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Original Article

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Antimicrobials Utilisation Trends and Surgical Site Infections in Open Abdominal Surgery

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Abstract

The open abdominal surgeries are more prone to many surgical site infections due to the therapy failure or aseptic conditions during surgery. The patients undergoing these surgeries are prescribed with more than one antimicrobials as empirical or prophylaxis. This irrationality in prescription can lead to surgical site infections and antimicrobial resistance. Hence, our study aims at evaluating the drug use of antimicrobials in the open abdominal surgery. This hospital based prospective observational study was carried out in the General Surgery department at a tertiary care hospital in India. The study included 114 subjects for a period of six months. The data was collected from various sources in a predesigned data collection forms. The prescriptions containing antibiotics were evaluated and the rationality was compared using John Hopkins Antibiotic Guidelines. Amongst the study population, 57.8% were inpatients and 42.1% were out-patients. The male patients were more (50.8%) and 78.9% of the study population underwent elective surgery. The most common surgery conducted was hernioplasty 48.2%. Majority of the prescription comprised of antibiotic therapy, amongst which the third generation Cephalosporins (70.96%) were prescribed the most, as prophylaxis. The drug utilisation evaluation helps to assess the appropriate selection of safe and effective antimicrobials which is significant in pre and post-operative cases. Hence our study supports the need for clinical pharmacist in the antimicrobial management, to study drug utilization pattern and develop antimicrobial stewardship for the rational prescription.

Keywords: Drug utilization evaluation; Antimicrobials; Surgical site infection.

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Introduction

A surgical unit is a setting where a large number of drugs are administered to patients and drug treatment are high [1]. In surgical practice, antimicrobial agents are usually administered in three situations as surgical prophylaxis, as an adjunct to operative treatment and as treatment of infection prophylaxis to reduce the incidence of surgical site infection. They are used more widely in abdominal surgeries such as appendicitis, Cholelithiasis, surgeries for hernia, fistula in Anal fistula, haemorrhoids, surgery for GI obstruction, cancer in abdomen and hernia mesh repair.

Surgical site infections [SSI] poses an increased risk of hospital acquired infections and may have

impact on economic burden due to additional incurring costs of OPD visits, length of hospital stay, increased intensity of treatment, laboratory investigations hospital discharge, additional costs of outpatient visits, emergency admissions, treatment and other health care requirements are borne by the patient [2,11,14]. SSI also produces delayed wound healing, augmented use of antibiotics and multidrug antibiotic resistance.

Antimicrobials are the main stay of treatment for the prevention and cure of SSI [3]. They form the backbone of any prescription for treating infection. Drug utilization studies aim to evaluate factors related to the prescribing, dispensing, administering and taking of medication (antimicrobials) associated events (either beneficial or adverse). Irrational use of antibiotics includes use of medically ineffective and inappropriate drugs unrelated to diagnosis, polypharmacy, expensive drugs, use of branded drugs instead of generic drugs, and excessive use and misuse of antimicrobials. Often, these are given at wrong time, dose and frequency that can result in increased incidence of adverse drug reactions, super infection, antimicrobial resistance, many drug related problems, delay in relief, increased hospital days, increased morbidity and mortality, and economic loss and is one of the reasons for increasing resistance to antimicrobials [15]. During the last decade, antibiotic resistance is on the rise [5]. This is due to the abuse of broad-spectrum antibiotics in first-line treatment or erroneous or use of multiple courses, prolonged duration of antibiotic treatment. Treatment guidelines assist physicians to prescribe medications in a rational manner.

A cohort study indicated that almost 40-60% of SSIs can be prevented with the appropriate use of surgical antimicrobial prophylaxis (AMP). Although 30-50% of antimicrobials are used 30-90% of them are used in correctly which attributed for 16% of SSIs in hospitals for surgical prophylaxis [16]. Common challenges faced when prescribing antibiotics are to choose the appropriate drug to eradicate the infecting microorganism and to continue the drug for the correct time period. This do not mean that all antibiotics use should blindly be reduced, proper selection of antibiotics should be made which requires good clinical judgement and in-depth information about pharmacological and microbiological factors. Regrettably, the prescription of antibiotics is made without much thought about the pharmacological features of the drug or the range of microorganisms infecting the surgical site [7].

The aim of the study is to evaluate drug utilisation pattern of antimicrobials in open abdominal surgeries and to report ADR's in those patients in a tertiary care hospital.

Methodolodgy

The study was conducted both in patients and out patients of the general surgery department of the tertiary care hospital in Bangalore. It was hospital based prospective and observational study conducted for a period of six months. Institutional ethical committee (ECR/215/Inst/KA/2013/ RR-16) approval was obtained before conducting the study.

A written informed consent was taken from patient for data collection. A Predesigned patient profile form was used to enter all patient details like patients demographics, date of admission and discharge, reason for admission, past medical history and their duration, food habits, allergies, known ADRs, lab reports and the surgical procedures. The inclusion criteria of the study included inpatients and outpatients who were prescribed with one or more antimicrobials and who had undergone open abdominal surgeries. The patient who did not give their consent to participate was excluded.

The prescriptions containing antimicrobials were evaluated for the category of antimicrobial prescribed, most common antimicrobial used along with their combination. OT notes and the case sheets were used to obtain the details of pre-operative, intra-operative, and post-operative prophylactic antimicrobials.

The patients during the hospital stay and OPD visit were examined for any new clinical manifestations or symptoms in order to identify adverse drug reactions (ADR) associated with the given therapy. WHO Probability Assessment Scale was used to assess the identified ADR's, the relationship between suspected drug and reaction were established using Naranjo's causality assessment scale which is further classified into certain/definite, probable and possible. The patients who were included in the study, assessed by the treating surgeon for any pus exudates, erythematous appearance and intactness of wound of ruling out any surgical site infections were recorded. The isolates collected from the sample which includes swabs, blood, and pus of the infected wound site were collected and submitted at the microbiological lab. Further, standard tests such as Gram's staining, catalase, DNase, growth

on mannitol salt agar, slide and tube coagulase were done to identify the culture. Kirby Bauer disc diffusion method (1996) against various antibiotics, antibiotic susceptibility pattern of all the confirmed strains were documented and after incubation for 24 hours at 37^{0}C the results were interpreted. Using the guidelines published by the Clinical and Laboratory Standards Institute, the zone diameters measured around each disk were interpreted and analysed. Microsoft word and excel were used to generate tables, pie charts, bar diagrams and data analysis.

