of time after stopping the medication, and therefore, it is important to understand the role of medications in patients with such manifestations.

Keywords: Oral contraceptives, Anasarca, Drug-induced edema, Urinary tract infection, Iron deficiency anemia, Estrogen, Renin-angiotensin-aldosterone system

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Introduction

Oral contraceptives are one of the most frequently used reversible forms of contraceptives, which are used for the prevention of pregnancy and for the routine management of various gynecological complaints in women [1]. Though they are generally well tolerated, certain cases may show a range of side effects, which are generally mild and self-limiting. However, in some cases, severe complications such as hypertension, hypoalbuminemia, venous thromboembolism, and gallbladder and liver dysfunction have been reported [2]. It has been observed that estrogen, which is present in oral contraceptives, causes fluid retention through sodium and water retention, which activates the Renin-Angiotensin-Aldosterone System (RAAS), which leads to peripheral edema and weight gain, and in very rare cases, anasarca, which is a form of generalized edema, characterized by the swelling of the body as a result of the excessive retention of fluid in the tissues [3]. Drug-induced anasarca is not generally recognized, and its early identification is important to ensure proper management and resolution of the condition.

Here we present a rare case of drug induced anasarca in a young female patient, along with iron deficiency anemia and urinary tract infection.

Methodology

This case study was performed by carrying out a retrospective analysis of the clinical data of the patient who was admitted to the Department of General

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Medicine. The information regarding the patient's demographic data, clinical presentation, investigations, treatment given, and follow-up was collected from the patient's clinical records and the hospital database.

A detailed clinical evaluation was done at the time of admission. This includes the entire history taking, with special emphasis on the intake of medications in the recent past, especially oral contraceptive pills. Physical examination and vital sign recording, baseline investigations were done and analyzed. These include hematological parameters, renal function tests, liver function tests, electrolytes, inflammatory markers, and microbiological studies such as urine and blood cultures.

Causality Assessment

To determine the likelihood of drug-induced anasarca, the temporal correlation between the appearance of symptoms and the recent use of the oral contraceptive pill was carefully assessed. It was observed that the patient improved when the suspected medication was stopped and this was documented to support the causal association.

Literature Assessment

The data collected was analyzed descriptively, and the results obtained were compared to the previously published literature on fluid retention caused by oral contraceptive use and drug-induced edema to present the results of the present case study.

Case Report

Clinical presentation

A 24-year-old female presented to the casualty department with complaints of gradual onset of bilateral lower limb swelling over the past week, accompanied by fever for the past five days and generalized fatigue for the past three days. The patient was apparently healthy 1 week back, when she started developing gradual onset of bilateral lower limb edema. There was no history of trauma, chest pain, palpitations, shortness of breath, decreased urine output. On further history taking, the patient revealed that she had started taking oral contraceptive pills a week prior to the onset of the symptoms.

ON EXAMINATION:

Physical examination revealed stable vitals signs with a blood pressure of 110/80 mmHg, pulse rate of 98/min, and a temperature of 98.4°F. The general physical examination revealed the presence of bilateral lower limb pitting edema without any pain, skin color changes were Seen.

Cardiovascular, respiratory, abdominal, and neurological systemic examinations were within normal limits.

Investigations

Laboratory investigations revealed hemoglobin of 9 g/dL, with a packed cell volume of 27.9% and peripheral blood counts revealed normocytic normochromic anemia. The total leukocyte count was raised at 21,326 cells/mm³, with neutrophil predominance suggestive of underlying infection and the platelet counts were 376,000/mm³ in normal limits.

Parameter	Measured value	Normal range
Hemoglobin	9 g/dl	12 to 16 g/dl
Packed cell volume	27.9%	36% to 46%
Total leukocyte count	21,326 cells/mm³	4000 to 11000 cells/mm³
Platelet count	3,76000 /mm³	1.5 lakhs/mm³ to 4.5 lakhs/mm³

Table 1. Complete Blood Count findings

Renal function tests and electrolytes showed blood Urea 13.2 mg/dL, Serum Creatinine 0.5 mg/dL, Uric Acid 2.4 mg/dL, Sodium 132 mEq/L, Potassium 4.4 mEq/L, Chloride 101 mEq/L and were within normal range.

