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SAFETY PROFILE OF ASPIRIN FOR THE PERIOD OF 2010-2019

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ABSTRACT

Among hospitalised patients, adverse drug reactions (ADRs) constitute a significant source of morbidity and death. ADRs in internal medicine units at a third-level university hospital were to be described in terms of their occurrence, severity, and cause in this study. Internal medicine units conducted a descriptive research using a structured approach, a review of clinical data, and interviews with hospitalised patients. To determine causation for patient adverse events, the Naranjo method was used. ADRs were also categorised using the Rawlins and Thompson standards. The research consisted of 21 case reports of patients, 11 males and 10 women. After applying the Naranjo algorithm to adverse events, 0 definite, 20 probable and 1 possible were identified ADRs. In the two case studies we found ADRs as lethal to the patient. The frequency of ADRs was comparable to that which was noted in earlier studies conducted in internal medicine departments. To effectively detect and prevent ADRs, pharmacological surveillance activities in hospital wards must be systematised.

Keywords: Adverse Drug Reactions, Safety Profile, Aspirin, Naranjo method, World Health Organization

INTRODUCTION

Adverse drug reactions (ADRs) are described as "any harmful or undesired response to a medication, occurring at doses used for prophylaxis, diagnosis, and treatment in humans" by the World Health Organisation (WHO) **[1]**. ADRs were ranked between the fourth and sixth leading causes of mortality in the US in 1994, trailing only cardiovascular disease, cancer, accidents, and violence. Numerous epidemiological studies have been conducted in an effort to determine the

severity, incidence, and direct and indirect costs of ADRs in hospital and ambulatory settings as a result of the large rise in commercially accessible drugs in recent years. The prevalence of adverse drug reactions (ADRs) in hospitalised patients has been reported to range from 1.2% to 45%. The wide variation in prevalence reported in studies is primarily attributable to methodological variations in the data collection and the use of non-standardized criteria to diagnose the presence of adverse drug reactions **[1-3]**. With little information on adverse effects in people in Latin American countries, the majority of research on ADR detection has been done in the USA and Europe.

Latin American countries have developed some research to look at ADRs. At a third-level hospital in Bogotá, Tribio *et al*. recently reported a 25.1% frequency of adverse effects in hospitalised patients in internal medicine wards. They discovered that patients with ADRs had longer hospital stays, which directly or indirectly raised hospital costs5. In third-level internal medicine wards in Brazil, a cohort study found that 43% of hospitalised patients had adverse responses to at least one drug. Patients in internal medicine wards have adverse drug reactions (ADRs) often because they tend to be older, have several chronic diseases, and take multiple medications (polypharmacy), which puts them at an increased risk of harmful effects and interactions between drugs and illnesses **[2-5]**.

The lack of pharmacological surveillance studies and inadequate reporting of adverse events to the Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA) [National Institute of Food and Drug Surveillance] are two factors contributing to the lack of knowledge regarding the prevalence, incidence, and mortality of ADRs in hospitalised patients in Colombia and other Latin American countries. In order to describe the prevalence and clinical features of ADRs in internal medicine hospital wards at a university hospital, this study was carried out. Along with the severity of the adverse responses, possibly avoidable side effects, and unfavourable drug-drug and drug-illness interactions, the classes of drugs most commonly linked to ADRs were also found **[1, 5]**.

MATERIALS AND METHODS

During 2010-2019, a safety profile study of Aspirin was conducted. This research includes all suspected adverse drug reactions (ADRs) related to NSAIDS medicine in all type of patients with different age group that were recognised and reported by various departments of hospitals. Drug responses brought on by prescription mistakes, the use of complementary or alternative medicine, and

specialties like oncology, dentistry, and surgery are not included. Case sheets, investigative reports of patients who had experienced an ADR, personal interviews with patients or the patient's companion, historical history of medication usage, and personal interviews with reporting individuals or physicians were used to gather the data for the study.

The "Naranjo causality assessment scale" was used to determine the causes of the reported ADRs. According to the Naranjo Algorithm, a medication response can be categorised as either certain, likely, or plausible. The modified Hartwig and Siegel Scale categorises the severity of an adverse drug response (ADR) as mild, moderate, or severe with varying degrees in accordance with elements such as the need for a change in therapy, the length of the hospital stay, and the handicap brought on by the ADR. There are different case studies reported for the Aspirin which is given below:

Case Studies for Aspirin from 2010-2019

Case Study 1

Following will be the key elements of line listing.

1) Case study: Fixed drug eruptions are common cutaneous adverse drug reactions, commonly caused by anticonvulsants, antibiotics and analgesics.
2) Country: India
3) Patient Details
    a) Age: 27Years
    b) Gender: Male
4) Medical history: Headache
5) Surgical History: No
6) Suspected Adverse Drug Reaction: History of rash followed by itching since one day after taking the Aspirin 350mg tablets one by one within eight hours. On examination, 5-6 ulcerative, hyperpigmented lessions with erythematous border were found on both lower limbs.
7) Preferred Term: Hyperpigmented lessions
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: In the present case report, the patient presented with FDE immediately after oral administration of Aspirin and completely cured after stopping the drug.
12) Drug Reaction (definite, probable and possible): Probable **[6]**