Results

In the present study, the prescriptions of 114 patients who underwent general abdominal surgical procedures were enrolled and the prescribing pattern was analysed. Out of which 58 patients (50.8%) were males. Majority of the patients were in the age group of 36-50 years with 35 patients (30%) followed by 30 (26.5%) patients in the 51-60 age group (Fig. 1). The major diagnosis observed was hernia 55 (48.2%) followed by cholelithiasis 26 (22.8%) (Fig. 2). Among the different types of surgeries performed 78.9% of the study population underwent elective surgery.

Prescription analysis was done and among the 139 antimicrobials prescribed, it was observed that antibiotics (82.01%) and antiprotozoal drugs 12 (25%) were most commonly prescribed. Out of the different classes of antibiotics, cephalosporins 76 (67.8%) were most frequently advised in which ceftriaxone 38 (36%) were most commonly used (Table 1). This was followed by metronidazole 9 (11.4%) in the antiprotozoal class. Antibiotics were prescribed as single and combination therapy, of which monotherapy (112, 80.5%) was most preponderant. Among the different combination therapies used, it was observed that ornidazole+ofloxacin 30 (38.9%) was the most commonly used followed by cefuroxime +clavulanic acid 8 (42.1%).

Ceftriaxone induced diarrhoea (37.5%) was the highest observed adverse effect. Whilst surgical site infections were witnessed in 15 (13.15%) patients acquired and majority of them (41.4%) had grade IV severity.

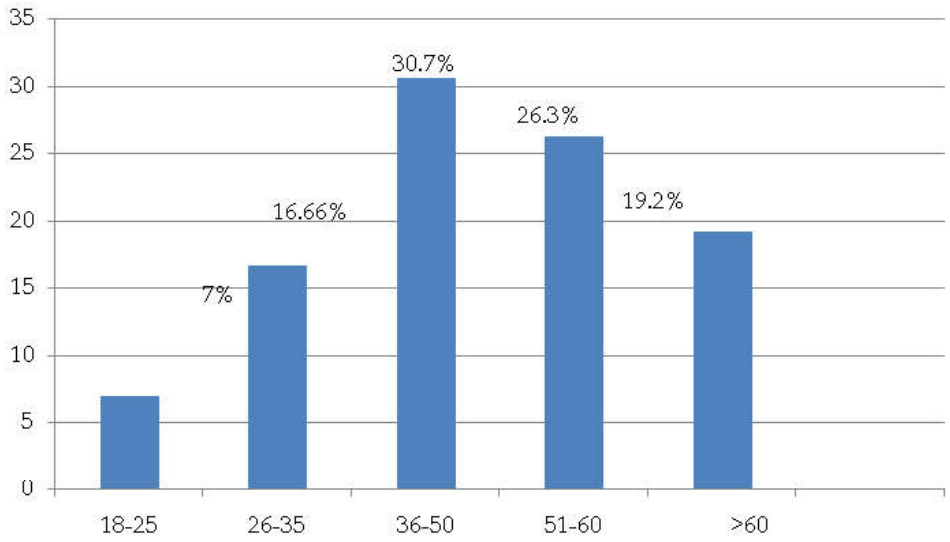

Fig. 1: Age Group Categorization

Table 1: Antibiotic Monotherapy

Sl. NO	Antibiotic class	N	%
1	Cephalosporins	76	67.8%
2	Antiprotozoal	12	10.7
3	Beta lactam	7	6.41
4	Oxazolidinones	1	0.89
5	Aminoglycosides	6	5.3
6	Fluroquinolones	10	8.9
	Total	112	100