The liver function tests revealed mildly elevated transaminase with AST levels of 44 U/L and elevated ALT levels of 165 U/L. The total protein was 5.59 g/dL, and albumin was 3.1 g/dL. The lipid profile revealed mild dyslipidemia with an HDL of 32 mg/dL and a total cholesterol of 144 mg/dL, LDL cholesterol of 87 mg/dL, and triglycerides of 117 mg/dL.

Parameter	Measured value	Normal range
AST	44 U/L	10 to 40 U/L
ALT	165 U/L	7 to 56 U/L
Total protein	5.59 g/dl	6 to 8 g/dl
Albumin	3.1g/dl	3.5 to 5 g/dl
HDL	32 mg/dl	>40 mg/dl

Table 2. Liver Function Test and Lipid Profile Findings

The patient had significantly elevated inflammatory markers, including CRP of 17.1 mg/L and an elevated ESR of 126 mm/hr, indicating active infection or inflammation.

Urine culture revealed Escherichia coli confirming urinary tract infection, while blood cultures were negative. The autoimmune profile, including an ANA profile, was normal, while nephrology evaluation for proteinuria was advised.

Course in the hospital

During the course of stay in the hospital, the patient was administered IV antibiotics for the treatment of urinary tract infection, proton pump inhibitors, and iron supplements for anemia. The offending drug, which was in this case an oral contraceptive pill, was discontinued as a precautionary measure due to the possibility of the causative agent of edema being an adverse side effect of the drug. The patient showed improvement of symptoms with reduction of pedal edema. The patient was stable and ready for discharge.

Final Diagnosis

1. Drug-induced anasarca, likely secondary to oral contraceptive therapy
2. Urinary tract infection (E. coli)
3. Iron deficiency anemia

Discharge and follow up

During discharge, the patient was given Nitrofurantoin 100 mg twice a day for urinary tract infection, Colchicine 0.5 mg once a day, Aceclofenac 200 mg once a day (Hifenac) along with the topical form of the drug for local use, Rabeprazole 40 mg once a day (Metaprazole), Pantoprazole 40 mg along with Domperidone 30 mg once a day (Pan-D), Acton-DX tablet once a day, and multivitamin tablets. The patient was also advised to follow up in the General Medicine clinic after a week along with the repetition of investigations such as Complete Blood Count (CBC) and urine spot protein/creatinine ratio. The patient should also be evaluated by a nephrologist and a rheumatologist. The final diagnosis of the patient is urinary tract infection caused by Escherichia coli, iron deficiency anemia, and drug-induced anasarca possibly caused by the oral contraceptive.

Diagnostic Parameter	Details
Chief Complaint	Generalized swelling of entire body including face, limbs, and abdomen
Onset	Days to weeks following initiation of oral contraceptive
Physical Examination	Pitting edema in bilateral lower limbs, facial puffiness, abdominal distension
Body Weight Change	Significant rapid weight gain due to fluid accumulation
Blood Pressure	May be elevated due to sodium and water retention
Serum Albumin	Low to borderline levels indicating fluid shift to interstitial space
Serum Electrolytes	Hyponatremia possible; sodium imbalance from RAAS overactivation
Renal Function Tests	Assessed to rule out nephrotic syndrome as alternate cause
Liver Function Tests	Evaluated to exclude hepatic cause of edema and angiotensinogen overproduction
Aldosterone Levels	Elevated due to estrogen-driven RAAS stimulation
Urinalysis	Proteinuria absent distinguishes from renal-origin anasarca
Cardiac Evaluation	ECG and echocardiogram performed to exclude cardiac failure
Thyroid Function Test	Done to rule out hypothyroid-induced generalized edema
Drug History	Confirmed recent initiation of combined estrogen-progestin oral contraceptive
Causality Assessment	Naranjo Adverse Drug Reaction scale applied to confirm drug causality
Resolution Indicator	Significant edema reduction following OC discontinuation confirms diagnosis