Case Study 2

1) Case study: Anacin induced adverse drug reaction
2) Country: Nigeria
3) Patient Details
    a) Age: 26 Years
    b) Gender: Female
4) Medical history: She noticed injury on her gum following an attempt to chew a fish bone

5) Surgical History: No
6) Suspected Adverse Drug Reaction: Bilateral-periorbital swellings, reddish eyes, visual impairment, headache and pains secondary to ingestion of 300mg Anacin, a brand of acetylsalicylic acid.
7) Preferred Term: Bilateral-periorbital swellings
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Anacin may induce idiosyncratic adverse reaction, hence, health care providers should be aware of the potential deleterious effect of Anacin while prescribing same for patients with previous history of allergic reactions.
12) Drug Reaction (definite, probable and possible): Probable **[7]**

Case Study 3

1) Case study: Aspirin misuse
2) Country: UK
3) Patient Details
    a) Age: 49 Years
    b) Gender: Male
4) Medical history: He had no significant past medical history and lived in a group home.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: He presented to the emergency department with ataxia and confusion following ingestion of an unknown amount of Aspirin.
7) Preferred Term: Ataxia
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: With the continued high prevalence of NPM/OTC misuse, it remains important for clinicians to be able to identify signs and symptoms of Aspirin-use disorders using directed questions and toxicology screening, which remains a vital diagnostic element. Clinicians should be prepared to recommend effective treatment modalities and educate patients about the risks and consequences associated with non-medical Aspirin use.
12) Drug Reaction (definite, probable and possible): Probable **[8]**

Case Study 4

1) Case study: Adverse drug interaction between Aspirin and Furosemide: A case report
2) Country: India
3) Patient Details
    a) Age: 60 Years
    b) Gender: Female
4) Medical history: She is known case of (k/c/o) hypertension and diabetes mellitus since 5 years on mediations, i.e., tablet atenolol -5 mg (1-0-0), tablet amlodipine- 5 mg (1-0-0), and tablet metformin - 500 mg (1-0-1).
5) Surgical History: No

6) Suspected Adverse Drug Reaction: Female patient admitted to the female general medicine ward with the complaints of chest pain since 6 pm, and she was apparently well 1 day back then given a history of chest pain since 6 pm which is a burning type of pain and also a history of breathlessness since 6 pm. The patient's appetite was reduced and sleep was disturbed.
7) Preferred Term: Acute left ventricular failure, ischemic heart disease with old hypertension, and type 2 diabetes mellitus.
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Aspirin may attenuate the action of furosemide and may cause acute renal failure in cases of pre-existing hypovolemia or dehydration.
12) Drug Reaction (definite, probable and possible): Possible **[9]**

Case Study 5

1) Case study: Medication error case scenario
2) Country: UN
3) Patient Details
    a) Age: 65 Years
    b) Gender: Female
4) Medical history: She had a heart attack five years ago. At her previous visit three weeks ago she was complaining of muscle pain, which she developed while working on her farm. She was given a non-steroidal anti-inflammatory drug (NSAID), diclofenac. Her other medications included Aspirin, and three medicines for her heart condition (simvastatin, a medicine to reduce her serum cholesterol; enalapril, an angiotensin-converting enzyme (ACE) inhibitor; and atenolol, a beta blocker).
5) Surgical History: No
6) Suspected Adverse Drug Reaction: She was admitted to hospital as she developed symptoms of blood loss (such as fatigue and dark stools). She was provisionally diagnosed as having a bleeding peptic ulcer due to her NSAID, and her doctor discontinued diclofenac and prescribed omeprazole, a proton pump inhibitor.
7) Preferred Term: Fatigue and dark stools
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: The clinic confirmed that the NSAID, which should have been discontinued (deprescribed), had been continued by mistake. This time she was given a medication list when she left the hospital which included all the medications she needed to take and was advised about which medications had been discontinued and why.

12) Drug Reaction (definite, probable and possible): Probable [10]

Case Study 6

1) Case study: Severe hepatoxicity caused by Aspirin overdose a case report
2) Country: China
3) Patient Details
    a) Age: 61 Years
    b) Gender: Male
4) Medical history: Two days spontaneous fever
5) Surgical History: No
6) Suspected Adverse Drug Reaction: The patient developed gradually worsening epigastric pain, and vomited approximately 200 ml of bloody gastric content 3 h after the pain began. The abdominal pain and vomiting were persistent, leading the patient to seek medical care.
7) Preferred Term: Epigastric pain
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Two years later, the patient died of chronic liver failure.
12) Drug Reaction (definite, probable and possible): Probable **[11]**

Case Study 7

1) Case study: Bleeding Complication of Triple Therapy of Rivaroxaban, Prasugrel, and Aspirin a case report and general discussion.
2) Country: Europe
3) Patient Details
    a) Age: 55 Years
    b) Gender: Male
4) Medical history: History of paroxysmal atrial fibrillation but had previously refused warfarin therapy. His past medical history was otherwise significant for congestive heart failure preserved ejection fraction, coronary artery disease treated with a bare metal stent six months prior, diabetes mellitus type 2, hypertension, gout, and chronic kidney disease stage 3 (creatinine clearance 30). His home medications included prasugrel, Aspirin atorvastatin, clonidine, furosemide, potassium chloride, amlodipine, insulin, allopurinol, and hydralazine.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: Intractable nausea and vomiting and was found to be in atrial fibrillation with rapid ventricular response
7) Preferred Term:
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Care should be taken in selecting a regimen most appropriate for the patient, remembering that there are no methods for monitoring newer oral anticoagulants. This is especially true in patients with other comorbidities that

increase bleeding risk, such as chronic kidney disease.