Table 1: illustrates the pattern of antibiotic monotherapy

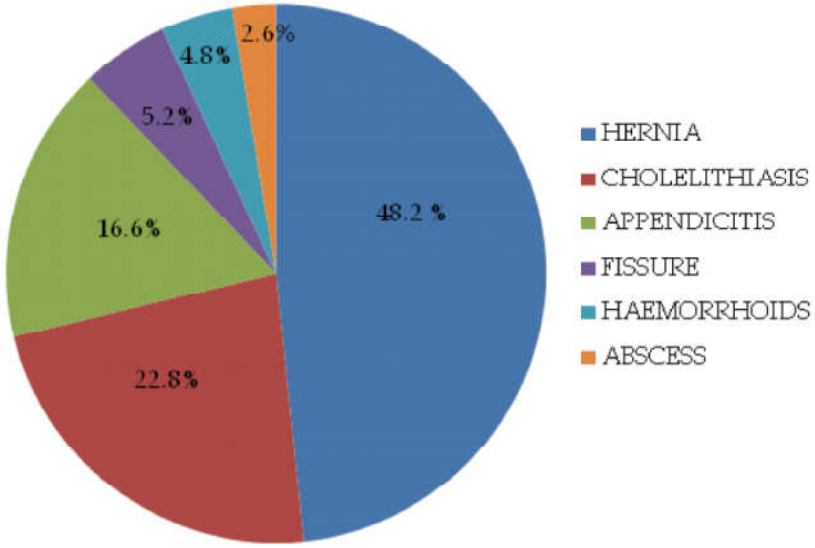

Fig. 2: Disease Pattern

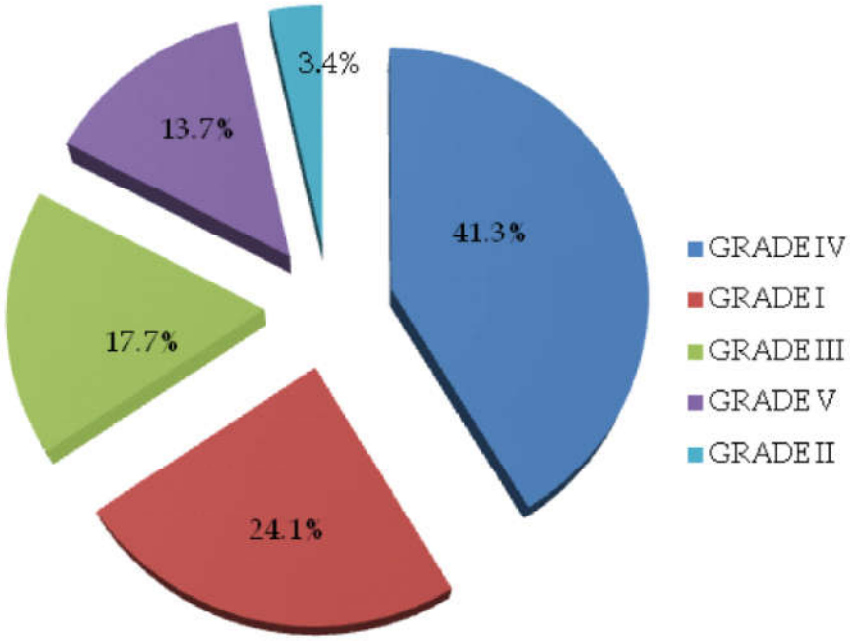

Fig. 3: Surgical Site Infection

Table 2: Antibiotic Combination Therapy

Sl. No	Antibiotic combination	Number of patients	%
1	Ornidazole and ofloxacin	40	45.5
2	Amoxicillin and clavulanic acid	9	10.2
3	Piperacillin and tazobactum	6	6.9
4	Ceftriaxone and sulbactam	20	22.7
5	Cefoperazone and sulbactam	5	5.6
6	Cefuroxime and clavulanic acid	8	9.1
	Total	88	100

Table 2: Depicts the pattern of antibiotic combination therapy

Discussion

Antimicrobials are considered to be one of the most important part of modern medical care and play a crucial role in the treatment of infectious disease or as prophylaxis. Surgical antimicrobial prophylaxis refers to a very short course of an antimicrobial therapy which is started prior to surgery, to prevent infections at the surgical site.

Our present study focuses on the use of antimicrobials in patients undergoing open abdominal surgery in a tertiary care hospital. According to our study 70 (51.8%) were found to be male patients and 65 (48.1%) patients were females. This is similar to a study done by Tabiri et al. [8]. where the male patients was found to be more (77.7%). Majority of the patients in our study population was within the age group of 36-50 years (30.7%) followed by 51-60 years (26.3%), which is in accordance to the fact that the chances of acquiring infections increases with age.

In our study, majority (78.9%) of patients had an elective procedure which was similar to the results of the study conducted by H.S. Rehan et al. [9]. They conducted a prospective observational study to assess pattern of prophylactic antibiotics in different surgeries. Among the surgical procedures was conducted in our study hernioplasty (48.2%) was the most common surgery encountered, which is allied to a study conducted by Brethis et al. [8].

All subjects in the current study received prophylactic antimicrobials prior to the surgery and the antimicrobial therapy was continued after the surgery. In our present study (82%) of our subjects received antibiotic monotherapy, prescriptions with two antibiotic drug combinations 23 (16.45%) and more than 3 drug combinations 2 (1.43%) this is similar to a study conducted by Bengari et al. [8] whose results revealed 30% of his subjects received monotherapy, 44 (46.81%), 14 (14.89%) prescriptions had three antibiotic drugs combinations and 6 (6.38%) prescriptions were more than three antibiotic drug combinations. Our study showed higher usage of monotherapy, which may uphold the fact of single and appropriate selection of antibiotic, has been followed at our hospital setting satisfying one of the criteria for rational use of antibiotic.

The most commonly used antimicrobial prophylaxis in surgery according to Indian Council of Medical Research Department of Health Research New Delhi, India 2017 is cefazolin excluding conditions of severe beta-lactum allergy, known MRSA colonization and surgical areas with organisms that cannot be treated with cefazolin alone (e.g., appendectomy, colorectal. In cases requiring additional coverage of microbes, combinations like cefazolin plus metronidazole or cefoxitin, or ertapenem can be used. Hospital specific and patient specific antibiotic resistance would warrant the use of additional antibiotics. In the current study, number of antibiotic used were 139 (82%), 76 (69%) in which of third generation cephalosporin 76 (67.8%) and of 12 (10.7%) metronidazole were used. The results were in par with the study conducted by Ayesha Parveen et al. who did a six months prospective observational study on prescribing patterns of antibiotics in post-operative patients in a teaching hospital [3]. The total numbers of antibiotics used were 420 in which 37.1% of third generation cephalosporin and 31.4% of metronidazole were used. The study concludes that most common use of cephalosporins and metronidazole seems to be effective in reducing the surgical site infection and other complications. Patients in surgical wards develop infections post-surgery. Many of the infections are caused by bacteria that are highly virulent. As a result there is a need for prophylactic or empirical treatment with antibiotics that can cover broad spectrum of pathogens. However use of third generation was extensive, which may result in the development of resistance to these agents in the near future.

It was observed that ornidazole+ofloxacin 30 (38.9%) was the most commonly used combination therapy followed by cefuroxime +clavulanic acid 8 (42.1%). This result is contradictory to the study conducted by Ayesha Parveen [3] et al. who did a 6 months prospective observational study on prescribing patterns of antibiotics in post-operative patients in a teaching hospital and they found that cefeperazone+sulbactum (47%) combination was used the highest. Ornidazole ofloxacin combination is comparatively less costly when compared to other combinations which might explain the increased prescription of the same.