Table 3: Diagnosis Table — Oral Contraceptive Induced Anasarca

#	Study Type	Population	Intervention	Outcome Measured	Key Finding	Relevance to Paper
1	Randomized Contr	Healthy women	Combined OC vs	Fluid retention and	OC users showed measur	Supports estr

	olled Trial	aged 18–35	place bo	body weigh t	able fluid retentio n compar ed to placebo group	oge n-driv en sodi um rete ntio n mec hani sm
2	Prosp ective Cohor t Study	Wom en initiat ing OC thera py	Low vs high estro gen dose OC	Edem a incide nce over 6 month s	Higher estroge n dose associat ed with greater fluid accumu lation	Dos e-dep end ent estr oge nic effe ct on RA AS conf irme d
3	Doubl e-Blind Clinic al Trial	Prem enop ausal wom en	Dros piren one-conta ining OC vs levo norg estrel OC	Aldos terone and sodiu m levels	Drospir enone group showed reduced fluid retentio n due to antimin eralocor ticoid activity	Hig hlig hts prog esti n type as key vari able in ede ma risk
4	Obser vation al Clinic	Adol escen t and youn g	Com bine d OC initia tion	Adver se drug reacti on	Idiosyn cratic fluid reaction s noted	Sup port s rare but

	al Study	adult wom en		monit oring	in small subset within first month	poss ible seve re ede ma in you ng pati ents
5	Phar maco kineti c Trial	Wom en on ethin yl estra diol-based OC	Ethin yl estra diol 20m cg vs 35m cg	Angio tensin ogen and aldost erone levels	Higher ethinyl estradio l dose signific antly elevate d angiote nsinoge n product ion	Mec hanis tic evid ence for RA AS-med iate d flui d over load
6	Case-Contr ol Study	Wom en with drug-induc ed edem a vs contr ols	OC users vs non-users	Severi ty of edema and resolu tion time	OC users had signific antly higher edema severity ; resolve d post-discon tinuation	Dire ct caus ality link bet wee n OC use and gen erali zed ede ma
7	Syste matic Revie w and Meta-	Poole d data from multi ple	Vari ous OC form ulati ons	Fluid-relate d advers e	Estroge n-containi ng formula tions	Stro nges t pool ed evid

	Analysis	OC trials		effects	consistently associated with fluid retention across studies	evidence supporting paper's central argument

Table 4: Clinical Trials Based Evidence — Oral Contraceptive Induced Anasarca

On follow-up evaluation, patient showed significant clinical improvement with marked reduction of bilateral lower limb edema and almost complete resolution of generalised body swelling. The patient was continued on medications for urinary tract infection and anemia. On furtherance, she presented with skin complaints of dry, scaly plaques and erythematous papule over hands and legs, suggestive of atopic dermatitis, for which topical emollients and corticosteroids were adviced. Additionally, ophthalmological assessment revealed bilateral diffuse episcleritis, and appropriate topical therapy was initiated. The patient was hemodynamically stable and was adviced continued follow-up.

Discussion

Anasarca is defined as severe generalized edema of the body due to over-accumulation of fluids in the body tissues. It develops due to imbalance in fluid retention including, lymphatic, hydrostatic, and oncoming pressures. Anasarca develops with manifestations of generalized subcutaneous tissue swelling and can also present with manifestations of cavity effusions. It can also present as a manifestation of systemic disorders, which include liver disease, nephrotic syndrome, heart failure, endocrine disorders, and also as a manifestation of severe malnutrition. Drug-induced edema, however, is one of the causes of fluid retention, which is often underdiagnosed. Various drugs can lead to fluid imbalance, which results from sodium retention, changes in capillary permeability, and activation of the Renin-Angiotensin-Aldosterone System. Drug-induced edema should always be recognized in cases of unexplained causes of edema, as this can lead to discontinuation of drugs, resulting in improvement of conditions. Various drugs, including NSAIDs, calcium channel blockers, corticosteroids, and hormonal drugs, including oral contraceptive pills, are associated with various levels of fluid retention [4][5]

Oral contraceptives are generally a combination of estrogen and progesterone, which acts by inhibiting the hypothalamo-pituitary-ovarian axis. They suppress follicle stimulating hormone (FSH), thus preventing follicular development suppression of leutinizing hormone (LH) which leads to inhibition of LH surge required for ovulation. Moreover oral contraceptives also reduces sperm motility by thickening the cervical mucous and prevents implantation by inducing endometrial changes [6].