12) Drug Reaction (definite, probable and possible): Probable **[12]**

Case Study 8

1) Case study: Case report of Aspirin overdose. Bezor formation and controversies of multiple-dose activated charcoal in salicylate poisoning
2) Country: China
3) Patient Details
    a) Age: 33 Years
    b) Gender: Male
4) Medical history: No medical history. A suicidal attempt.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: He had ingested 90 tablets of regular preparation Aspirin (500 mg/tablet) around five hours before arrival. He complained of epigastric discomfort, nausea and tinnitus. He had drunk a can of beer which was around 500 ml but he denied co-ingestion of other medications.
7) Preferred Term: epigastric discomfort, nausea and tinnitus
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Aspirin overdose may lead to bezoar formation in the gut. A delayed and erratic absorption of Aspirin in a regular preparation was clearly demonstrated in our case.
12) Drug Reaction (definite, probable and possible): Probable **[13]**

Case Study 9

1) Case study: Rescue of anaphylaxis after oral Aspirin ingestion
2) Country: China
3) Patient Details
    a) Age: 52 Years
    b) Gender: Male
4) Medical history: No relevant prior medical record history presented with a traumatic spleen rupture and was admitted for emergency splenectomy.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: On postoperative day 11, he ingested one-half of a 25-mg enteric coated tablet of Aspirin 30 min after dinner, in accordance with his doctor's advice, and his platelet count increased to a maximum concentration of 704×109/L. Our successful practical experience is to always use Aspirin and low molecular dextran as an anti-platelet regimen when the platelet count is ≥ 500×109/L to reduce the risk of venous thrombosis formation. Severe anaphylaxis to oral Aspirin occurs unexpectedly and prophylactically, evoking the following series of symptoms, as emerged in the present case: uncontrollable motions and a sense of dying, accompanied by

dizziness, precordia distress, upper abdominal pain combined with vomiting, nausea, and defecation, along with dyspnea without wheezing. Incredibly, two transient, but extremely intense, hyperspasmia events occurred and lasted about 3–5 minutes each. Simultaneously, his blood pressure and oxygen saturation (SaO2) decreased to 70– 80/40 mmHg and 70–80%, respectively. However, his face became flush and he complained of body-wide pruritus, even though no obvious urticaria was observed at that time. Electrocardiography indicated atrial tachycardia.

7) Preferred Term: Anaphylaxis
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Anaphylaxis to Aspirin is a rare, but life-threatening, reaction. Based on our experience, we propose that the mechanism of Aspirin allergy may be related to vascular spasm based on unique presentations. It is most important to assess allergy risk to ultimately determine the risk or Aspirin therapy. Also, it is necessary to adopt standardized emergency measures to avoid anaphylaxis to Aspirin. Focusing attention on these adverse effects of Aspirin should be helpful to address anaphylactic progression to improve success of emergent intervention
12) Drug Reaction (definite, probable and possible): Probable **[14]**

Case Study 10

1) Case study: Aspirin induced intraoral burn, A rare case report with emphasis on its diagnosis.
2) Country: India
3) Patient Details
    a) Age: 35 Years
    b) Gender: Female
4) Medical history: She gave the history of toothache for which she placed Aspirin powder below the tongue.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: Developed the ulcer, which was painful. On local examination there was sloughing of oral mucosa on ventral aspect of tongue for approximately 3x4cms and associated with whitish slough on buccal mucosa correlating with diagnosis of Aspirin burn. We prescribed her topical steroid and anesthetic application (Kenacort 0.1% and Dologel CT) along with multivitamin preparation and she responded well.
7) Preferred Term: Oral ulcer
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes

11) Outcome: Patients history plays the most important role to reach the diagnosis so it is crucial to obtain the detailed patient history.
12) Drug Reaction (definite, probable and possible): Probable **[15]**

Case Study 11

1) Case study: A case of Aspirin exacerbated respiratory disease (AERD) with Aspirin-induced Hypersensitivity Vasculitis
2) Country: California
3) Patient Details
    a) Age: 38 Years
    b) Gender: Female
4) Medical history: History of prior nasal polypectomy and Aspirin desensitization without complication, underwent a second polypectomy and Aspirin desensitization for recurrent nasal polyposis
5) Surgical History: No
6) Suspected Adverse Drug Reaction: After the second Aspirin desensitization, she developed an urticarial rash, which persisted despite maximal antihistamine therapy. Additionally, while on daily Aspirin, the patient continued to have uncontrolled asthma despite therapy on inhaled corticosteroids, long acting beta-agonists, inhaled tiotropium, and oral montelukast. Thus, she underwent bronchothermoplasty, during which she discontinued Aspirin and had resolution of her urticaria. However, the urticaria returned with increasing severity after her third Aspirin desensitization procedure. Skin biopsy showed perivascular neutrophilic infiltrate with a suggestion of fibrinoid necrosis, suspicious for urticarial vasculitis and urticarial hypersensitivity reaction. Aspirin was discontinued with complete resolution of skin lesions.
7) Preferred Term: Aspirin-induced hypersensitivity vasculitis
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Aspirin-induced hypersensitivity vasculitis in a patient with AERD. We are currently discussing further treatment options for AERD in this patient who cannot tolerate conventional therapy with Aspirin.
12) Drug Reaction (definite, probable and possible): Probable **[16]**

