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Highlights

Rare Cause of Abdominal Pain

Clinical and Economic Evidence

Discovering Thoughts, Inventing Future

VOLUME 22 ISSUE 3 VERSION 1.0

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Evans Syndrome- Rare Cause of Abdominal Pain: A Case Report

By Bodhrun Naher, Md. Rafiqul Islam, Ferdous Ara Begum, Md. Rukunuzzaman & Md. Wahiduzzaman Mazumder

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Abstarct- Evan's syndrome is a rare and chronic autoimmune disease characterized by autoimmune hemolytic anemia and immune thrombocytopenic purpura with a positive Coomb's test in the absence of an underlying etiology. There is no preferential distribution of Evans syndrome by age, gender, or ethnic group. The best treatment options for Evans syndrome depend on many factors, including the severity of the condition; presence of signs and symptoms and person's response to therapies. We present a case of a 12 year old adolescent girl with abdominal pain, diagnosed as a case of Evans syndrome based on the clinical features, Coombs test, hemolytic anemia and thrombocytopenia.

Keywords: autoimmune hemolytic anemia; immune thrombocytopenic purpura; coomb's test.

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Evans Syndrome- Rare Cause of Abdominal Pain: A Case Report

Bodhrun Naher [α], Md. Rafiqul Islam [σ], Ferdous Ara Begum [ρ], Md. Rukunuzzaman [ω], & Md. Wahiduzzaman Mazumder [¥]

Abstract- **Evan's syndrome is a rare and chronic autoimmune disease characterized by autoimmune hemolytic anemia and immune thrombocytopenic purpura with a positive Coomb's test in the absence of an underlying etiology. There is no preferential distribution of Evans syndrome by age, gender, or ethnic group. The best treatment options for Evans syndrome depend on many factors, including the severity of the condition; presence of signs and symptoms and person's response to therapies. We present a case of a 12 year old adolescent girl with abdominal pain, diagnosed as a case of Evans syndrome based on the clinical features, Coombs test, hemolytic anemia and thrombocytopenia.**

Keywords: autoimmune hemolytic anemia; immune thrombocytopenic purpura; coomb's test.

I. Introduction

Evans syndrome is an uncommon condition defined by the combination (either simultaneously or sequentially) of direct antiglobulin test positive autoimmune haemolytic anaemia (AIHA), immune thrombocytopenia (ITP) and/or immune neutropenia in the absence of a known underlying etiology. There is evidence to support abnormalities in both cellular and humoral immunity in Evans syndrome[1]. Its chronic course is characterized by recurrent relapses and remissions. Evans syndrome is a diagnosis of exclusion. This means that a diagnosis is made in people with Coombs positive haemolytic anaemia and thrombocytopenia related to an abnormal immune response, other conditions with similar signs and symptoms have been ruled out. Various blood tests and in some cases, a bone marrow may be needed to exclude other conditions.

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II. Case Report

Maria,12 years old adolescent girl, 2nd issue of non consanguineous parents, admitted into Pediatric Gastroenterology and Nutrition department with the complaints of severe, agonizing, epigatric pain without any radiation and relieved slightly after leaning forward for 5 days, associated with non projectile, non bilious vomiting. She had no H/O of fever, cough, oral ulceration, joint pain, alopecia, but she had malaise, fatigue for last 15 days. Maria was severely pale, moderately icteric, no lymphphadenopathy, stigmata of chronic liver disease was absent. Maria had tenderness in epigastric region with just palpable spleen and no other organomegaly or ascites. Laboratory findings:

- CBC: ESR=120 mm, Hct= 23.5%, Hb=7.5gm/dl, MCV=84.5fL, MCH=27 pg, MCHC=31.9gm/dl, RDW- CV=14.6%, WBC=4500/cmm, N=63%, L=30%, M=05%, E=02%, B=00%, Platelet=80000/μL.
- PBF showed features consistent with immune haemolytic anaemia with thrombocytopenia and marked roulaeux formation.
- Reticulocyte count was about 4.79%.
- Direct Coomb's test (DAT) was positive, Indirect coomb's test (IAT) was negative.
- LDH-2905 U/L
- Hemoglobin electrophoresis revealed normal finding
- Serum bilirubin was 8.4 mg/dl, serum ALT-23 U/L, ceruloplasmin-44 mg/dl, s.albumin-4.35 g/dl,INR-1.12
- Serum Lipase-86 U/L,
- Fasting lipid profile , RBS, Serum electrolytes and Creatinine were within normal range
- Viral markers for Hepatitis A, B, C and E were negative
- IgG was14.3 g/l
- ANA, Anti –ds-DNA, Anti smooth muscle antibody and anti LKM1 were negative
- Flow cytometry for PNH evaluation was not consistent with a diagnosis of PNH
- S. Iron= 208.98 μgm/dl (raised); S. Ferritin=443.0 ngm/ml (raised); TIBC= 295 μgm/dl (Normal).
- *Urine* R/M/E showed Color=straw, Albumin=trace, Urobilinogen= 1+, Bilirubin- +++, Pus cell=2-4, RBC=plenty.

- Bone marrow shows Dimorphic erythroid and megakaryocytic hyperplasia.
- USG of whole abdomen – periportal echogenicity of Liver is increased. Parenchymal echogenicity is decreased. Multiple ill defined hyperechoic areas are noted in the right lobe of Liver.
- CT scan of whole abdomen with contrast- Hepatosplenomegaly with multiple hepatic SOLs and irregular heterogenous enhancement of spleen with abdominal lymphadenopathy.

She received total 3 bags blood within 10 days for correction of anaemia but her condition was deteriorating. Her general condition was improved after Injection Methyl Prednisolone 30 mg/kg/day for 5 days followed by oral prednisolone 1.5 mg/kg/day continued up to normalization of CBC then slow tapering. Follow up CBC after 7 days showed increased haemoglobin and platelet level without blood transfusion.CBC: ESR=5 mm, Hct= 24.0%, Hb=12.1 gm/dl, MCV=87.3fL, MCH=27.6 pg, MCHC=31.7 gm/dL, RDW- CV=16.4%, WBC=6000/cmm, N=50%, L=42%, M=05%, E=03%, B=00%, Platelet= 180000/μL and USG of whole abdomen revealed no mass lesions in liver but spleen is enlarged in size with altered echotexture in inferior pole. Maria was diagnosed as Evans syndrome on the basis of clinical picture and laboratory investigations.

III. Discussion

Autoimmune hemolytic anemia (AIHA) is an immune disorder which is characterised by circulating antibodies against antigens on the red blood cells (RBCs) membrane resulting in shortened life span of the RBC [2]. Robert Evans first described an association between idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia in 1951. It was characterized by simultaneous destruction of the body's own red blood cells, white blood cells, platelets, neutrophils which causes Autoimmune Hemolytic Anemia (AIHA) and Idiopathic Thrombocytopenia Purpura (ITP) or immune neutropenia in absence of any cause [3].

Evans syndrome is predominantly a disease of pediatric age group[4]. There is evidence to support abnormalities in both cellular and humoral immunity in Evans syndrome. Both CD4 and CD8 lymphocytes were reduced; increased constitutive production of interleukin-10 and interferon-y caused activation of autoreactive, antibody-producing B cells. Despite the frequency of haemopoietic cell-specific autoantibodies in patients with Evans syndrome, there is very little information about the identity of target antigens.

Patients may present with AIHA or ITP either separately or concomitantly. Neutropenia occurs in up to 55% of patients at presentation, or pancytopenia (14%). The development of the second cytopenia may occur months to years after the first immune cytopenia and may delay diagnosis. Usual features of haemolytic anaemia i.e: pallor, lethargy, jaundice, heart failure in severe cases; and features of thrombocytopenia i.e: petechiae, bruising, mucocutaneous bleeding may be present. The lymphadenopathy and organomegaly (hepatomegaly and/or splenomegaly) may be chronic or intermittent and in some cases may only be apparent during episodes of acute exacerbation[2-6].

A full blood count will confirm the presence of cytopenias and a blood film should be examined for features of AIHA (polychromasia, spherocytes) and to exclude other underlying diagnoses (malignancies, micro angiopathic haemolytic anaemia, congenital haemolytic and thrombocytopenic conditions).

Features of haemolysis should be sought including a raised reticulocyte count, unconjugated hyperbilirubinaemia and decreased haptoglobins. The direct antiglobulin test (DAT) is almost invariably positive (although often weakly so), even in the absence of haemolytic anaemia, and may be positive for IgG and/or complement (C3)[3-6]. The indirect antiglobulin test may also be positive in 52-83% of patients[5,10].

Assays for antiplatelet and antigranulocyte antibodies have shown varied results[11]. In a report of 32 adult patients with AIHA, showed antiplatelet antibodies in 91% (demonstrated by thromboagglutination and indirect antiglobulin consumption tests) and leucocyte antibodies in 81% (demonstrated by a cytotoxicity test). Common variable immunodeficiency (CVID) and IgA deficiency, which have been reported to develop acquired cytopenias[12,13], and also as a baseline prior to immunomodulatory therapy.

As Evans syndrome is a diagnosis of exclusion so other confounding factors such as malignancies, infections and rhematological disorders should be ruled out. A bone marrow examination (aspiration/biopsy) necessary to rule out causes of aplastic anemia or an infiltrative disorder. Bone marrow aspiration usually shows a mild to moderate erythroid hyperplasia. Megakaryocytes may be normal to increased in number which indicates an increased destruction of platelets in the peripheral blood as the cause of thrombo-cytopenia[6].