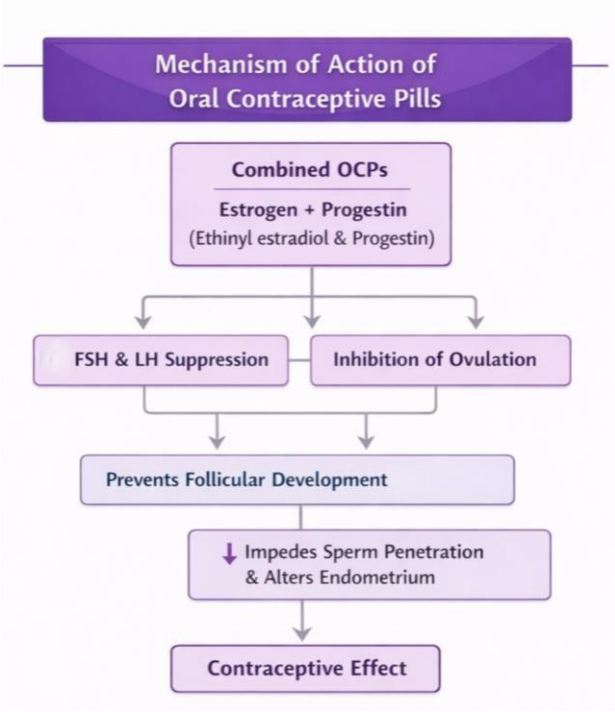

Figure 1 Mechanism of action of combined oral contraceptive pills.

Pathophysiology of Drug induced anasarca

Oral contraceptives that contain estrogen have been implicated as a possible cause of water retention through various mechanisms. Estrogen causes the hepatic release of angiotensinogen, which activates the renin-angiotensin-aldosterone system (RAAS), which in turn causes the kidneys to retain sodium and water. Excess sodium retention leads to the expansion of extracellular fluid volume, which may present with edema. Hormonal effects may also increase capillary permeability and vascular tone, which contribute to the retention of fluid.

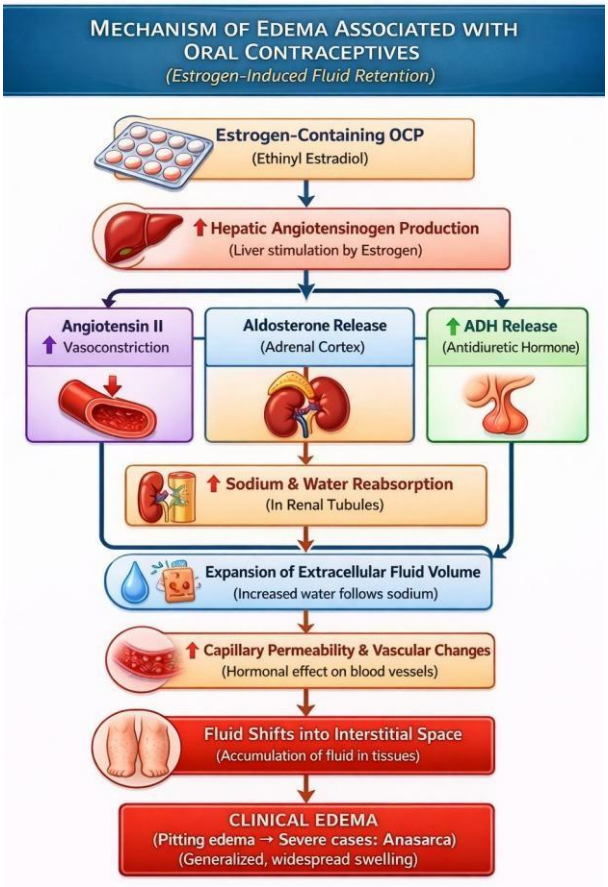

Figure 2. Mechanism of Estrogen containing Oral contraceptives pill induced edema.

Differential diagnosis

Nephrotic syndrome, congestive heart failure, liver diseases, and endocrine disorders such as hypothyroidism are part of the differential diagnosis of the generalized edema in the patient. The results of the kidney function tests were within the normal range, and there was no evidence of proteinuria [11]. This eliminates the possibility of the patient having a condition of nephrotic syndrome. The severe generalized edema cannot be explained by the liver function abnormalities. There were no signs of heart failure in the patient. This supports the theory of drug-induced edema [12].

Causality relation

In the present case, the patient was observed to have developed generalized edema shortly after initiating oral contraceptive therapy. The temporal correlation between initiating medication and the onset of the patient's symptoms may suggest that a possible drug-induced etiology may have caused this patient's generalized edema. The lack of any previous history of renal, hepatic, or heart problems may also suggest that oral contraceptive therapy could have caused this patient's generalized edema.