Selection of appropriate and effective pre-op prophylactic antibiotic and post-op definitive antibiotic treatment is essentials to reduce the risk of SSI in patients post-operatively. In addition to this, patient medication adherence and other factors play a pivotal role in minimizing the occurrence of SSI. Among the study population 13.15% of the patients acquired surgical site infections, similar results were observed in a study conducted by H.S. Rehan et al. in which it was found that 12% of the patients complained of purulent discharge at the

incision site and surgical site infection was reported in 14% of cases. Whereas in a study conducted by Bansal showed only 6% of SSI. Surgical site infections were analyzed using Southampton scoring system in which it was observed that 40% was Grade-I (Erythema) followed by 33.3% of Grade-IV (PUS). The use of antimicrobials in all the cases was empirical. SSI warrants the increased use of antibiotics as treatment which in turn can lead to increased cost of therapy and prolonged hospital stay. Antimicrobial prophylaxis is helpful to prevent surgical site infections. In our study it was observed that majority of the surgical site infections were treated with supportive therapy and severe conditions were treated with antimicrobials.

The adverse drug reactions of antibiotics were observed in 8.1% of our study population. In our study it was found out that diarrhea (37.5%), itching and rashes (15%) were more prevalent while the study conducted by Ramya et al. (2013) revealed that most common organs affected were skin (69%) and GIT (8%).

It was observed that Cephalosporins (37.5%) were the most ADR causing drug followed by linezolid (15%) which belongs to the class of oxazolidinones this is similar to a study conducted by M. Shamna et al. in the year 2014, which showed that cephalosporins were the most common drugs causing ADR (35%) [10].

Conclusion

The study shows that majority of the prescription contained cephalosporins followed by metronidazole which can be due to the fact that they are broad spectrum antibiotics. Most of the patients in the study were diagnosed with hernia and cholilitheasis for which the antibiotics were prescribed without conducting relevant culture sensitivity test. The major surgical procedures were elective which lead to the prescription of more than one antibiotics in most of the cases. More than average numbers of the drugs in the evaluated prescriptions were prescribed by brand names. Thus the empirical treatment without the culture sensitivity test and the usage of branded products instead of generic drugs increases the cost of the treatment and may lead to antibiotic resistance. Hence the prescribing practices that are a reflection of a health care practitioner's abilities to discriminate among various choices of drugs should be evaluated and monitored carefully to promote the rational drug use.

Limitations

The study was carried out only for a short period of time and included a small sample size. Also the study was restricted to open abdominal surgery.

Abbreviations

SSI Surgical Site Infection, ICMR-Indian Council of Medical Research, ADR- Adverse Drug Reaction, MRSA-Methicillin-resistant Staphylococcus aureus.

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Review Article

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Diclofenac Induced Severe Pancreatitis: A Rare Case Study

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Abstract

Acute pancreatitis is sudden inflammation of the pancreas that may be mild or life threatening but usually subsides. Acute Pancreatitis is an acute inflammatory process of the pancreas with varying involvement of regional tissues or remote organ systems. Gallstones and alcohol abuse are the main causes of acute pancreatitis. Severe abdominal pain is the predominant symptom. Blood tests and imaging tests, such as computed tomography, help the doctor make the diagnosis. Whether mild, moderate, or severe, acute pancreatitis usually requires hospitalization. Here case reported with a history of tooth removal and given analgesic – NSAIDS – Diclofenac post intake patient develop severe pain abdomen, vomiting and restlessness. Patient being hospitalized for the same and regular investigation done suggestive of Acute Pancreatitis. Patient recovered as per standard treatment given.

Keywords: Acute Pancreatitis; Diclofenac; Serum Amylase; Serum Lipase; NPO.

How to cite this article:

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Incidence of acute pancreatitis in England, Denmark and USA ranges between 5 & 30 per 100,000 populations with highest incidence recorded in the United states and Finland.

The estimated incidences are however in accurate because the diagnosis of mild diseases may be missed and death may occur before diagnosis in 10% of people with severe disease [1].

The increased incidence of pancreatitis, coupled with new treatment options, poses a challenge for primary care physicians. Twenty fivepercent of patient suffer from the severe form of the disease with local or systemic complications, resulting in mortality rate ranging from 2-10%.

Increased mortality and morbidity are associated with organ failure in 50% of severe acute pancreatitis cases [2].

The two most common causes of acute pancreatitis are choleliathisis and alcohol. The other causes includes drugs (Azathioprine, Corticosteroids, etc.) [3].

Regardless of the etiology, pancreatic enzymes (Including Trypsin, Phospholipase A2 & Elastase) become activated within the gland itself. The enzymes can damage tissue and activated complement and inflammatory cascade, producing cytokines. This process causes inflammation, edema, and sometimes necrosis. In mild pancreatitis, inflammation is confined to the pancreas; the mortality rate is 10 to 50%. After 5 to 7 days, necrotic pancreatic tissue may become infected by enteric bacteria. The chances of developing infected pancreatic necrosis depend the extent of necrosis [4].

Activated enzymes and cytokines that enter the peritoneal cavity cause a chemical burn and results in exudation of fluid in third space; those that enter the systemic circulation causes a

systemic inflammatory response that can result in acute respiratory distress syndrome and renal failure. The systemic effects are mainly the result of increased capillary permeability and decreased vascular tome, which result from the released cytokines and chemokines. Phospholipasae A [2] is thought to injure alveolar membranes of the lungs. Here case reports a 56 years old male non alcoholic, non smoker, vegetarian no history any surgery had history of severe toothache and undergone tooth eruption and has been given diclofenac as a analgesics. Post analgesic consumption patient develop severe pain abdomen, persisting vomiting and abdominal distension.

On Examination

- Pulse – 126 BPM.
- Blood Pressure – 156/90 mm of Hg.
- SpO_2 – 96% at RA.
- Temperature – Afebrile.

CVS – S1 & S2 – NAS.

R/S – NVBS, B/L EAE.