Case Study 12

1) Case study: Single NSAID, Induced Serum Sickness-like reaction to Naproxen in a patient able to tolerate both Aspirin and ibuprofen
2) Country: New York
3) Patient Details
    a) Age: 64 Years
    b) Gender: Female
4) Medical history: Serum sickness like reaction to either naproxen or

cyclobenzaprine three years before presentation in our clinic. Ten days after she received both medications for cervical radiculopathy, she developed severe polyarthritis, fever, and myalgias, and had elevated levels of CRP.

5) Surgical History: No
6) Suspected Adverse Drug Reaction: At our clinic, patient wanted to know if she could tolerate other NSAIDs. She underwent successful Aspirin and ibuprofen challenges in our office in separate visits, and since then she continued Aspirin daily and ibuprofen as needed. Complement levels, CRP, chemistry and CBC were normal at weekly follow up appointments. Naproxen challenge was initiated and she tolerated 100mg daily for seven days. Her dose was increased to 250 mg at subsequent visit, and after three days she developed stiff neck, headache, myalgias, arthralgias, and low-grade fever. Laboratory results showed elevated CRP (1.6 mg/dl, baseline 0.1 mg/dl), lymphocytopenia, thrombocytopenia, and mild transaminitis. Findings resolved after naproxen discontinuation and short steroid course. Patient was advised to avoid naproxen in the future.
7) Preferred Term: Serum sickness like reaction
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: This is the first reported case of a single NSAID-induced serum sickness-like reaction. The different chemical structures of naproxen (two benzene rings), ibuprofen and Aspirin (each has one benzene ring) probably influence the specific immune response, which may explain the different reaction to these NSAIDs.
12) Drug Reaction (definite, probable and possible): Probable **[17]**

Case Study 13

1) Case study: Kounis syndrome induced by oral intake of Aspirin, a case report and literature review
2) Country: Morocco
3) Patient Details
    a) Age: 49 Years
    b) Gender: Female
4) Medical history: Left hip pain for which patient took Aspirin 1 g couple of hours prior to her current presentation.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: Patient presented to the emergency department with severe chest pain and shortness of breath. Further history reveals that she experiences similar symptoms of chest pain and shorness of breath after taking Aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs). Physical exam reveals

bilateral expiratory lung wheezing. Chest X ray was unremarkable, ECG showed ST segment elevation in the inferior leads. The new occurrence of asthma attacks associated with asprin consumption was finalty related to Samter's syndrome. Sinus tomography and a nasal endoscopy revealed the presence of bilateral nasal polyposis confirming the diagnosis of the Aspirin-exacerbated respiratory disease (AERD) diagnosed as the coexistence of asthma, nasal polyps and Aspirin allergy.

7) Preferred Term: Kounis syndrome
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: We are reporting a rare clinical entity of coronary spasm caused by taking non-steroidal anti-inflammatory resulting in acute myocardial infarction, and in which case the only eviction of the allergen has led to the cessation of symptoms.
12) Drug Reaction (definite, probable and possible): Probable **[18]**

Case Study 14

1) Case study: Rush immunotherapy for Aspirin desensitization without IFN-gamma
2) Country: USA
3) Patient Details
    a) Age: 82 Years
    b) Gender: Female
4) Medical history: History of hypertension, benign prostate hypertrophy, duodenal adenoma and gastrointestinal bleeding. The patient showed chest pain one day before admission.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: Male patient was admitted to the intensive care unit with a myocardial infarction. He visited the department of cardiology, internal medicine and was admitted to the intensive care unit with the impression of acute myocardial infarction. However, at the dawn of admission day #3, chest pain was aggravated again. ST segment elevation in EKG was appeared with chest pain. Heparinization was started. Percutaneous cardiac intervention was indicated and administration of Aspirin was necessary but the patient had Aspirin hypersensitivity and requested consultation to Allergy and Clinical Immunology Center, Cheju Halla General Hospital.
7) Preferred Term: Myocardial infarction
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Desensitization was successful up to the dose of 300 mg for 3 h and at the day 5th of admission, the patient received a percutaneous

transcoronary angioplasty (PTCA) with 2nd generation DES stent at proximal circumflex artery of major left coronary artery successfully with medication of Aspirin at the dose of 100 mg daily.