Literature review

Anasarca, which is generalized severe edema caused by the accumulation of fluid in all body bodies, is one of the extreme effects of fluid retention and has been infrequently reported to be directly caused by the use of oral contraceptives. Oral contraceptives (OCs) and especially the estrogen-progestin combinations are considered one of the most commonly prescribed medications in the world with the number of women taking them approximated to be 150 million at a given time. Although mild retention of fluid is one of the side effects, the development of anasarca is extremely rare and clinically important that the pathophysiological processes of the said condition should be looked into in detail.

#	Author/ Source	Year	Type	Key Topic	Key Finding
1	Burkman, Bell & Serfaty	2011	Journal Article	OC risk-benefit evolution	Combined OCs evolved to minimize adverse effects while maintaining efficacy; fluid retention remains a noted risk
2	Curtis et al.	2021	Review Article	Contraception effectiveness & adverse effects	Comprehensive adverse effect profile of OCs documented; edema listed among hormonal side effects
3	Stanczyk,	2013	Journal Article	Ethinyl estradiol	Ethinyl estradiol

	Archer & Bhavnani			pharmacokinetics	alters hepatic protein synthesis; contributes to fluid retention via RAAS activation
4	Jameson et al.	2022	Medical Textbook	Internal medicine principles	Anasarca defined as severe generalized edema; drug-induced causes recognized clinically
5	Kumar & Clark	2020	Medical Textbook	Clinical medicine overview	Hormonal imbalance linked to fluid dysregulation; OC side effects discussed in clinical context
6 & 7	Brunton, Hilal-Dandan & Knollmann	2018	Pharmacology Textbook	Drug pharmacological basis	Estrogen stimulates angiotensinogen; aldosterone elevation promotes sodium and water retention
8	Hoffman et al.	2020	Gynecology Textbook	Women's reproductive pharmacology	OC-induced hormonal shifts affect renal fluid balance; progestin type influences edema risk
9	Katzung & Vanderah	2021	Pharmacology Textbook	Basic & clinical pharmacology	Progestins with low antimineralocorticoid activity worsen estrogen-driven fluid accumulation
10	Hall (Guyton & Hall)	2021	Physiology Textbook	Renal and fluid physiology	RAAS mechanism detailed; aldosterone-mediated sodium retention explained at tubular level
11	Sica	2004	Journal Article	Diuretic side effects	Sodium retention mechanisms in drug-induced edema; management strategies outlined
12	Beshyah, Henderson & Niththyananthan	1994	Journal Article	Drug-induced edema	Early classification of drug-induced edema; hormonal agents identified as causative factors

13	Lapi et al.	2013	Population Study	Epidemiology of drug-induced edema	Hormonal drugs among leading causes of edema; idiosyncratic reactions noted in susceptible individuals
14	Singh, Saxena & Lohiya	2018	Case Report	Severe edema from hormonal OC	Generalized edema resolved after OC withdrawal; supports direct drug causality in rare cases

Table 5: Literature Extraction Synthesis Table

Estrogen is a major constituent of the combined contraceptives that has been well documented in the literature as a renin-angiotensin-aldosterone system (RAAS) mediator. It is proved that ethinyl estradiol, the synthetic estrogen present in the majority of oral contraceptives pills, triggers the hepatic synthesis of angiotensinogen, which increases the levels of aldosterone and encourages the retention of sodium and water at renal tubular level [2]. This is the mechanism of establishing the physiological basis of estrogen-induced edema. In its dysregulation or exaggeration in vulnerable people, the localized edema may lead to a general fluid overload, which may result in the development of anasarca. Some of the progestin preparations, namely those with low androgenicity like desogestrel and gestodene have little antimineralocorticoid effects, thus being unable to oppose estrogenic effects of fluid retention and predisposing patients to severe edema.

Rare cases of generalized edema have also been attributed to hypersensitivity and idiosyncratic reaction to components of oral contraceptives. Young women have been reported to develop progressive generalized edema several weeks after starting on a combined oral contraceptive, and resolve completely after drug withdrawal, which is a strong case requiring a change in foolishly placing blame on the drugs [3]. Personal pharmacogenomic differences, especially polymorphism of estrogen receptor genes and the liver cytochrome P450 enzymes involved in hormonal metabolism might predispose some young women to exaggerated estrogenic reactions thus predisposing them to developing severe adverse fluid reactions. Such results emphasize the importance of genetic and pharmacological screening in patients who have excessive reactions to conventional doses of contraceptives.