Our patient Maria presented with abdominal pain, vomiting, generalized weakness and jaundice. Her CBC showed severely anaemic, thrombocytopenia, PBF showed features consistent with immune haemolytic anaemia with thrombocytopenia and marked roulaeux formation. Reticulocyte count and LDH was raised. Direct Coomb's test (DAT) was positive and Hemoglobin electrophoresis revealed normal finding. Liver function test was normal except bilirubin. Viral, autoimmune and Wilson disease markers for Hepatitis was negative. Serum Lipase, Fasting lipid profile, RBS, Serum electrolytes and Creatinine were within normal range. Flow cytometry for PNH evaluation was not consistent

with a diagnosis of PNH. Urine R/M/E showed plenty of RBC. Bone marrow showed Dimorphic erythroid and megakaryocytic hyperplasia. USG of whole abdomen – periportal echogenicity of Liver was increased. Parenchymal echogenicity was decreased. Multiple ill defined hyperechoic areas were noted in the right lobe of Liver. CT scan of whole abdomen with contrast showed Hepatosplenomegaly with multiple hepatic SOLs and irregular heterogenous enhancement of spleen with abdominal lymphadenopathy.

Our patient's general condition was improved after injection methyl prednisolone 30mg/kg/day for 5 days followed by oral prednisolone 1.5 mg/kg/day continue upto normalization of CBC then slow tapering. Follow up CBC after 7 days showed increased haemoglobin and platelet level without blood transfusion and USG of whole abdomen revealed no mass lesions in liver but spleen is enlarged in size with altered echotexture in inferior pole.

Evans syndrome is managed by Corticosteroids and/ or intravenous immunoglobulins as the first-line therapy. Most patients respond to this line of treatment although relapses are quite common. The second line therapy includes immunosuppressive drug. Recently, some patients have been treated with rituximab. Rituximab is one such drug that can be tried in cases of refractory Evans syndrome. Rituximab is a chimeric anti-CD20 monoclonal antibody with human IgG1 and k constant regions and murine variable regions [8,9]. It causes selective depletion of B cells through complement and antibody-dependent cell-mediated cytotoxicity and induction of apoptosis.

In long-term follow-up most authors described more frequent episodes of ITP compared with episodes of AIHA. Causes of death were mainly related to haemorrhage or sepsis and reassuringly, given the degree of immune dysregulation seen in many patients, none of the patients described in these long-term studies (mainly of children) developed malignancy.

Splenectomy may also be considered although long-term remissions are less frequent than in uncomplicated ITP. For severe and refractory cases, stem cell transplantation (SCT) offers the only chance of long-term cure. A fully developed Evans syndrome should be associated with a Coomb's positive hemolytic anemia which is essential for definitive diagnosis. Although rare, Evans syndrome should be suspected and investigated for in patients presenting with autoimmune haemolytic anaemia or autoimmune thrombocytopenia concurrently or sequentially. Patients of either of these disorders individually should therefore be thoroughly investigated for the other so as not to miss a diagnosis of Evans syndrome. Long term follow up is essential in such cases as the patient is at a risk of developing other auto immune problems [4].

IV. Conclusion

Although a rare disorder, Evans syndrome should always be considered in cases presenting with AIHA or AITP occurring simultaneously or in follow up after excluding the causes of unknown etiology. Hence the early diagnosis, knowledge of its presentation and constant follow up is crucial for this syndrome.

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Awareness and Practice of Personel Protective Equipment use during Covid-19 among Health Care Personnel in India: A Systematic Review

By Bhawna Solanki, Kabiru Lawali, Abhishek Lachyan, Nilofar Rasheed, Ajoke Akinola, Neelam Rao Bharti & Anjali Chauhan

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Abstarct- *Background:* Personal protective equipment (PPE) is the most insightful concern for frontline healthcare providers for the treatment of patients with coronavirus disease (COVID–19), to avoid transmission. The average person with COVID-19 infection is known to infect 1, 5 to 3, 5 people. The capacity of an entire hospital to be significantly diminished by a single COVID-19 infection of healthcare staff. Many health care personnel do not know what is safe to wear. With a growing number of doctor's fatalities, we aimed at increasing awareness and practice of health care personnel on the issues across the use of PPE by evaluating their awareness and practice using a validated questionnaire.

Methodology: The research approach used is quantitative; this is because the data obtained is a quantifiable data. The information collected is from sampling methods from an online validated questionnaire.

Keywords: *Awareness, Practice, COVID-19 Pandemic, Protective Personnel Equipment [PPE], Health Care Personnel.*

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Abstract- Background: Personal protective equipment (PPE) is the most insightful concern for frontline healthcare providers for the treatment of patients with coronavirus disease (COVID–19), to avoid transmission. The average person with COVID-19 infection is known to infect 1, 5 to 3, 5 people. The capacity of an entire hospital to be significantly diminished by a single COVID-19 infection of healthcare staff. Many health care personnel do not know what is safe to wear. With a growing number of doctor's fatalities, we aimed at increasing awareness and practice of health care personnel on the issues across the use of PPE by evaluating their awareness and practice using a validated questionnaire.

Methodology: The research approach used is quantitative; this is because the data obtained is a quantifiable data. The information collected is from sampling methods from an online validated questionnaire. The method of review is based on the PRISMA; Data analysis was done using descriptive and inferential statistical methods to meet the objectives of the study. Findings were presented in the form of Tables and figures. Using SPSS and EXCEL.

Result: The study analyzed 132 health care workers(HCW), of which 76.5% (105) were found to be male and 23.5%(27) female, the majority of the respondents are married 77.27%(102). Medical doctors, Medical lab personnel represent the highest percentage of 20.45%(27) each, with pharmacists, health officers, and physiotherapists having 15.15%(20), 19.69%(26), and 17.43%(23) respectively. the level of awareness of the respondents was analyzed. 75.72 % of health care workers are aware of personal protective equipment, 77% are aware of the role personal protective equipment play in the prevention of the spread of COVID-19, 5% are not aware.

Conclusion: The level of awareness is quite high as seen from the results, and also there is a need to educate more regarding the use of PPE despite their uncomfortably stated by few HCWs. The practical use of PPE during this pandemic is also much as the result shown. Their availability is a matter of great importance as there is a shortage of overall equipment due to high demand.

Keywords: Awareness, Practice, COVID-19 Pandemic, Protective Personnel Equipment [PPE], Health Care Personnel.

I. Introduction

On 11th March 2020 the World Health Organization declared the COVID-19 outbreak a public health emergency of international concern[1],[2]. The outbreak started in mainland China in December 2019, with a regional emphasis at Wuhan City, Hubei[3]. 29, 54,222 cases and 2, 02,597 deaths from coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had been identified worldwide as of April 28th, 2020[4]. Clinical trials of hospitalized patients found that patients often exhibit symptoms consistent with viral pneumonia at the onset of COVID-19, most frequently fever, cough, sore throat, myalgia, and fatigue. The SARS-CoV-2 incubation period will last for 2-3 weeks. The virus spreads through human-human interaction by infected people and physical contact, coughing, sneezing, droplets/aerosols.[5] No, any effective antiviral medication or vaccine has been produced to date[6].

Current studies have indicated that the most frequent signs are respiratory symptoms of COVID-19 such as fever, dry cough, and dyspnea, very close to

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the 2003 extreme acute respiratory syndrome (SARS) and 2012 Middle East respiratory syndrome (MERS), which strongly suggests the virus' droplet transmission and contact transmission [7],[8]. In addition to the standard respiratory disorder, less common features such as diarrhea, nausea, vomiting, and abdominal pain have been reported in different degrees and different sample populations.[9] Transmission by droplets occurs when a person is in close contact (within 1 meter) with another person who has developed respiratory symptoms (coughing or sneezing) due to infection with COVID-19 and is thus at risk of exposure of his/her mucosa (mouth and nose) or conjunctiva(eyes) to potentially infectious respiratory droplets (generally known to be greater than 5-10 μm). Droplet transmission can also occur near the infected individual, via fomites (clothes, utensils, furniture, stethoscope, thermometer, etc. [10],[11].

India registered the first COVID-19 case in Kerala on 30 January, which grew to three cases by 3 February; all were students who had returned from Wuhan. Apart from these, there was no noticeable change in transmissions in February. On 4 March 22 new cases, including 14 infected members of an Italian tourist party were reported [12].

In March, after many people with travel experience to affected countries, the transmissions increased, and their contacts tested positive. A 76-year-old man with a travel background to Saudi Arabia on 12 March became India's first COVID-19 fatality.[13],[14]

A Sikh preacher, who had a travelling history to Italy and Germany, turned into a "mega spreader" by attending a Sikh festival in Anandpur Sahib on 10–12 March. Twenty-seven COVID-19 cases were traced back to him. More than 40,000 people were quarantined on 27 March in 20 villages in Punjab to contain the spread[15].

A religious congregation event at Tablighi Jamaat in Delhi, which had taken place earlier in March, emerged as a new virus super spreader event on 31 March, after various cases across the country were traced back to it. The Ministry of Health announced on 18 April that there were 4,291 cases directly related to the incident[16].

Around 4,000 stranded pilgrims returned from Hazur Sahib in Nanded, Maharashtra. on 2 May in Punjab, many of them tested positive, including 27 bus drivers and drivers who had been part of the scheme for transport. On 13 May 1,225 pilgrims had been tested positive[17].