P/A – Distended Diffuse tenderness, BS – Reduced.

Investigations – At the time admission.

CBC - TLC – 16200 Cubic/mm, Serum Amylase – 6632 IU/L, Serum Lipase– 4322 IU/L, Creatinine – 2.05mg/Dl, K+ 4.5, NA + 134

Table 1 shows classical recovery - clinically and laboratory wise.

Patient hospitalized and treated as per standard protocols.

- NPO
- RT Aspiration.
- IV – Fluids as maintenance round the clock.
- Foleys catheter for the Urine output.
- Meropenam – 500mg Q8H.
- PPI – 40mg IV Q 12H.

Probable Mechanism of Diclofenac Causing Pancreatitis

Drugs associated with pancreatitis have been classified into three groups. In the first group the association is regarded as definite and fulfils the criteria ofpancreatitis developing during treatment with the drug, disappearing upon drug withdrawal and, recurring again when the drug is reintroduced. In the second category a probable association is thought to exist when some but not all the above conditions are fulfilled; the third group contains drugs which have been proposed as causes of pancreatitis, but the published evidence is either inadequate or contradictory. Acute pancreatitis in the patient described was probably due to diclofenac consumption. A definite causative association could only have been established after rechallenging the patient with the drug. Deliberate subjection of a patient to a potentially serious or lethal disease can be ethically justified only if the drug in question-and only that drug-is essential for treatment of a serious illness [5,6].

Conclusion

Pancreatitis is life threatening conditions, most common factors being alcohol and gall stones but we need to even consider rare incidence such as diclofenac as reported here.

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Table 1:

	Serum Amylase	Serum Lipase	TLC	K +	NA ++	Creatinine
Day 1	6632 IU/L.	4322 IU/L	16200	4.5 meq/L	134 meq/L	2.05 mg/dl
Day 2	4467 IU/L.	3453 IU/L	14400	4.5 meq/L	137meq/L	1.95 mg/dl
Day 3	2178 IU/L.	2422 IU/L	12200	4.5 meq/L	142meq/L	1.76 mg/dl
Day 4	879 IU/L.	834 IU/L	11700	4.5 meq/L	138meq/L	1.56
Day 5	356 IU/L.	345 IU/L	8200	4.5 meq/L	140 meq/L	1.3 mg/dl
Day 6	67 IU/L.	135 IU/L	7276			

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Case Report

Gastroenterology International
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An Uncommon Cause of Chronic Diarrhoea

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Abstract

A 9 year old female patient presented with history of chronic diarrhea for 4 years. She had no pain abdomen or blood in stools. She had significant weight loss. She was previously evaluated with stool examination, upper gastrointestinal endoscopy, colonoscopy, computed tomography of abdomen, even then the etiology could not be identified. She continued to have diarrhea and weight loss and then presented to our hospital. Endoscopy demonstrated diffuse nodularity in the second part of duodenum. Tissue transglutaminase antibody for celiac disease was negative. Histopathological examination of duodenal biopsy showed multiple clumps of Giardia lamblia trophozoites which was confirmatory for chronic giardiasis. Then she was treated with oral tinidazole (2 grams, single dose) which with she had improvement in symptoms with weight gain.

Keywords: Giardiasis; Diarrhoea; Giardia Lamblia; Endoscopy; Chronic Diarrhoea.

How to cite this article:

S Abarjitha, Arun AC, Jenish Rajma et al. An Uncommon Cause of Chronic Diarrhoea. Gastroenterology International. 2018;3(1-2):17-18.

Introduction

Diarrhea is defined as the increased frequency of passage of abnormally liquid stools and its volume more than 200 grams per day. When it extends more than 4 weeks, then it is termed as chronic diarrhea. It can be categorized on being due to disease of colon or small bowel or to malabsorption. Here we present a case, where the diarrhea was caused by one of the forgotten etiologies.

Case Report

A 9 year old female child presented with chief complaints of diarrhea for 4 years. The diarrhea was intermittent, watery, associated with significant weight loss. There was no abdominal pain, no blood in stools and also there is no history of steatorrhea. The history of weight loss showed the possibility of malabsorption. Complete Hemogram showed iron deficiency which is also suggestive of malabsorption. She was previously evaluated elsewhere 4 years back, where stool examination, upper gastrointestinal endoscopy, colonoscopy, computed tomography of abdomen were normal. She came to our hospital with persisting diarrhea and weight loss.

General examination showed pallor, mild pitting edema, no icterus, lymphadenopathy and clubbing. Abdominal examination was also found to be normal. Hematological investigation showed hemoglobin of 7.7%, Mean corpuscular volume- 66, Total count- 4900 per micro litre, Platelets -2.5 lakhs per micro litre. Renal function test and liver function test were normal.

There are many differential diagnosis for chronic diarrhea. For painful diarrhea, differential diagnosis includes chronic pancreatitis, amoebiasis,

inflammatory bowel disease, eosinophilic enteritis, autoimmune enteropathy. For painless diarrhea, differential diagnosis includes celiac disease, tropical sprue, microscopic colitis, lactose intolerance. Immunoglobulin a Tissue transglutaminase antibody for celiac disease was negative and hence it ruled out celiac disease. Hydrogen breath test was negative which ruled out lactose intolerance. Following this, upper gastro-intestinal endoscopy was taken. It showed diffuse nodularity in the second part of duodenum and biopsy was taken.

Duodenal biopsy revealed focal dense lymphoid aggregates with germinal centers in lamina propria. Then a large number of basophilic pear shaped symmetrical structures were present in the intervillous space (Fig 1). This confirmed the presence of trophozoites of Giardia lamblia. So the final diagnosis was chronic giardiasis which caused malabsorption and weight loss. She was treated with a single dose of tinidazole (2 gram) and nitazoxanide (500 milligram) twice daily for 3 days with which she had improvement in symptoms with weight gain.