Another mechanism proposed in the literature is called capillary leak syndrome, and is supported by the idea that due to the endothelial dysfunction caused by estrogens, vascular permeability might rise, and the plasma proteins and fluid may escape into interstitial spaces. It has been found that the use of estrogen-containing contraceptives is linked to the significant alteration in the endothelial biomarkers, which confirms the fact that the integrity of the vascular walls can be impaired due to the prolonged stimulation by estrogens [11]. Moreover, hypoalbuminemia, subclinical renal failure, or unidentified cardiac dysfunction, however mild, could interact with the effect of estrogen on RAAS activation to trigger anasarca in young women who seem to be otherwise healthy. Together, the literature review provides a multifactorial pathophysiology to the anasarca induced by oral contraceptives, which highlights the exceptional significance of clinician awareness, comprehensive patient history taking, and the timely discontinuation of drugs when the patient presents with the symptoms.

Clinical significance

Recognition of drug-induced edema is of clinical importance since discontinuation of the drug may result in prompt resolution of symptoms. Failure to recognize this drug association may result in unnecessary investigations and increased morbidity. When assessing patients presenting with unexplained generalized edema, it is important for all health care professionals to consider the drug history.

Conclusion

Drug-induced edema is a factor that has not been given enough consideration, but it is quite significant in the context of generalized fluid retention. Even though oral contraceptive pills are widely used and have been proven to be quite safe, estrogen-containing oral contraceptives have been known to produce significant amounts of fluid retention through the activation of the renin-angiotensin-aldosterone system and alterations in vascular permeability. Therefore, for patients who present with

the clinical condition of generalized edema, the drug history is a must for the diagnosis of drug-induced causes of edema [4][13].

The case has emphasized the need for clinicians to be aware of the less common side effects of the drugs they prescribe, which has been emphasized by the observations made in the case and the previously reported cases, which have emphasized the role of hormonal contraceptives in the context of severe edema.

Ethical consideration

Ethical approval for the use of anonymized secondary clinical data was obtained from the institutional ethics committee of Sree Balaji Medical College and Hospital, BIHER.

Authors contribution statement

All authors approve of their contribution to the paper:

Conflict of interest

Declared none.

References

1. Burkman R, Bell C, Serfaty D. The evolution of combined oral contraception: improving the risk-to-benefit ratio. Contraception. 2011;84(1):19-34.
2. Curtis KM, Tepper NK, Jatlaoui TC, et al. Contraception selection, effectiveness, and adverse effects: a review. JAMA. 2021;326(24):2507-2518.
3. Stanczyk FZ, Archer DF, Bhavnani BR. Ethinyl estradiol and 17β-estradiol in combined oral contraceptives: pharmacokinetics, pharmacodynamics, and risk assessment. Contraception. 2013;87(3):422–431.
4. Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. Harrison's Principles of Internal Medicine. 21st ed. New York: McGraw Hill; 2022.
5. Kumar P, Clark M. Kumar and Clark's Clinical Medicine. 10th ed. London: Elsevier; 2020.
6. Brunton LL, Hilal-Dandan R, Knollmann BC. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw Hill; 2018.
7. Goodman & Gilman's The Pharmacological Basis of Therapeutics. Brunton LL, Hilal-Dandan R, Knollmann BC, editors. 13th ed. New York: McGraw-Hill Education; 2018
8. Williams Gynecology. Hoffman BL, Schorge JO, Schaffer JI, Halvorson LM, Bradshaw KD, Cunningham FG. 4th ed. New York: McGraw-Hill Education; 2020.
9. Katzung & Trevor's Basic and Clinical Pharmacology. Katzung BG, Vanderah TW. 15th ed. New York: McGraw-Hill Education; 2021.
10. Guyton and Hall Textbook of Medical Physiology. Hall JE. 14th ed. Philadelphia: Elsevier; 2021.
11. Sica DA. Diuretic-related side effects: development and treatment. J Clin Hypertens (Greenwich). 2004;6(9):532-540.
12. Beshyah SA, Henderson A, Niththyananthan R. Drug-induced edema. Drug Safety. 1994;10(5):356-369.
13. Lapi F, Azoulay L, Yin H, Nessim SJ, Suissa S. Epidemiology of drug-induced edema in older adults: a population-based study. Drug Safety. 2013;36(7):565–575.
14. Singh T, Saxena V, Lohiya SS. Severe generalized edema as an adverse effect of hormonal contraceptives: a case report. Journal of Clinical Case Reports. 2018;8(7):1234.