12) Drug Reaction (definite, probable and possible): Probable **[19]**

Case Study 15

1) Case study: Rush immunotherapy for Aspirin desensitization using IFN-gamma
2) Country: USA
3) Patient Details
    a) Age: 62 Years
    b) Gender: Male
4) Medical history: Percutaneous coronary intervention
5) Surgical History: No
6) Suspected Adverse Drug Reaction: In the past history, angioedema was developed by taking analgesics (NSAID) after tooth extraction. The patient also had a drug allergy to acetaminophen. The patient showed angioedema and generalized urticarial after taking Aspirin for the percutaneous coronary intervention. A pharmacologic consultation by Clinical Pharmacy Coordinator at Central Valley Specialty Hospital (Modesto, CA USA) concerning pharmacologic and toxic side effects of the accumulation doses during the desensitization for Aspirin, having been given the information of the patients status, especially about the expected effects of IFN-gamma on acute myocardial syndrome was requested.
7) Preferred Term: angioedema and generalized urticarial
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: When the patient showed allergic reaction repetitively at a certain dose, IFN-gamma was administered before the challenge and was not used thereafter when patient did not show allergic reaction after impediment dose. In drug allergies, IFN-gamma was used only at the impediment of desensitization process.
12) Drug Reaction (definite, probable and possible): Probable **[19]**

Case Study 16

1) Case study: Case report, Aspirin and Ibuprofen a Potential Life threatening Drug interaction after coronary stent implantation.
2) Country: Austria
3) Patient Details
    a) Age: 79 Years
    b) Gender: Male
4) Medical history: The history of our patient was remarkable and included already 2 events of stent-thrombosis in the past. Furthermore, presence of multiple and overlapping stents have to

be discussed as an additional risk-factor for stent-thrombosis in our patient.

5) Surgical History: No
6) Suspected Adverse Drug Reaction: Since the patient had suffered his 3rd stent thrombosis, a platelet function test was performed. The effect of Aspirin was measured using the PFA 100 test. Collagen/Epinephrine closure time of only 84 sec. was found, which indicated an insufficient antiplatelet effect of Aspirin. In order to assess the effect of ticagrelor, the Platelet VASP/P2Y12 test was performed and showed a moderate effect of ticagrelor (Platelet Reactivity Index of 52%).
7) Preferred Term: Acute myocardial infarction
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Studies also have shown that other NSAIDs like indomethacin, mefenamic acid, tiaprofenic acid and naproxen may influence the antiplatelet-effect of Aspirin while diclofenac, paracetamol and celecoxib seem to be safe when added to Aspirin.
12) Drug Reaction (definite, probable and possible): Probable **[20]**

Case Study 17

1) Case study: Case report on cardiovascular side effects of Aspirin.
2) Country: India
3) Patient Details
    a) Age: 29 Years
    b) Gender: Female
4) Medical history: The history of migraine
5) Surgical History: No
6) Suspected Adverse Drug Reaction: She developed chest pain, tachycardia and orthopnea following Aspirin consumption at doses of 1500mg per day for several days.
7) Preferred Term: Tachycardia and orthopnea
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: After discontinuation of Aspirin therapy, the patient's symptoms promptly resolved. The patient consented to a pharmacological challenge test which once again triggered the symptoms.
12) Drug Reaction (definite, probable and possible): Probable **[21]**

Case Study 18

1) Case study: Case report on Reye's syndrome a rare but serious pediatric condition
2) Country: New Jersey
3) Patient Details
    a) Age: 12 year
    b) Gender: Male
4) Medical history: Flu-like symptoms of mild fever, headache, and generalised aches for five days

5) Surgical History: No
6) Suspected Adverse Drug Reaction: He was given Aspirin (300 mg every four hours for 24 hours) after which his symptoms seemed to resolve. However, 12 hours later he began vomiting, and this continued almost hourly for 24 hours, at which time his parents sought medical help
7) Preferred Term: Reye's syndrome
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: The confusion resolved within 48 hours, and over the next few days his liver test results became normal. However, the boy remained tired and lethargic and it was three months before he had recovered sufficiently to return to school full time.
12) Drug Reaction (definite, probable and possible): Probable **[22]**

Case Study 19

1) Case study: Case report on Reye's syndrome a rare but serious pediatric condition
2) Country: New Jersey
3) Patient Details
    a) Age: 9 month
    b) Gender: Male
4) Medical history: He had had a low grade fever for about 24 hours, and his mother had given him 150 mg Aspirin on one occasion.
5) Surgical History: No
6) Suspected Adverse Drug Reaction: Twelve hours later he began to vomit and this persisted for 24 hours. When the general practitioner examined him the boy was limp and lifeless, and hypoglycaemia was confirmed.
7) Preferred Term: Reye's syndrome
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: Twelve hours after admission to hospital he had a brief generalised seizure; it was not associated with hypoglycaemia, and his cerebrospinal fluid was normal. The seizure responded to intravenous diazepam, and treatment with phenobarbitone was continued for several days. After 24 hours the boy was fully conscious and he subsequently made a full recovery.
12) Drug Reaction (definite, probable and possible): Probable **[22]**

Case Study 20

1) Case study: Case report on Reye's syndrome a rare but serious pediatric condition
2) Country: New Jersey
3) Patient Details
    a) Age: 12 year
    b) Gender: Male
4) Medical history: For 4 days, he had been suffering from a viral syndrome,

with fever (39°C) and nasal discharge, which was treated by self-administration of 250 mg of Aspirin.