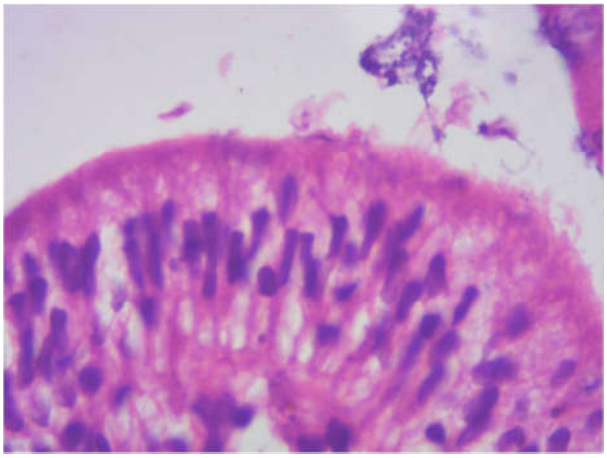

Fig. 1:

Discussion

In this era of non-communicable diseases, infectious diseases are often forgotten. However infectious diseases are still common in the tropical countries [1]. This case is a prototype of the fact that older infectious disorders should not be forgotten in the differential diagnosis. Giardia is the commonest parasitic diarrheal pathogen affecting humans and a frequent cause of waterborne/ foodborne parasitic diseases worldwide [2]. Prevalence of giardiasis is higher in children, living in poor, low hygiene settings in developing countries, and in travelers returning from highly endemic areas. The clinical picture of giardiasis is heterogeneous, with high variability in severity of clinical disease [3]. In this patient, Giardiasis had been ignored initially because the stool examination was negative. This is due to the fact that there is intermittent shedding of trophozoites in stool.

Conclusion

In patients with chronic diarrhea, it is difficult to arrive at a single diagnosis, because there are many etiologies which may cause chronic diarrhea. In this era of autoimmune diseases, malignancies and non communicable diseases, infectious diseases should not be forgotten. Also while investigating any patient, all treatable causes should be actively looked for. Giardiasis is re-emerging in many of the low incidence countries with drug resistance being a main concern.

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Case Report

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A Rare Occurrence of Synchronous Adenocarcinoma Gall Bladder along with Squamous Cell Carcinoma Cervix

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Abstract

Multiple primary malignant neoplasms (MPMN) is the term used to describe malignancies arising from two or more different organs with different histology and have no relation which each other. Incidences of such cases have been occasionally in the literature. Organs affected in such cases do differ in accordance to prevalence of disease in the particular region, with metachronous occurrences being more common than synchronous malignancies. Carcinoma gall bladder and Carcinoma cervix are the two most common neoplasms affecting the females in Northern India. The synchronous appearance of both malignancies together is a rare phenomenon which has never been described earlier in available literature search. We describe synchronous occurrence of locally advanced adenocarcinoma gall bladder with locally advanced squamous cell carcinoma cervix and the diagnostic as well management challenges we encountered in this case report. 50 year old post menopausal female presented with complains of pain in right upper abdomen with a palpable abdominal lump and foul smelling vaginal discharge. On examination there was a lump in right hypochondrium with an ulcerative proliferative growth in cervix. Radiological imaging showed gall bladder mass with adjacent hepatic infiltration and cervical growth invading base of bladder and right parametrium causing right hydrouteronephrosis. Image guided core needle biopsy of gall bladder revealed adenocarcinoma and punch biopsy of cervix revealed squamous cell carcinoma. With increasing life expectancy and improvement in imaging modalities there is a gradual increase in reporting of such cases. Proper Clinical assessment is needed to rule out recurrence in case of metachronous malignancies or metastasis in case of synchronous malignancies from index cancers to classify it as multiple primary malignant neoplasms. These cases not only pose a diagnostic dilemma but also difficulty in management. With more awareness and better reporting regarding the phenomena we may be able to formulate personalized treatment plans to treat these patients of MPMN

Keywords: Synchronous; Multiple Primary Neoplasms; Carcinoma; Gall Bladder; Cervix.

How to cite this article:

Jeetendar Paryani, Parijat Suryavanshi, Shashi Singh Pawar. A Rare Occurrence of Synchronous Adenocarcinoma Gall Bladder along with Squamous Cell Carcinoma Cervix. Gastroenterology International. 2018;3(1-2):19-22.

Introduction

The phenomenon of two or more cancers occurring in the same patient without any relation between them is termed as Multiple Primary Malignant Neoplasms (MPMN). The reporting of such cases is gradually on the rise. The common histological types may vary according to local prevalence of cancers in a particular region.

Carcinoma gall bladder is the most common malignancy of the biliary tract and one of commonest malignancies of the gastrointestinal tract [1]. It is characterised by with marked variation in incidence in distribution in different parts of the world with exceptionally high incidence in females of North Indian Gangetic plains [1].

Carcinoma cervix is one of most common cancer in developing nations [2,3]. In India, it is most common cancer of women and mortality from it is quite high. This is because of the fact that most of cancers of cervix are diagnosed at an advanced stage [2,3].

Despite the high incidence of both these malignancies in North Indian females [1,2,3] synchronous occurrence of both these malignancies with different histological types has probably not been reported before.

We describe synchronous occurrence of locally advanced adenocarcinoma gall bladder with locally advanced squamous cell carcinoma cervix in this case report.

Case Report

50 year old post-menopausal female presented with chief complains of gradually worsening pain in right hypochondrium for last six months. Pain was intermittent colicky non radiating relieved by medication.

Patient also complained foul smelling vaginal discharge accompanied by complains of intermittent episodes of bleeding per vagina since 3-4 months. There was accompanying history of loss of appetite and weight loss over the period of last 2 months. There was no history of fever, jaundice, backache, urinary complains, vomiting or neck swelling.

On examination patient was poorly built and nourished with mild pallor. ECOG status was 2. Abdominal examination showed 6*6 cm firm globular gall bladder mass. There was no other palpable abdominal lump, no free fluid or supraclavicular nodes.