A popular subject – perhaps the most thought about, and emotive issue for front-line treatment professionals dealing with Coronavirus Disease Patients (COVID-19) – is a personal protective system (PPE). During the 2019 Corona Virus Pandemic (COVID-19), a lengthy and rising list of health care workers has lost their lives[18]. At the beginning of the outbreak, a significant proportion of health care staff became infected, probably secondary to a lack of awareness and inadequacy of personal protective equipment (PPE). For several nations throughout Europe, debates have started about how to optimally secure health care personnel. Coronavirus COVID-19 has travelled across the globe impacting public care services[19]. There are various recommendations for the protection of health care workers in each country or hospital. Nevertheless, no concrete standards for personal protective equipment (PPEs) and health protocols in the area of medicine have yet been created[20]. Health care practitioners should be trained and supported optimally from the guidelines. The average person with COVID-19 infection is known to infect 1, 5 to 3, 5 people. The capacity of an entire hospital to be significantly diminished by a single COVID-19 infection of healthcare staff. About 1300 health workers were contaminated in Wuhan, the outbreak area. More than 200 doctors have

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died of the illness in Italy to this day[21]. The likelihood of infection is more than three times the general population for health workers. Both healthcare staff is commonly known to wear standard surgical masks during any patient encounters. Also, the correct hand hygiene and disinfection are suggested to avoid excessive touch, preserve adequate space. Positive or suspicious patients with COVID-19 are isolated from non-infected patients in most hospitals[1, 2, 22].

There are a wide range of personal protective equipment (PPEs) globally varying from strong respiratory purifiers (PAPRs) to different facemasks, helmets, gowns, and gloves[20,23]. Epidemics of severe acute respiratory syndrome coronavirus 2003 (SARS-CoV-1) or Middle East Respiratory Syndrome Corona Virus (MERS) have historically occurred in countries (e.g., China, Taiwan, and South Korea), where suits for PAPR and Hazmat are available. Some of the most impressive value of PAPR is the re-usability of aerosol producing medical procedures (AGMPs), thus giving them safety .[18, 22, 24]

Covering more of the body leads to better protection. Though, this may contribute to additional exposure as it is generally correlated with greater difficulties in placing and extracting the personal protective equipment (PPEs) because the PPE becomes less easy .Covers are the worst to remove which provide the greatest security, accompanied by long skirts, skirts, and aprons. Respirators use with coverings can have more security than a cloth-covered mask, but are easier to use. Airier personal protective equipment (PPE) forms can contribute to identical pollution rates but can be rendered more comfortable. Coronavirus disease is predominantly transmitted by contact or droplet transmission. Coronavirus disease can become aerosolized by 'aerosol-generating procedures' and then the airborne transmission is possible [1,2,2025].

For certain countries, the lack of personal protective equipment (PPE) has contributed to healthcare workers being vulnerable to probable infections[26]. The usage of personal protective equipment (PPE) in emergency operations created questions regarding its impact on surgical performance, sense of safety, non-technical efficiency, general comfort, and surgical exhaustion [1].

Personal protective equipment (PPE) is only one part of a system to protect staff and other patients from COVID-19 transmission. Personal protective equipment (PPE) recommendations from international organizations are broadly consistent; personal protective equipment (PPE) use is not. Appropriate use of Personal protective equipment (PPE) significantly reduces the risk of viral transmission and infection. Personal protective equipment (PPE) should be matched to the potential mode of viral transmission – contact, droplet, or airborne. Many health care personnel do not know what is safe to wear[21] With a growing number of doctor's fatalities, we aimed at increasing awareness and practice of health care personnel on the issues across the use of PPE by evaluating their awareness and practice using a validated questionnaire.

II. Need for Study

- In epidemics of highly infectious diseases, such as Ebola Virus Disease (EVD) or Severe Acute Respiratory Syndrome (SARS), healthcare workers (HCW) are at much greater risk of infection than the general population, due to their contact with patients' contaminated body *fluids*. *Verbeek et el 2019*
- Lack of awareness and proper practice regarding the use of PPE can lead to hazard known as occupational hazard caused by improper negligence

III. Statement of Research Problem

The need for the use of these PPEs has increased over the years with increasing awareness of workplace hazards, and the difficulties associated with overdependence on other control measures which for some agents cannot be eliminated or even monitored. This is especially important in hospital settings where workers are often exposed to biohazards and other infectious agents like hepatitis B, hepatitis C, and HIV. Indeed, health facilities are rife with very hazardous agents: just recently COVID-19 disease, Lassa fever, and other infections caused high mortality among health workers in the affected countries in India and sub-region. Control of Coronavirus has become particularly difficult and several measures including the use of appropriate PPEs were used to contain it. Apart from biohazards, in hospitals, some departments work on

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radioactive materials (radiology department) and others that work on both biohazards and chemicals (laboratory department). Some hospitals have therefore established policies on PPE.[4]

Nosocomial infections transmitted by direct contact can be prevented by adapting standard precaution guidelines. Appropriate use of PPE is the easiest way to prevent contact from secretions and transfer of pathogens which is mainly the mode of transmission of COVID-19. It's important to assess the level of compliance with the use of PPE by various HCWs who make direct contact with COVID-19 patients. Based on the available evidence, the COVID-19 virus is transmitted between people through close contact and droplets, though further studies are being carried out to know whether it is airborne. The people most at risk of infection are those who are in close contact with a COVID-19 patient or who care for COVID-19 patients, hence this study attempted [7].

IV. Aim

This study aims to evaluate the awareness and the practice of personal protective equipment use during COVID-19 among health care personnel.

V. Objectives

To determine the level of awareness among health care personnel on the use of PPE

To evaluate the practice in the use of PPE among health care workers

Hypothesis

H1=There will be a significant correlation between awareness and practice of use of PPE among health care workers.

H0=There will be no significant correlation between awareness and practice of use of PPE among health care workers in the treatment of COVID-19.

VI. Methodology

a) Search Strategy

The method of review is based on the PRISMA [27]format (preferred reporting item for systematic reviews and meta-analysis). In the search for the topic, using google scholar search engine, from the identified keywords. Such as awareness, the practice of PPE, COVID-19, and health care personnel. It was decided that all and at most three out of five keywords to be used in the search for the articles related. As two researchers were consulted for the review, the first researcher worked on the literature search and the second on the technical aspect which was the extraction of articles. The initial search after entering of the title (Awareness and practice of PPE use during among health care personnel "Personal Protective Equipment COVID 19") produced 16,900 results of which custom range was applied to capture current data with 5 years, from 2016 to August 2020 and this yielded 8, 070 results. On observation of the articles, several of them did not match the search criteria. Therefore, an advanced search was applied to narrow down the subject and be more specific. The advanced search was applied "with all the words", "Personal Protective Equipment COVID 19", with words occurring anywhere in the article and dated between 2016 till 2020 were reviewed and it resulted in twenty-five articles, sorted by relevance.

b) Research Approach

The research approach used is quantitative; this is because the data obtained is a quantifiable data. The information collected is from sampling methods from an online validated questionnaire.

c) Research Design

A longitudinal cohort study in a form a prospective study was designed and used as data collection was obtained throughout specific time across the same category of individuals.

d) Variables

The variables are independent. This is because the variable obtained are stable and unaffected by the other variables that were measured. It refers to the condition that the experiment is systematically manipulated. It is a presumed cause.

[27] Kublashvili K, Tsikarishvili K, Uriadmkopeli K, Kobalia S. EDITORIAL 3 Gábor Halmai Illiberalism in East-Central Europe 11 Kanstantsin Dzehtsiarou COVID-19 and the European Convention on Human Rights 53 n.d.

Schematic representation of the study

Table 3: Research Frame Work time status

S/N	Activity	Time Frame											Responsible person
		Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	
01	Research topic development												Health care worker
02	Concept development and approval												Health care worker and supervisor
03	Research proposal writing					Final exam							Health care worker and supervisor
04	Submission of research proposal												Health care worker
05	Data collection												Health care worker and supervisor
06	Data analysis												Health care worker and supervisor
07	Dissertation writing												Health care worker and supervisor
08	Submission of dissertation and dissemination of results												Hospital health care worker

e) The Setting of the Study

The study was carried out among health care workers that work in a hospital setting as they are the first in line in the battle against COVID-19. These HCWs include Physicians, hospital pharmacist, radiologist, physiotherapist, lab technicians among others

f) Sample and Sampling Technique

The sample was calculated using a Cochran formula.

$$n = \frac{n_0}{1 + \frac{(n_0 - 1)}{N}}$$

Equation 1

Where n=adjusted sample size
N= Population size
$N_{0=}$ sample size
The sampling obtained

g) Inclusion Criteria

- Health care workers
- Age between 19 years to 60 years
- Those that are willing to participate
- Those that can read and write and gives consent for

h) Exclusion Criteria

- Those that are not health care personnel
- Age below 19 years
- Those that are not willing to participate

i) Tool/Instruments

A self-designed questionnaire was used which is validated by medical experts. The questionnaire was designed in such a way that it provides information related to socio-demographic data, attitude, and practice of HCWs concerning personnel protective equipment used in taking care of patients with COVID-19. The questionnaire consists of a three-part, the first part being the sociodemographic data, then awareness, followed by practice. The results are presented in a tabular form

j) Content Validity

Attached is a copy of the validity content, a questionnaire which is validated by a seven (7) medical doctors and three (3) health officers, making 10 in total.

k) Pilot Study

A result of 20 respondents as specified in the outline provided by the school and guide was used as a pilot study. Necessary corrections made during the presentation were implemented and as such the current result provided updated information.

l) Data Collection Process

An online validated questionnaire was used which as stated was validated by medical experts. A google doc form was constructed shared among the targeted respondents listed above, who fulfil the inclusion criteria.

m) Plan for Data Analysis

Data analysis was done using descriptive and inferential statistical methods to meet the objectives of the study. Findings were presented in the form of Tables and figures. Using SPSS and EXCEL.