5) Surgical History: No
6) Suspected Adverse Drug Reaction: Twelve hours after admission to hospital he had a brief generalised seizure; it was not associated with hypoglycaemia, and his cerebrospinal fluid was normal. The seizure responded to intravenous diazepam, and treatment with phenobarbitone was continued for several days. After 24 hours the boy was fully conscious and he subsequently made a full recovery. Two days before hospital admission, he was no lonfer febrile but suffered from vomiting and complete digestive intolerance. The next day, he presented with haematemesis, which motivated admission to the emergency ward. Upon admission, his temperature was 35.8°C, his pulse was 110 per minute, and blood pressure was 128/73 mmHg.
7) Preferred Term: Reye's syndrome
8) Serious/ Non-serious: Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: In the early evening, neurovegetative disturbances appeared with mydriasis, which were initially reversible with osmotherapie and neuroanesthesia, and then irreversible 12 h after admission. A cranial Doppler examination demonstrated evidence of massive cerebral oedema. He died 2 days after admission
12) Drug Reaction (definite, probable and possible): Probable **[22]**

Case Study 21

1) Case study: Case report on Reye's syndrome in children on long-term Aspirin treatment
2) Country: UK
3) Patient Details
    a) Age: 2.5 year
    b) Gender: Female
4) Medical history: In long-term Aspirin treatment initiated by the regional unit for Kawasaki disease developed fever and vesicular rash
5) Surgical History: No
6) Suspected Adverse Drug Reaction: Chicken pox was considered as differential diagnosis and management options were considered in light of the above summary.
7) Preferred Term: Reye's syndrome
8) Serious/ Non-serious: Non-Serious
9) Unexpected: No
10) Expected: Yes
11) Outcome: All children with long-term Aspirin treatment and with an unclear history of chickenpox should be screened for varicella immunity. If indicated, they should receive varicella vaccine on a priority basis. All these children should also receive yearly

intramuscular inactivated influenza vaccine.

12) Drug Reaction (definite, probable and possible): Probable **[22]**

RESULT AND DISCUSSION

During the period of 2010-2019, 21 adverse drug reaction case studies of Aspirin was reported. **Table 1** shows the report of adverse drug reactions.

The incidence rate of NSAIDs adverse reactions was found to be 10-25% over the research period, with a total of 21 (Aspirin) adverse reactions to NSAIDS medicines recorded among patients between the ages of 1 and 85 years. Additionally, 11 female patients (47.62%) were outnumbered by roughly 10 (52.38%) male patients when ADRs occurred by Aspirin and 9 female patients (60.00%) were outnumbered. Results are shown in **Table 2**. Results showed in **Table 3** that skin 5 (23.81%), GIT 5 (23.81%) and CNS 10 (47.62%) were the organ systems most severely impacted by Aspirin adverse effects. All the case studies showed that the route of administration of NSAIDS was oral by which it causes adverse drug reactions **(Figure 1)**.

The suspected drug Aspirin was removed in 21 (100%) of the instances, while the suspected drug was left alone in 0 (0%) and the dose was changed in 0 (0%). According to this study, 19 patients (90.47%) recovered from ADRs, and 2 (9.52%) patients had fatal ADRs of Aspirin. 0% of these cases were discovered to be unknown for both the drugs **(Table 4-6) (Figure 3)**.

Table 1: List of Aspirin ADRs Reported During the Study Period 2010-2019

S. No.	Gender	Age	Country	ADR reported	Reason for Taking	Drug Reaction
1.	Male	27	India	Rash followed by itching	Headache	Probable
2.	Female	26	Nigeria	Bilateral-periorbital swellings	Injury on her gum	Probable
3.	Male	49	UK	Ataxia	Misuse	Probable
4.	Female	60	India	Acute left ventricular failure, ischemic heart disease	Hypertension	Possible
5.	Female	65	UN	Blood loss (Fatigue and dark stools)	Muscle pain	Probable
6.	Male	61	China	Epigastric Pain and bloody Vomit	Fever	Probable
7.	Male	55	Europe	Intractable nausea and vomiting, atrial fibrillation with rapid ventricular response	Hypertension and kidney diseases	Probable
8.	Male	33	China	epigastric discomfort, nausea and tinnitus	Suicidal attempt	Probable
9.	Male	52	China	Anaphylaxis	traumatic spleen rupture	Probable
10.	Female	35	India	Mouth ulcer	Toothache	Probable
11.	Female	38	California	Aspirin-induced hypersensitivity vasculitis and Utricaria	Nasal polypectomy	Probable
12.	Female	64	New York	NSAID induced Serum Sickness	Serum Sickness like reaction	Probable

13.	Female	49	Morocco	Kounis syndrome	Left hip pain	Probable
14.	Female	82	USA	Myocardial infarction	Hypertension	Probable
15.	Male	62	USA	angioedema and generalized urticarial	percutaneous coronary intervention	Probable
16.	Male	79	Austria	Acute myocardial infarction	stent-thrombosis	Probable
17.	Female	29	India	Tachycardia and orthopnea	Migraine	Probable
18.	Male	12	New Jersey	Vomiting	Flu-like symptoms of mild fever, headache, and generalised aches	Probable
19.	Male	0.9	New Jersey	Vomiting and seizures	Low grade fever	Probable
20.	Male	12	New Jersey	generalised seizure, vomiting and haematemesis	viral syndrome, with fever (39°C) and nasal discharge	Probable
21.	Female	2.5	UK	Chicken pox	Kawasaki disease developed fever and vesicular rash	Probable