Per vaginal examination revealed circumferential ulceratio-proliferative growth in cervix obliterating bilateral fornixes and finger staining with blood. Contrast enhanced CT scan of Whole Abdomen was suggestive of space occupying lesion 4*4 cm predominantly in body region of gall bladder with adjacent liver infiltration and fascial planes obscured with duodenum. Cervix and uterus replaced by a heterogeneous mass (6*4*3 cm) infiltrating the parametrium. Lesion was also invading the right ureterovesical junction base of bladder and rectum with loss of fascial planes. Right moderate hydrouteronephrosis was also present.

Liver Function Test and kidney function tests was within normal limits. Other investigation were also within normal limits Punch biopsy was done from cervix which was suggestive for well differentiated Squamous cell carcinoma. Ultrasound guided Core needle biopsy was also done from gall bladder mass which was suggestive of infiltrating adenocarcinoma.

The case was discussed in multi-disciplinary meeting to decide for the future course of management. In view of locally advanced nature of both malignancies and poor performance status the patient was decided to be started on palliative cisplatin based chemotherapy. But after two cycles of chemotherapy patient succumbed to the disease.

Fig. 1: CECT scan showing Gall bladder mass infiltrating the surrounding liver with ill-defined interface with surrounding structures. Also it shows Right hydronephrosis.

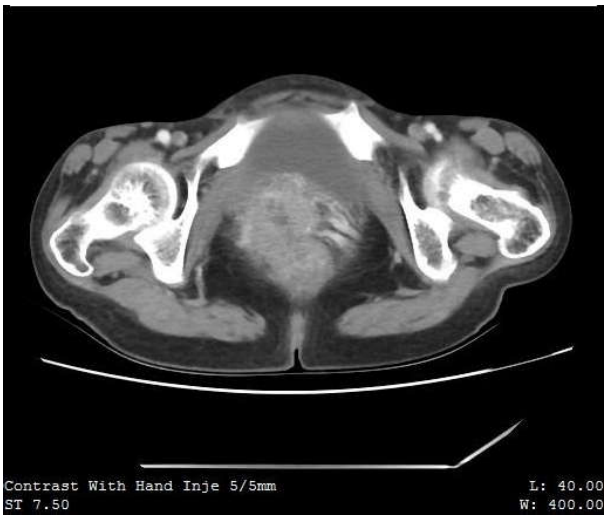

Fig. 2: Showing cervical mass invading the right parametrium and base of bladder

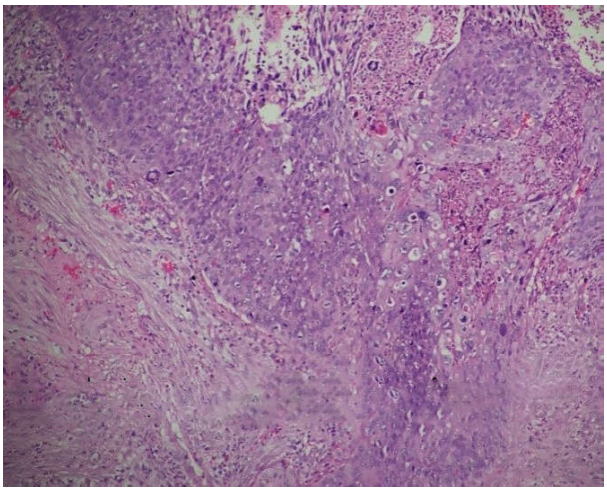

Fig. 3: showing 10x Zoom of microscopic image of punch biopsy of cervix of the patient suggestive of Squamous cell carcinoma.

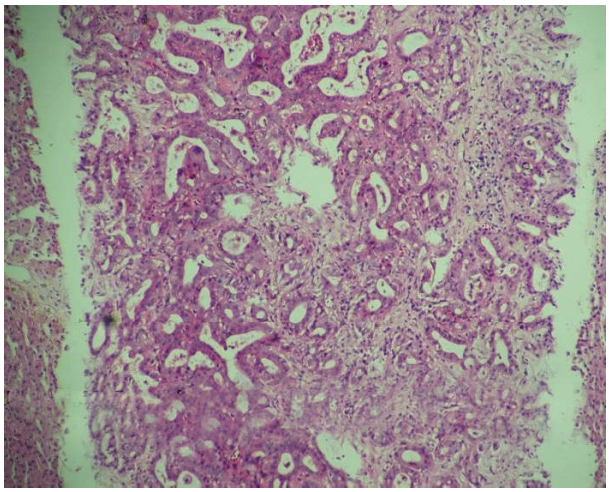

Fig. 4: 20x Zoom of microscopic image of punch biopsy of cervix of the patient suggestive of Squamous cell carcinoma

Discussion

With the increasing life expectancy and better imaging modalities available, incidence of cases detected with two or more primaries is on the rise. Spratt and Hoag found that the reported prevalence varies from 0.7% to 11.7% and concluded that, empirically, persons living to extreme age are more likely to have multiple cancers [6].

Clinically such cancers maybe confused with recurrence or the metastasis from the index malignancy as in both of these conditions occurrence of new lesions at different parts of body is considered as part of the metastatic spread.

To avoid such conditions Warren established criteria for diagonosis of MPMN which were updated by Liu Fusheng, 1) each tumour must be malignant, 2) each tumor must have its own pathological features, 3) tumors must occur in different parts or organs which are not continuous with each other 4) each tumor must have its own metastatic pathway and the diagnosis of metastatic or recurrent tumours should be carefully excluded [4,5,6].

Incidence of such neoplasms is seen mostly in 5th to 6th decade with slight female predisposition. [6,7]. The favourable site of MPMNs may vary according to geographic prevalence of cancers in a particular region. In the study by L.L Xu the original tumor sites were most commonly observed in the digestive system, followed by the breast, respiratory system, reproductive system, and head and neck [5]. Also in the same study the occurrence of malignancy in different organ system was more likely to metachronous than synchronous. In another study, location of the index cancer was breast followed by genital malignancy [6]. In an another study conducted in India head neck cancers were the most common index cancer and breast most common second location [7].