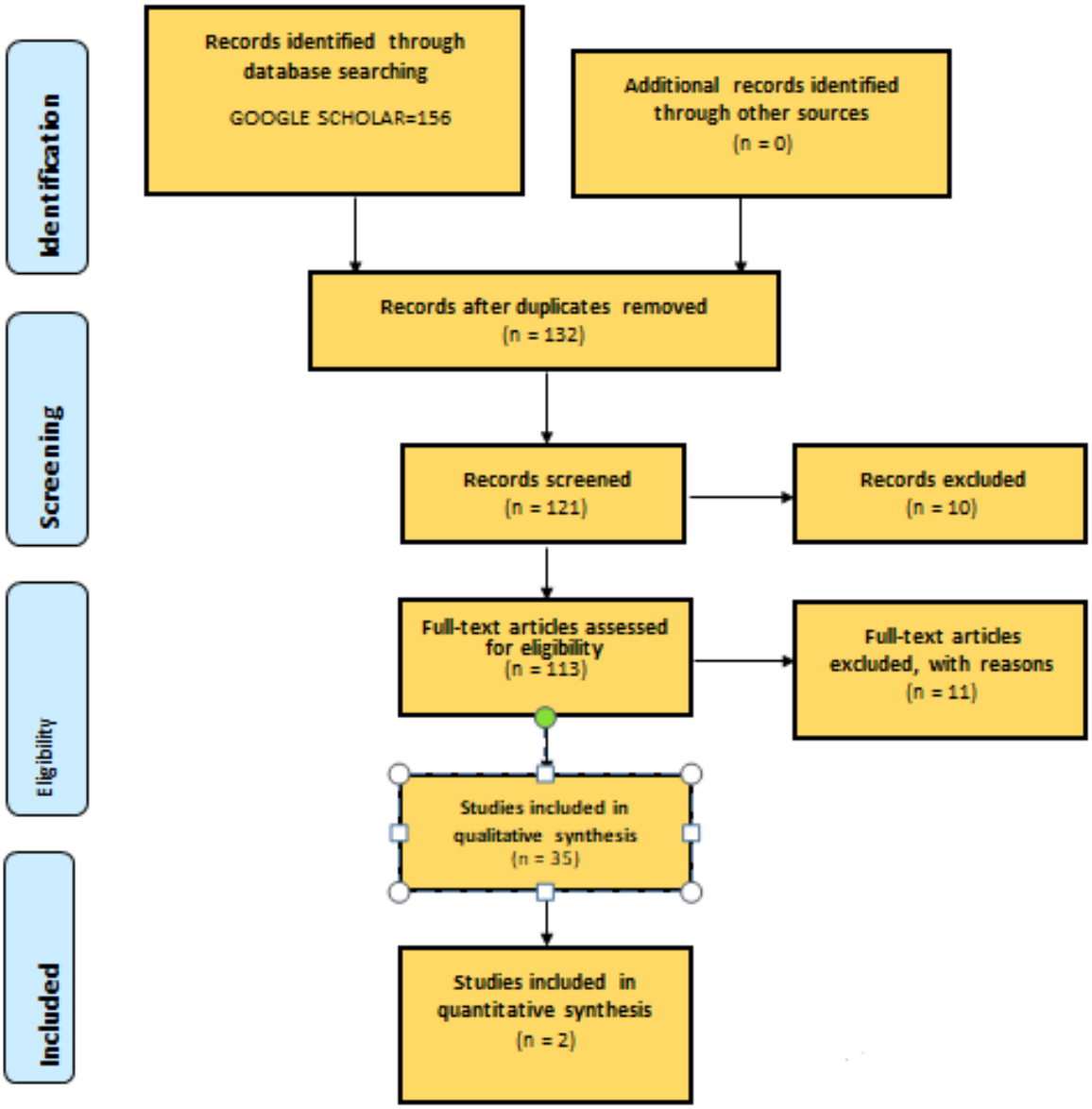

Figure 1: PRISMA Flow Diagram. Legend: The PRIMSA diagram details our search and selection process applied during the overview

VII. Results

Table 1: Demographic Table

Indicators	Frequency (%)
	N=132
Gender	
Male	101(76.5)
Female	31 (23.5)
	N=132
Age	
18-25	23(17.4)
26-30	69(52.3)
31-35	11(8.33)
36-40	5(3.8)
41-45	10(7.58)
46 Above	13(9.85)
Duration of current career field	N=132
<1	30(22.72)
1-5	85(64.39)
6-10	12(9.10)
11-15	5(3.79)
16-20	0
	N=132
Degree and above	125(94.69)
High school (9-10)	7(5.31)
Educational Level Correspondents	
Married	102(77.27)
Unmarried	30(22.73)
	N= 132
Profession	**Frequency(%)**
Medical doctors	27(20.45)
Medical lab personnel	27(20.45)
Pharmacists	20(15.15)
Health officers	26(19.69)
Medical students	4(3.04)
Physiotherapy	23(17.43)
Radiology	5(3.79)
Working department	N= 132
Laboratory unit	41(31.07)
Radiology unit	13(9.85)
Emergency unit	20(15.15)
Physiotherapy	19(14.39)
Surgical ward	27(20.45)
Neurology	12(9.09)

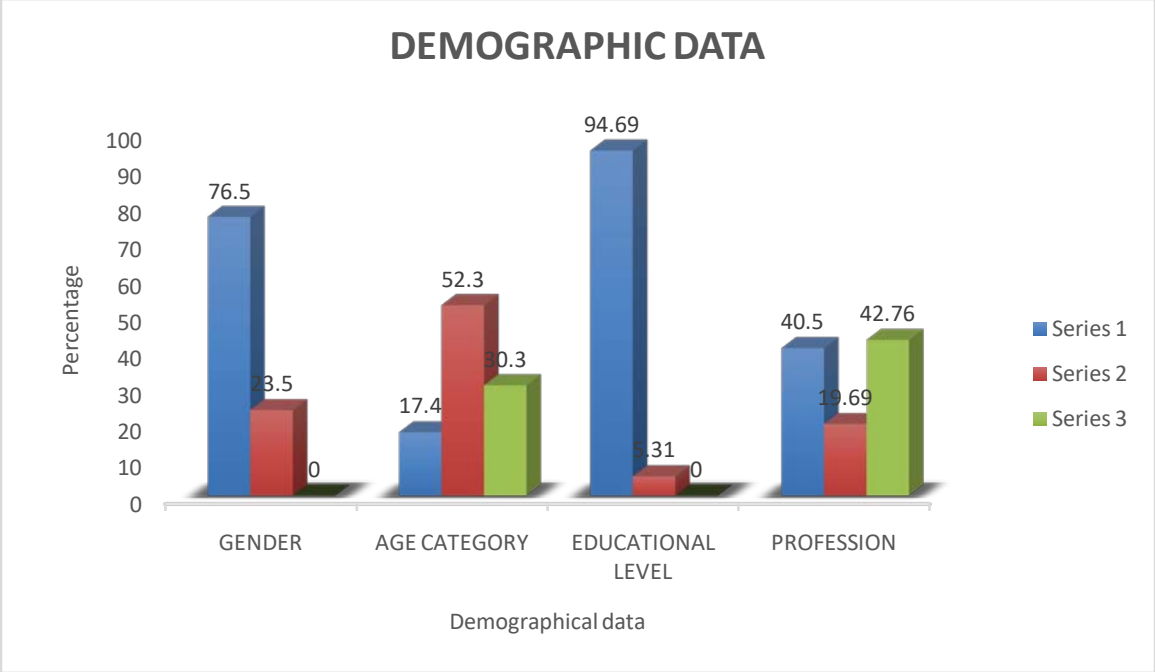

Figure 2: Demographic data

The gender chart represents 76.5% being male and 23.5% female. 52.3% having the highest age range between 26-30 years old. 94.69% of the correspondents are educated with at least a degree. Doctors and pharmacist accounting for 40.5% and others account for 42.76%.