Table 2: Division of ADRs of Aspirin Based on Gender of the Patients

S. No.	Sex	Number (Out of 21)	Percentage
1	Male	11	52.38
2	Female	10	47.62

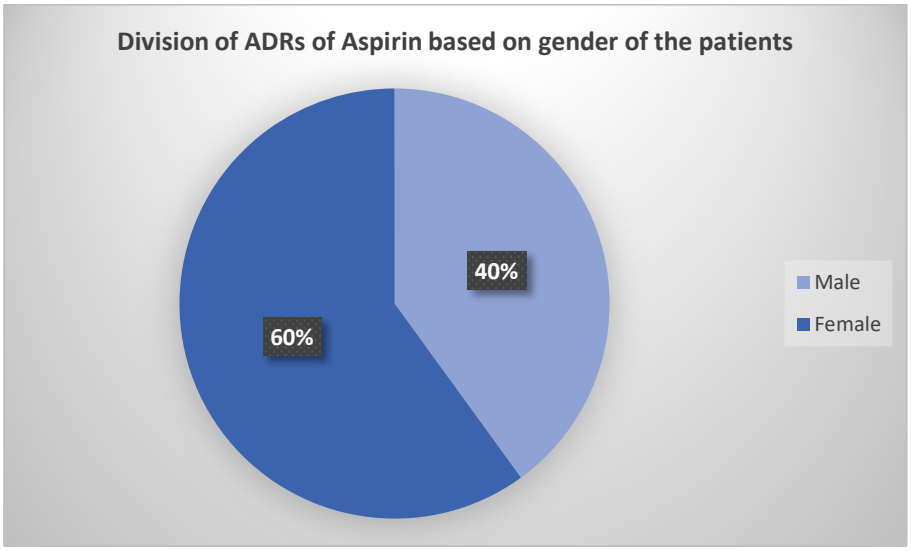

Figure 1: Division of ADRs of Aspirin based on gender of the patients

Table 3: Organ System Affected Due to ADRs of Aspirin

S. No.	Organ System	Aspirin	
		Number	Percentage
1	GIT	5	23.81
2	Skin	5	23.81
3	Nephrotoxicity	0	0
4	CNS	10	47.62
5	Respiratory	0	0
6	Haematological	1	4.76
7	Other	0	0

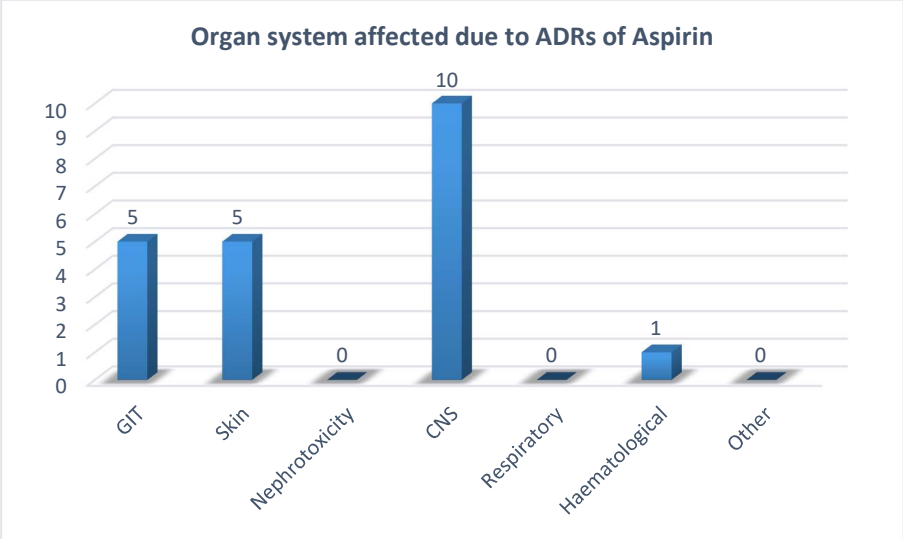

Figure 2: Organ System Affected Due to ADRs of Aspirin

Table 4: Route of Administration (ROA) of NSAIDS Agents that Cause ADRs

S. No.	ROA	Aspirin	
		Number	Percentage
1	Oral	21	100%
2	Parenteral	0	0%

Table 5: Fate of Suspected Drugs

S. No.	Fate of suspected drug	Aspirin	
		Number	Percentage
1	Drug withdrawn	21	100%
2	Dose altered	0	0%
3	No change	0	0%

Table 6: Outcome of ADRs

S. No.	Management of ADRs	Aspirin	
		Number	Percentage
1	Recovered	19	90.47%
2	Fatal	2	9.52%
3	Unknown	0	0%

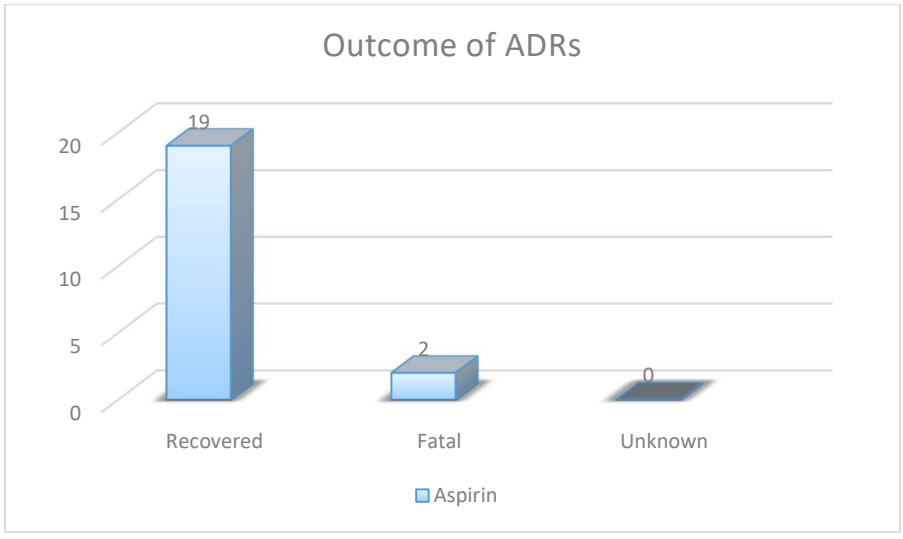

Figure 3: Outcome of ADRs

Table 7: Causality Assessment of ADRs (Using Naranjo Scale)