Stage of presentation is usually advanced for one or both malignancies [6]. Some studies suggest that second cancer might also be diagnosed at early stage [7]. This phenomena can be explained by increase hospital visits and tests for index malignancy leading to earlier detection of second cancers. This appears truer for metachronous cancers. In synchronous cancers the findings of second cancer is usually incidental and are more likely to present at advanced stage. In our case report patient presented with locally advanced stage of both malignancies. The stage of Gall bladder cancer appeared to be T3N0 (III A) and that of cervix appeared to be FIGO III B.

On the analysis of various studies describing MPMN, the incidence of gall bladder cancer as index cancer was very low and synchronous occurrence of gall bladder with reproductive system was rare. [5,6,7]. On extensive search of literature we could not find the synchronous occurrence of gall bladder cancer cervical cancer. This could be the first case report of MPMN describing the synchronous occurrence of these two malignancies.

Detailed clinical and radiological evaluation may help to avoid misdiagnosis and missed diagnosis. Care should be taken to establish the difference between metastasis and recurrence of carcinomas from MPMN.

In management of such cases the treatment of each tumor should be done according to its stage irrespective of the other tumour. The stage of disease and site selection should be used to determine optimal surgically based treatment options, combined with chemotherapy, radiotherapy, biological therapy, and other methods to improve survival [6,7].

The occurrence of synchronous malignancies complicates the stage wise management of the disease more so if the management requires the use of different modalities of treatment. As in our case definitive treatment the gall bladder cancer necessitated a major hepatobiliary surgery whereas carcinoma cervix mandated for concurrent chemo radiation .But such treatment for one primary would have definitely delayed the treatment of the other malignancy. The poor performance status caused by burden of both malignancies made us decide for palliative chemotherapy as the treatment option after multi-disciplinary meeting.

As more data keeps on gathering towards such cases certainly future may be differently and yet more effectively able to deal with the phenomena of Multiple Primary Malignant Neoplasms.

Conclusion

Multiple primary malignant neoplasms (MPMN) is defined as malignancies arising from two or more different organs with different histology. Synchronous occurrence of locally advanced adenocarcinoma gall bladder with locally advanced squamous cell carcinoma cervix has not been described before. With increasing life expectancy and improvement in imaging modalities there is a gradual increase in reporting of such cases. With more awareness and better reporting regarding the phenomena we may be able to formulate personalized treatment plans to treat these patients of MPMN.

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The methods section should include only information that was available at the time the plan or protocol for the study was written such as study approach, design, type of sample, sample size, sampling technique, setting of the study, description of data collection tools and methods; all information obtained during the conduct of the study belongs in the Results section.

Reports of randomized clinical trials should be based on the CONSORT Statement (http:// www. consort-statement. org). When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 2000 (available at http://www.wma. net/e/policy/l 7-c_e.html).

Results

Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Extra or supplementary materials and technical details can be placed in an appendix where it will be accessible but will not interrupt the flow of the text; alternatively, it can be published only in the electronic version of the journal.

Discussion

Include summary of key findings (primary outcome measures, secondary outcome measures, results as they relate to a prior hypothesis); Strengths and limitations of the study (study question, study design, data collection, analysis and interpretation); Interpretation and implications in the context of the totality of evidence (is there a systematic review to refer to, if not, could one be reasonably done here and now?, What this study adds to the available evidence, effects on patient care and health policy, possible mechanisms)? Controversies raised by this study; and Future research directions (for this particular research collaboration, underlying mechanisms, clinical research). Do not repeat in detail data or other material given in the Introduction or the Results section.

References

List references in alphabetical order. Each listed reference should be cited in text (not in alphabetic order), and each text citation should be listed in the References section. Identify references in text, tables, and legends by Arabic numerals in square bracket (e.g. [10]). Please refer to ICMJE Guidelines (http://www.nlm.nih.gov/bsd/uniform_ requirements.html) for more examples.

Standard journal article

[1] Flink H, Tegelberg Å, Thörn M, Lagerlöf F. Effect of oral iron supplementation on unstimulated salivary flow rate: A randomized, double-blind, placebo-controlled trial. J Oral Pathol Med 2006; 35: 540-7.

[2] Twetman S, Axelsson S, Dahlgren H, Holm AK, Källestål C, Lagerlöf F, et al. Caries-preventive effect of fluoride toothpaste: A systematic review. Acta Odontol Scand 2003; 61: 347-55.

Article in supplement or special issue

[3] Fleischer W, Reimer K. Povidone iodine antisepsis. State of the art. Dermatology 1997; 195 Suppl 2: 3-9.

Corporate (collective) author

[4] American Academy of Periodontology. Sonic and ultrasonic scalers in periodontics. J Periodontol 2000; 71: 1792-801.

Unpublished article

[5] Garoushi S, Lassila LV, Tezvergil A, Vallittu PK. Static and fatigue compression test for particulate filler composite resin with fiber-reinforced composite substructure. Dent Mater 2006.

Personal author(s)

[6] Hosmer D, Lemeshow S. Applied logistic regression, 2nd edn. New York: Wiley-Interscience; 2000.

Chapter in book

[7] Nauntofte B, Tenovuo J, Lagerlöf F. Secretion and composition of saliva. In: Fejerskov O,

Kidd EAM, editors. Dental caries: The disease and its clinical management. Oxford: Blackwell Munksgaard; 2003. p. 7-27.

No author given

[8] World Health Organization. Oral health surveys - basic methods, 4th edn. Geneva: World Health Organization; 1997.

Reference from electronic media

[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/theme_health/HSQ20.pdf (accessed Jan 24, 2005): 7-18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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Tables should be self-explanatory and should not duplicate textual material.

Tables with more than 10 columns and 25 rows are not acceptable.

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Explain in footnotes all non-standard abbreviations that are used in each table.

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