Table 2: Awareness of Correspondents

S/n	AWARENESS	YES(%)	NO(%)	NOT SURE(%)	VERY MUCH (%)	LITTLE BIT (%)
1	Do you know what personal protective equipment is	75.72	2.50	0	18.94	3.20
2	Do you know the role of personal protective equipment in the prevention of Covid-19?	77.00	17.50	2.5	0	2.5
3	Do you know that additional precautions are required by health care workers to protect themselves from Covid-19?	90	5	2.5	2.5	0
4	Do you know that the type of personal protective equipment used for COVID-19 patients varies among personnel?	84.6	10.3	0	5.1	0
5	Do you know that the lack of use of Personal protective equipment can lead to an occupational hazard related to COVID-19?	80	5	2.5	7.5	5
6	Does Personal protective equipment always available to you?	27	62.2	2.7	2.7	5.4
7	Do you know that personal protective equipment interferes with the ability to do a job?	92.5	2.5	2.5	2.5	0

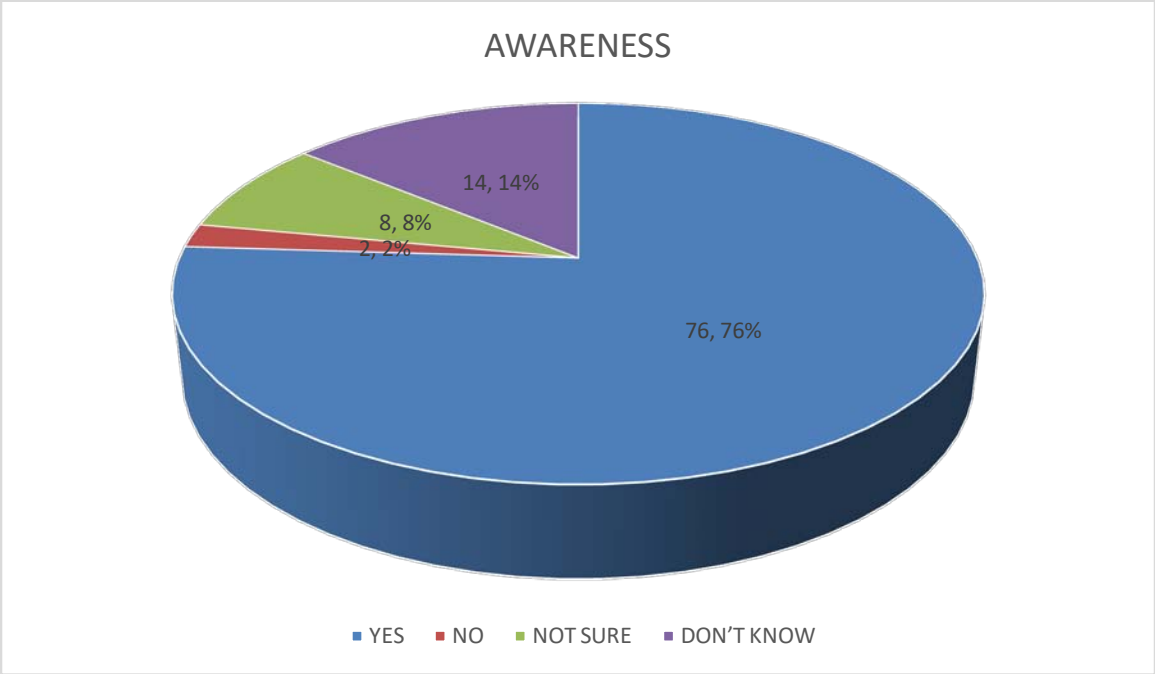

Figure 3: Average Awareness of the correspondents 76% averagely answered 'YES' as they are aware of what PPE are used while 14% not sure

Table 3: Practices of Correspondents

S/N	PRACTICE	YES (%)	NO (%)	NOT SURE (%)	MAYBE (%)	I DON'T KNOW (%)
1	Do you think wearing personal protective equipment is uncomfortable for you?	37.88	49.24	20.45	0	0
2	Do you think personal protective equipment provides a physical barrier to COVID-19?	84.85	7.56	3.79	3.79	0
3	Do you believe your job performance is affected by wearing personal protective equipment?	41	43.6	12.6	2.6	0
4	Did you experience any difficulties, incidents, or accidents while using personal protective equipment?	23.1	59	5.1		12.8
5	Do you think that posters in the working area are important in reminding you to wear personal protective equipment?	87.2	0	5.1	5.1	2.6
6	Do you regularly wear personal protective equipment?	85	15	0	0	0
7	Do you share your protective equipment?	5	85	2.5	5	2.5

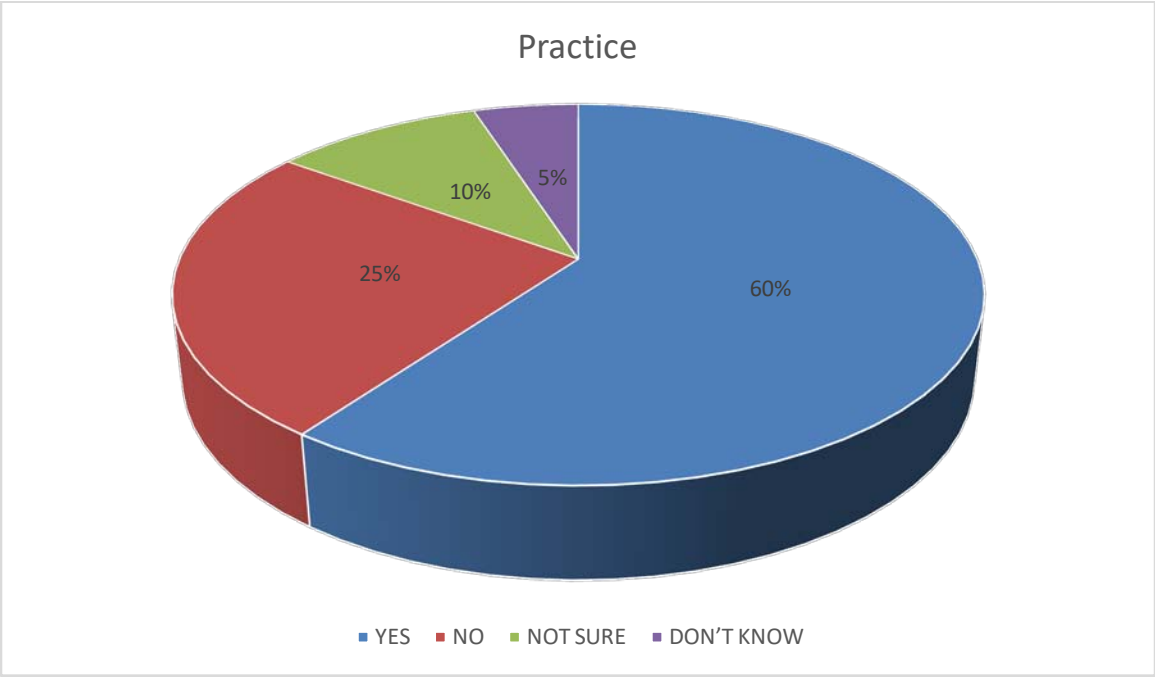

Figure 4: Average Practice of Correspondent

In terms of practice, 60% of our correspondents are practicing while 25% are not.

Table 4: Chi Square Table between Education Variable and Practice Variable

Crosstab						
Practice-based on literacy and education						
		Do you think wearing personnel protective equipment is uncomfortable for you?				
		yes	no	Not sure	maybe	I don't know
Years of practice	<1	36	9	4	5	74
	1-5	26	8	3	0	57
	6-10	27	5	1	3	36
	11>	10	3	0	0	13
Total		89	25	8	8	132

Chi-Square Tests			
	Value	Degree of freedom	Asymptotic Significance (2-sided)
Pearson Chi-Square	7.354[a]	9	.600
Likelihood Ratio	10.560	9	.307
Linear-by-Linear Association	.338	1	.561
N of Valid Cases	180		

Crosstab

Table 4 shows the demographic and professional characteristics data of the health care workers. The study analyzed 132 health care workers(HCW), of which 76.5% (105) were found to be male and 23.5%(27) female, this is due to the data obtained from random sampling among the HCW. 52.3% (69) of the HCWs are from the age limit of 26-30 which has the highest percentage and 3.8% (5) age limit 36-40 is the lowest. This is by a study on Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare workers, which also shows a higher percentage of men as compared to women at the age group of 26-30 years [23]. The experience of the HCWs was analyzed, 1-5 years being the highest with 64.39 %(85) followed by those with < 1year having 30(22.72%). Those with high school education represent 5.31 %(7) and 94.69%(125) have at least a degree. This is also following a study on the use of personal protective equipment by health care workers in a

disease outbreak, showing that the majority of health workers associated with disease outbreak are degree holders, this shows that people are educated, and shows that at the beginning of the outbreak, a significant proportion of health care staff became infected, probably secondary to a lack of awareness and inadequacy of personal protective equipment (PPE) [1]. The majority of the respondents are married 77.27%(102). Medical doctors, Medical lab personnel represent the highest percentage of 20.45%(27) each, with pharmacists, health officers, and physiotherapists having 15.15%(20), 19.69%(26), and 17.43%(23) respectively, this is following another study on Reasons for healthcare workers becoming infected with novel coronavirus disease (COVID-19) in China showing that most healthcare workers affected are Medical doctors and Medical lab personnel[22] The analysis shows that HCWs from the laboratory unit is the highest responders 31.07%(41) followed by those from the surgical ward and emergency unit with 20.45%(27) and 15.15%(20) respectively.

There is a high level of awareness among the HCW recorded as seen from Table No.2, this can be attributed to the fact that COVID-19 is a pandemic disease and the method of which it can be transmitted as defined by the World Health Organization (WHO) is through physical contact with the infected patient[1] Though PPE prevents the risk of exposure as health workers are more at risk to be infected. The media also plays a vital role in increasing the level of awareness regarding the importance of PPE in the fight against COVID-19, as various outlets provide knowledge to the society, health workers inclusive on the preventive measures required to protect oneself against the pandemic.