S. No.	Drug Reaction	Aspirin	
		Number	Percentage
1	Definite	0	0%
2	Probable	20	95.23%
3	Possible	1	4.76%

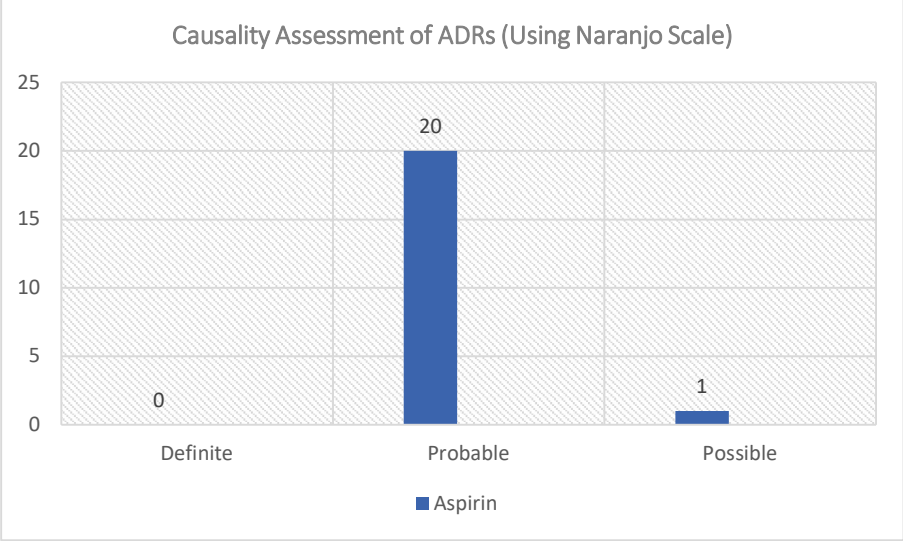

Figure 4: Causality Assessment of ADRs (Using Naranjo Scale)

According to the Naranjo scale, 0 cases were definite for both the drugs, 20 cases of Aspirn (95.23%) were probable and 1 (4.76%) case of Aspirin was possible.

For decades, rheumatological and other disorders have been treated with nonsteroidal anti-inflammatory medications (NSAIDs) to reduce pain and inflammation. They have adverse effects on the kidneys and the cardiovascular system in addition to gastrointestinal (GI) issues (ranging from modest dyspepsia to serious ulcers, bleeding, and perforation). NSAIDs are a class of medications that block the COX-1 and COX-2 isoforms of the cyclooxygenase enzyme. Since conventional NSAIDs are nonselective, they bind to both isoforms and inhibit them, although COX-1 is inhibited more strongly than COX-2. Side effects are caused by COX-1 inhibition, whereas therapeutic outcomes are brought on by COX-2 inhibition. The development of COX-2 selective medications is the outcome of this.

Due to the rising use of anti-inflammatory in these departments for the treatment and prevention of different illnesses, a higher number of NSAIDs adverse drug reactions have been identified in the general patient medicine department. The study also indicated that the GIT, CNS and skin were the two major areas affected by the recorded NSAIDs adverse medication effects.

Because of the risk benefit ratio in particular patients, and in some cases, the use of NSAIDS was based on the culture and

sensitivity reports, the analysis of the fate of the suspected drugs revealed that the drug was withdrawn in many cases and dose altered in some while no change was made with the suspected drug in others. The findings showed that the most common class of NSAIDS to account for adverse drug reactions in patients was Aspirin.

CONCLUSION

Adverse drug responses are a difficulty for maintaining drug safety and are one of the drug-related issues in the hospital environment. The majority of inpatient prescriptions are for NSAIDS, which are also the most inappropriately given medicine class. To encourage children's wise use of NSAIDS, it is important to ensure that hospital-based NSAIDS recommendations are implemented and strictly followed. To guarantee medication safety, the health system should encourage the spontaneous reporting of adverse drug reactions, accurate documentation, and regular reporting to regional pharmacovigilance centres.

The medicines that are most frequently prescribed are those that are most frequently connected to ADRs in children. During the study period, the paediatric department often prescribed class of NSAIDS medicines includes Aspirin, Etoricoxib etc.

The study came to the conclusion that in our hospital context, spontaneous reporting of adverse drug reactions is quite excellent. ADRs have the potential to raise the expense of patient care and can resemble illness, leading to pointless investigations and treatment delays. A clinical chemist who has received the necessary training is actively involved in identifying adverse drug reactions and educating healthcare providers about the need of reporting ADRs, especially those that are significant or uncommon.

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