On the questionnaire, the level of awareness of the respondents was analyzed. 75.72 % of health care workers are aware of personal protective equipment, 77% are aware of the role personal protective equipment play in the prevention of the spread of COVID-19, 5% are not aware, which shows that more education and awareness is needed, this is in conjunction to the fact that an average person with COVID-19 infection is known to infect 1-5 to 3-5 people. The capacity of an entire hospital to be significantly diminished by a single COVID-19 infection of healthcare staff [2] 90% of health care workers are mindful of the added precaution health workers need to protect themselves from COVID-19. The cause of occupational hazards due to the lack of personal protective equipment is a known fact for 80% of the population, though 5% still shows no knowledge on that aspect (reason), some studies show that covering more of the body leads to better protection. Though this may contribute to additional exposure as it is generally correlated with greater difficulties in placing and extracting the personal protective equipment (PPEs) because the PPE becomes less easy[20]. The availability of personal protective equipment amongst health care workers is very low according to our study, this is very alarming due to how fast the disease is spreading and how highly expose health workers are. According to a report by WHO, there is a quite shortage of overall availability of PPE during the outbreak of COVID-19 and a recommendation of management of PPE should be coordinated through essential national and international supply chain management mechanisms, this explains the 68% of the respondents regarding the unavailability of the PPE [1] Another thing we discussed is the ability of the personal protective equipment to interfere with your work. 92.5% of the respondent shows how it affects their ability to do work, studies show how covers are the worst to remove which provide the greatest security, accompanied by long skirts, skirts, and aprons, Though, this may contribute to additional exposure as it is generally correlated with greater difficulties in placing and extracting the personal protective equipment (PPEs) because the PPE becomes less easy[1,2,20].

PPE used by HCWs includes gloves, medical masks, goggles or a face shield, and gowns, as well as for specific procedures, respirators (i.e. N95 or FFP2 standard or equivalent), and aprons (WHO,2020). In this study, 100% practice the use of at least one type of PPE. Regarding the comfortability experienced by HCWs when using PPE, 40% complained about breathing problems and prefer the N95 respirator over the regular surgical masks. The use of overall disposable gown to provide a physical barrier to microbes as well as COVID-19 was a common practice by 85% of the respondents. There is a wide range of personal protective equipment (PPEs) globally varying from strong respiratory purifiers (PAPRs) to different facemasks, helmets, gowns, and gloves. Epidemics of severe acute respiratory syndrome coronavirus 2003 (SARS-CoV-1) or Middle East Respiratory Syndrome Corona Virus (MERS) have historically occurred in countries (eg, China, Taiwan, and South Korea), where suits for PAPR and Hazmat are available. Some of the most impressive value of PAPR is the re-usability of aerosol producing medical procedures (AGMPs), thus giving them safety [53]. Job performance is affected by at least 41% of the respondents while 43.6 % experienced no such issues. To improve the practice, 87.2% stated that, the presence of reminder posters at their places of work significantly increases their ability to wear a PPE. Hence, 85% regularly wear their PPE.

VIII. Conclusion

In conclusion, the level of awareness is quite high as seen from the results, and also there is a need to educate more regarding the use of PPE despite their uncomfortably stated by few HCWs. The practical use of PPE during this pandemic is also much as the result shown. Their availability is a matter of great importance

as there is a shortage of overall equipment due to high demand.

IX. Recommendation

- Recommendation to the next researcher

1. A similar study can be conducted to access the awareness and practice of personal protective equipment use during COVID-19 among health care personnel and to find the actual impact of the transmission of the disease.
2. Along with an individual approach, all the health care personnel should be encouraged to participate in international and national awareness of personal protective equipment use during COVID-19

- Recommendation to the policymakers and health sector:

1. A public health approach that seeks to change the status and promote supportive strategies for better health and protection against diseases like COVID-19 which are easily transmitted.
2. Government legislation should increase awareness of personal protective equipment use during COVID-19, along with some guidelines in public places and advertisement of encouraging the use by both patients and healthcare workers.

Public Health Implication

- Public health is the science and art of preventing diseases, prolonging life, and improving human health through better education and awareness, policymaking, promoting a standard lifestyle, research, and prevention.
- The issue of personnel protective equipment and health care workers is an important integral part of public health care as a whole. Since the outbreak of COVID-19, health care workers have been the face in the fight and prevent the spreading of this disease.
- The finding of this study can help in planning an education program to raise awareness in the public regarding the safe use of personnel protective equipment, COVID-19, and its ill effect on health.
- The findings brought to light that if awareness and health education programs are implemented, it will help to change the negative behavior to positive and health situations. And still, the education of the youths remains the most effective policy and strategy on hygiene misconception.

Limitation of the Study

This study is only limited to those health workers that are only based in the hospital, which are the for the front in the fight against.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Ethics approval and consent to participate

There's no need for ethical approval for this review since no patient data will be collected. In this study author has thoroughly analyzed ethical issues including the plagiarism, confidentiality, malfeasance, data falsification and/or falsification, double publishing and/or submission, and duplication.

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Pileflebite: Uma Revisão Sistemática

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Summary- Introduction: Pylephlebitis is characterized as a portal vein thrombophlebitis, which occurs as a complication of intra-abdominal infections. It is more related to diverticulitis and appendicitis, being a rare complication with a high rate of morbidity and mortality.

Objective: To carry out a systematic review of pylephlebitis, taking into account its clinical, diagnostic and treatment aspects.

Methodology: The work consists of a systematic review, analyzing 20 articles on pylephlebitis, from 2013 to 2021.

Discussion: Pylephlebitis has nonspecific manifestations, making diagnosis and early treatment difficult. The management of the disease consists of using computed tomography, which has been shown to be the best diagnostic method, and early antibiotic therapy. The use of anticoagulation in the treatment is still much discussed.

Keywords: "*pylephlebitis*", "*appendicitis*", "*diverticulitis*", "*thrombophlebitis.*

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Strictly as per the compliance and regulations of:

Pileflebite: Uma Revisão Sistemática

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Resumo- Introdução: A pileflebite é caracterizada como uma tromboflebite da veia porta, que ocorre como uma complicação de infecções intra-abdominais. Está mais relacionada a diverticulite e a apendicite, sendo uma complicação rara e com alta taxa de morbidade e mortalidade.

Objetivo: Realizar uma revisão sistemática sobre pileflebite, levando em consideração seus aspectos clínicos, diagnósticos e de tratamento.

Metodologia: O trabalho consiste em uma revisão sistemática, analisando 20 artigos sobre pileflebite, no período de 2013 a 2021.

Discussão: A pileflebite cursa com manifestações inespecíficas dificultando o diagnóstico e tratamento precoce. O manejo da doença consiste na utilização da tomografia computadorizada, que vem se mostrando como o melhor método diagnóstico, e a antibioticoterapia precoce. O uso de anticoagulação no tratamento ainda é muito discutido.

Conclusão: Por conta da alta taxa de mortalidade, o diagnóstico e tratamento precoce são fundamentais, para uma melhor evolução da doença.

Palavras chaves: "pileflebite", "apendicite", "diverticulite", "tromboflebite".

Summary- Introduction: Pylephlebitis is characterized as a portal vein thrombophlebitis, which occurs as a complication of intra-abdominal infections. It is more related to diverticulitis and appendicitis, being a rare complication with a high rate of morbidity and mortality.

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Discussion: Pylephlebitis has nonspecific manifestations, making diagnosis and early treatment difficult. The management of the disease consists of using computed tomography, which has been shown to be the best diagnostic method, and early antibiotic therapy. The use of anticoagulation in the treatment is still much discussed.

Conclusion: Due to the high mortality rate, early diagnosis and treatment are essential for a better evolution of the disease.

Keywords: "pylephlebitis", "appendicitis", "diverticulitis", "thrombophlebitis.

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I. Introdução

A pileflebite é definida como uma tromboflebite séptica do sistema da veia porta advinda de uma infecção intra-abdominal ou pélvica[1]. É caracterizada como uma complicação rara, com incidência anual de 0,37 a 2,7 casos por 100.000 habitantes[2]. Apresenta alta taxa de morbidade e mortalidade (cerca de 25%), especialmente se não for reconhecida no início do tratamento[1].

Sua principal etiologia é a diverticulite, seguido da apendicite, colecistite, pancreatite e outras infecções intra abdominais[3]. Epidemiologicamente, há uma preferência em relação ao sexo masculino (60-70% dos casos) e acomete indivíduos entre 40 e 65 anos[2].

Com relação a sua manifestação clínica, muitas vezes apresenta-se de forma inespecífica, com febre, dor abdominal, náuseas e vômitos, o que acarreta em um atraso no diagnóstico e tratamento[4]. Há também algumas manifestações mais avançadas como icterícia e hepatomegalia[5]. Além disso, os exames laboratoriais também são inespecíficos, mostrando uma leucocitose, níveis elevados de enzimas hepáticas e bilirrubina e aumento de proteína C reativa[4]. Já os exames de imagem desempenham um papel importante no diagnóstico da pileflebite. A ultrassonografia com doppler vai detectar a diminuição de fluxo e a trombose, porém é um exame examinador dependente. A tomografia computadorizada com contraste, é o método de escolha, e consegue mostrar trombose da veia porta. Já a ressonância magnética só é utilizada quando as imagens anteriores mostram-se inconclusivas[4, 5, 6].

Atrasos no manejo da pileflebite são associados a uma taxa de mortalidade de até 25% e sabe-se que o principal problema em um portador de pileflebite é a infecção não controlada[7,8]. Assim, estabelecido o diagnóstico, deve-se iniciar a antibioticoterapia precoce de amplo espectro[8]. Estudos comprovam que, mesmo na ausência de uma bacteremia positiva, o uso de antibióticos reduziu a taxa de complicações potencialmente fatais como isquemia intestinal e abscessos hepáticos. Por tratar-se de uma condição de rara incidência, ainda não há diretrizes sobre a duração necessária de seu uso, variando, em média, de 4 a 6 semanas[7].

Além da antibioticoterapia, outras modalidades são vistas como possíveis pilares do tratamento da pileflebite: a anticoagulação e o tratamento cirúrgico[8,9,10]. O uso de anticoagulantes ainda é

controverso, pois, apesar de se mostrar benéfica em alguns estudos, em outros se demonstra que há a chance de complicações em 20% dos pacientes[8,9]. Já o tratamento cirúrgico é reservado, majoritariamente, para o tratamento do foco infeccioso intra-abdominal e para a drenagem de grandes coleções de fluidos e abscessos[8,10].

II. Metodologia

O trabalho consiste em uma revisão sistemática, em que foi realizado um levantamento bibliográfico, nos idiomas português, inglês e espanhol, no período de 2013 a 2021, utilizando as bases de dados Scielo e Pubmed. Foram selecionados 18 artigos de 23. Foi utilizado como critérios de exclusão o idioma (japonês) e artigos com mais de 10 anos.

As palavras chaves utilizadas foram: "pileflebite", "apendicite", "diverticulite", "tromboflebite".

Corroborando e respeitando o pré-estabelecido nas normas, regras e diretrizes propostas pelo Comitê de pesquisas envolvendo seres humanos, definidas na Resolução 510/16 do Conselho Nacional de Saúde – Ministério da Saúde, esta pesquisa foi submetida e aprovada no Comitê de Pesquisa da Universidade Santo.

III. Resultados

No estudo em questão foram analisados 18 artigos, incluindo relatos de caso e estudos retrospectivos, conforme mostra a tabela 1, abordando aspectos clínicos, diagnósticos e de tratamento da Pileflebite, descritos nos últimos 10 anos na literatura.

Tabela 1: Título, autor principal, ano, metodologias e resumo dos 18 artigos selecionados.

Pylephlebitis as a Rare Complication of Ulcerative Colitis: A Case Report	Leonard Hamera, 2019	Relato de caso	O artigo relata um caso de pileflebite como complicação de uma colite ulcerativa. O diagnóstico foi dado por tomografia computadorizada. Conclui que atualmente não há consenso sobre o manejo da doença. O tratamento foi feito com antibióticos e anticoagulantes, mesmo sem um consenso, porém o uso é feito através de manejos de relatos na literatura.
Pylephlebitis: incidence and prognosis in a tertiary hospital	Moncef Belhassen-Garcíaa, 2014	Estudo observacional retrospectivo	O estudo conclui que a pileflebite é uma complicação rara de infecções intra-abdominais (0,6% dos pacientes com infecções intra-abdominais), e tem alta mortalidade precoce, sendo a diverticulite o processo base mais frequente.
A case of pylephlebitis secondary to cecal diverticulitis	Byung Kook Lee, 2012	Relato de caso	O estudo relata um caso de pileflebite secundário à diverticulite. O tratamento foi com antibioticoterapia e anticoagulante. Conclui-se que o diagnóstico precoce é essencial para o tratamento. Antibióticos e anticoagulantes são a base do tratamento, mesmo sem um consenso.
Pylephlebitis: a Review of 95 Cases	Asad J Choudhry, 2015	Revisão retrospectiva de prontuários	O estudo revisa prontuários de 2002-2012 de pacientes diagnosticados com pileflebite e conclui como principal causa a pancreatite. O tratamento deve ser individualizado, porém refere o uso principalmente de ATB e anticoagulante.
Intestinal Infarction Caused by Thrombophlebitis of the Portomesenteric Veins as a Complication of Acute Gangrenous Appendicitis After Appendectomy: A Case Report	Rui Tang, 2015	Relato de caso	Esse artigo relata o caso de pileflebite pós apendicite e discute sobre quadro clínico (dor abdominal); conduta clínica, com uso de antibióticos e anticoagulantes, e cirurgia. Além de ressaltar a importância do diagnóstico precoce através de TC.
Pylephlebitis of a variant mesenteric vein complicating sigmoid diverticulitis.	Anna L. Falkowski, 2014	Relato de caso	O artigo relata o caso de uma tromboflebite supurativa da veia mesentérica inferior, como complicação da diverticulite sigmóide. O estudo conclui que a pileflebite é rara e geralmente ocorre como uma complicação de uma infecção intra-abdominal comum. A taxa de mortalidade é de

			aproximadamente 25%. Reforça a necessidade de TC de abdome. O tratamento pode ser conservador com antibiótico e anticoagulante (controverso) e cirúrgico em caso de isquemia.
Pylephlebitis Complicating Acute Appendicitis: Prompt Diagnosis with Contrast-Enhanced Computed Tomography	Furkan Ufuk, 2016	Relato de caso	O estudo relata o caso de uma pileflebite como complicação pós apendicite. O artigo conclui que o diagnóstico imediato e o tratamento da pileflebite são cruciais para reduzir a morbidade e a mortalidade. A tomografia computadorizada é essencial no diagnóstico precoce de pileflebite porque revela prontamente o trombo, visto que o quadro clínico é inespecífico. O tratamento precoce e agressivo com antibióticos de amplo espectro é necessário, e a terapia anticoagulante também pode ser usada para prevenir a isquemia intestinal.
Jejunal Diverticulosis Probably Leading to Pylephlebitis of the Superior Mesenteric Vein	Julia Bockmeyer, 2020	Relato de caso	O artigo conclui que a diverticulite e a apendicite são as principais causas. Cita o desafio do diagnóstico pelo quadro clínico inespecífico e ressalta a importância da antibioticoterapia e anticoagulação plena nos casos de pileflebite.
Clinical Manifestations of Superior Mesenteric Venous Thrombosis in the Era of Computed Tomography	Joon Whoi Cho, 2018	Estudo retrospectivo de prontuários	Estudo com análise de 41 prontuários por 17 anos. Conclui-se que as principais causas da doença são apendicite (51,9%) e diverticulite (25,9%). Ressalta a importância da tomografia computadorizada para o diagnóstico precoce. Além disso, ressalta sobre a importância do uso de antibiótico apropriado para o tratamento. O uso de anticoagulação foi citado como controverso, porém usado na maioria dos pacientes no presente estudo.
Mesenteric venous thrombosis as a complication of appendicitis in an adolescent	Seo Hee Yoon, 2019	Relato de caso	O artigo mostra um caso de pileflebite secundário a apendicite, o diagnóstico foi dado através de tomografia computadorizada. O tratamento foi feito com antibioticoterapia e anticoagulação. Conclui que o diagnóstico é de grande dificuldade pelo quadro clínico inespecífico, e o tratamento feito através do quadro clínico do paciente
Pylephlebitis and Crohn's disease: A rare case of septic shock.	Stefano Scaringi, 2017	Relato de caso	O artigo relata um caso raro de pileflebite secundário à doença de Crohn. O diagnóstico foi feito por tomografia computadorizada, após quadro clínico sugestivo. Conclui que o caso é extremamente raro e ressalta a importância do tratamento clínico com antibioticoterapia de amplo espectro iniciado o mais precoce possível.
Pylephlebitis Associated with Inferior Mesenteric Vein Thrombosis Treated Successfully with Anticoagulation and Antibiotics in a 37-Year-Old Male	Mohamed Abdallah, 2020	Relato de caso	O artigo relata um caso de pileflebite secundária de diverticulite. Foi diagnosticado através de tomografia computadorizada e tratada com antibioticoterapia e anticoagulantes mesmo sendo uma terapia ainda controversa.

An unusual increase of D-dimer level-pylephlebitis caused by acute appendicitis: a case report.	Weiqi Wang, 2020	Relato de caso	O artigo evidencia e discute sobre o aumento de D-dímero nos casos de pileflebite. Mesmo com um aumento significativo do D-dímero (14.037), o diagnóstico e a conduta do caso foram da mesma forma dos demais casos.
Pylephlebitis in a previously healthy emergency department patient with appendicitis	Christopher J Coyne, 2013	Relato de caso	O artigo conclui que é um tema de extrema importância, por ser uma emergência. Ressalta que o diagnóstico e início precoce de antibiótico é de grande importância, e podem melhorar os resultados no prognóstico da doença.
Diverticular Pylephlebitis and Polymicrobial Septicemia	Pradhum Ram, 2017	Relato de caso	O artigo relata um caso de sepse polimicrobiana resultante de pileflebite diverticular. Evidência a importância do diagnóstico precoce com tomografia computadorizada, o início precoce da antibioticoterapia e o uso oportuno de anticoagulantes.
Pylephlebitis	Jesse Hartpence, 2021	Artigo de revista	O artigo conclui que a pileflebite é uma complicação rara, sendo a diverticulite a etiologia mais comum. Possuem sintomas inespecíficos e o diagnóstico é feito por tomografia computadorizada. O tratamento é feito com antibioticoterapia de amplo espectro na maioria das vezes. O uso de anticoagulante ainda é controverso por não haver um consenso, porém mostra que pacientes que receberam a anticoagulação tiveram uma mortalidade mais baixa.
Pylephlebitis: a rare but possible complication of intra-abdominal infections	Susana Pérez-Bru, 2015	Estudo descritivo retrospectivo	O estudo com 4 pacientes, evidenciou que na maioria deles (3 pessoas), a etiologia da pileflebite foi colecistite e apenas 1 pessoa a etiologia foi apendicite aguda. Foi realizado cirurgia de emergência em um dos casos e os demais receberam o tratamento com antibioticoterapia empírica de amplo espectro. A terapia de anticoagulação foi realizada em todos os casos.
Superior mesenteric vein thrombosis as a complication of cecal diverticulitis: A case report	Soniya Pinto, 2016	Relato de caso	O artigo relata um caso de pileflebite secundário de diverticulite cecal. O diagnóstico foi feito através de ressonância magnética. O tratamento foi iniciado com antibioticoterapia e anticoagulação. O relato ressalta a importância da suspeita clínica e do diagnóstico precoce para melhor prognóstico da doença.

IV. Discussão

Quase todas as infecções intra-abdominais ou pélvicas envolvendo vísceras com drenagem pelo sistema venoso portal podem ser complicadas pela pileflebite. No início do século 20, a apendicite era a principal infecção relacionada a essa patologia, entretanto, isso acabou mudando com o avanço do diagnóstico precoce e eficácia dos antibióticos. Atualmente, a diverticulite é considerada a principal fonte de pileflebite, embora os casos tenham sido associados a outras condições inflamatórias e infecciosas, incluindo doença inflamatória intestinal, pancreatite, gastroenterite, colangite, úlcera péptica, abscesso hepático, amebíase e até mesmo casos associados a cateteres de veia umbilical e migração de banda gástrica ajustável[1,3].

A pileflebite é uma condição rara de patogenia ainda não bem definida, caracterizada pela trombose da veia porta secundária a uma infecção abdominal. Resulta de uma infecção não controlada nas regiões vizinhas ou drenadas pelo sistema portal. Inicialmente começando como tromboflebite de pequenas veias mesentéricas, o processo pode se espalhar para o sistema venoso portal e hematogênico para o fígado. A trombose das veias mesentéricas subsequentemente pode levar à isquemia mesentérica, infarto e necrose intestinal[5].

A doença pode cursar com diversas apresentações clínicas, desde assintomáticas, com o

diagnóstico incidental através de imagens, a formas graves com choque séptico e insuficiência hepática[8]. O principal quadro clínico é manifestado através de sintomas inespecíficos, incluindo fadiga, febre, dor abdominal, náusea e vômito, diarreia e anorexia[1, 2, 5, 8, 9]. Além da sintomatologia, também há achados de exame físico, como aumento da sensibilidade abdominal, esplenomegalia, hepatomegalia, ascite e icterícia, observados como consequência do envolvimento hepático disseminado além de poderem originar complicações adicionais como abscesso hepático ou colangite[1,5,9].

Além da sintomatologia, também há achados de exame físico, como aumento da sensibilidade abdominal, esplenomegalia, hepatomegalia, ascite e icterícia, observados como consequência do envolvimento hepático disseminado além de poderem originar complicações adicionais como abscesso hepático ou colangite[1,5,9].

Atualmente não há nenhum critério diagnóstico para pileflebite, assim como não há diretrizes para o manejo dessa patologia. Portanto, os planos de diagnóstico e tratamento são baseados em séries de casos e relatórios[1,9]. Ao revisar a literatura, percebemos que os exames de imagem são essenciais para o diagnóstico da Pileflebite[9]. Geralmente, tal diagnóstico é feito a partir de uma Tomografia computadorizada (TC) ou de uma ultrassonografia com Doppler (USG)[1].

O USG pode permitir a visualização do trombo na veia porta, ectasia da veia porta, rede de colaterais venosas, hepatoesplenomegalia e ascite. A TC com administração de contraste venoso, pode demonstrar gás no sistema porta e o trombo vascular hipodenso. Trombose de segmentos venosos portais intrahepáticos, veias mesentérica superior e esplênica é observada em 39%, 42% e 12% dos casos, respectivamente, enquanto a veia mesentérica inferior é pouco acometida isoladamente[2].

Apesar da sensibilidade e especificidade da TC e do USG no diagnóstico da Pileflebite serem desconhecidas, a TC é mais utilizada pois depende menos do operador e possibilita detectar outras complicações, como abscessos hepáticos e isquemia intestinal[1,3]. Outras modalidades menos utilizadas incluem RNM e PET/TC[1].

Os exames laboratoriais geralmente são inespecíficos, mas as alterações mais comuns incluem leucocitose inicial associada a anemia, elevação de fosfatase alcalina, AST, ALT e gama-glutamil transferase e normalmente sem aumento de bilirrubina[1,3].

As hemoculturas positivas são encontradas em 50–88% dos pacientes[3]. Os patógenos tipicamente identificados incluem *Escherichia coli*, *Streptococcus* spp., *Bacteroides*spp., *Proteus* spp., *Klebsiella* spp. e *Enterobacter* spp[2].

A base do tratamento da pileflebite, levando em consideração os artigos selecionados, consiste no uso de antibioticoterapia. É realizado antibiótico empírico de amplo espectro, com base na fonte de infecção, com duração de 4 semanas com base na possibilidade de formação de abscesso e até 6 semanas para abscessos conhecidos[9].

Já em relação ao uso da anticoagulação, os artigos abordados, não apresentam um consenso sobre. Acredita-se que o objetivo da anticoagulação seja para prevenção da progressão da trombose e para o tratamento das complicações da trombose da veia porta. No estudo de Kanellopoulou et al., foi observado que o uso precoce de anticoagulação foi associado a uma diminuição da taxa de mortalidade. Já no de Plemmons et al, não houve efeito significativo na mortalidade. E Batil et al, realizou um estudo retrospectivo com 44 pacientes, diagnosticados com pileflebite, para avaliar o uso de anticoagulação. Nesse estudo, foi concluído que a anticoagulação deve ser usada para pacientes com estado de hipercoagulabilidade por deficiência de fatores de coagulação, câncer ou quando houver envolvimento da veia mesentérica, pois está relacionado a um maior risco de infarto. Assim, não há um consenso sobre a realização de anticoagulação nos pacientes, devendo ser realizada de maneira individualizada, avaliando riscos e benefícios para o paciente[1, 5, 9, 10].

O uso de uma intervenção mais invasiva, como trombectomia cirúrgica ou colocação de dreno percutâneo na veia porta, em alguns casos pode ser necessário, porém, está relacionado a maiores taxas de recorrência[9].

Assim, o diagnóstico e tratamento precoce é fundamental, já que a doença pode evoluir com complicações, como formação de abscessos hepáticos, sepse e desenvolvimento de hipertensão portal[1, 9].

V. Conclusão

A pileflebite é uma complicação das infecções intra-abdominais, principalmente relacionada a diverticulite e apendicite. Por ser uma manifestação rara e com alta mortalidade, o diagnóstico precoce se torna essencial para uma melhor condução da doença. Porém, a clínica inespecífica dificulta o manejo precoce da doença.

Os artigos abordados, confluem sobre a parte clínica e diagnóstica da pileflebite. Porém, em relação ao tratamento, ainda não há um consenso sobre a utilização dos anticoagulantes. A falta de uma diretriz sobre o assunto leva a necessidade de individualizar a indicação do uso de anticoagulante, levando em conta os riscos e benefícios. Assim, a necessidade de novos estudos sobre os benefícios da anticoagulação nos pacientes com pileflebite, se torna essencial, já que a doença apresenta alta mortalidade e pode cursar com novas complicações.

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Surrogate Parameters, Instead of the Genetic Profile, for Recurrence Risk Evaluation in "Early-Stage Breast Cancer Cases" in a Middle – Income Country Like Argentina

By Roberto P. Meiss Kress MD, Roberto Chuit MD PhD & Ariel Gualtieri PhD

Abstarct- Breast Cancer (BC) is the most commonly diagnosed cancer amongst women worldwide and is a leading cause of death and disability among women in low- and middle-income countries (MICs) among which is Argentina. Nowadays in BC, beyond the standard determination of cancer stage according to the classic anatomical criteria of the TNM the study of genic profile (GP) of cancer has also been encouraged. Implementation of the multigene panels assay has led to a change in the manner in which chemotherapy is utilized mainly in patients with, early stage, *estrogen receptor (ER)-positive, Her2-neu negative, lymph node-negative* BC ensuring that patients at highest risk of recurrence are prescribed systemic treatment, while at the same time sparing low-risk patients potential adverse events from therapy unlikely to influence their survival. Multigene panels can provide better risk discrimination relative to clinic-pathological factors. Unfortunately, all these tests are expensive.

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Surrogate Parameters, Instead of the Genetic Profile, for Recurrence Risk Evaluation in "Early-Stage Breast Cancer Cases" in a Middle – Income Country Like Argentina

Roberto P. Meiss Kress MD [α], Roberto Chuit MD PhD [σ] & Ariel Gualtieri PhD [ρ]

Abstract- Breast Cancer (BC) is the most commonly diagnosed cancer amongst women worldwide and is a leading cause of death and disability among women in low- and middle-income countries (MICs) among which is Argentina. Nowadays in BC, beyond the standard determination of cancer stage according to the classic anatomical criteria of the TNM the study of genic profile (GP) of cancer has also been encouraged. Implementation of the multigene panels assay has led to a change in the manner in which chemotherapy is utilized mainly in patients with, early stage, *estrogen receptor (ER)-positive, Her2-neu negative, lymph node-negative* BC ensuring that patients at highest risk of recurrence are prescribed systemic treatment, while at the same time sparing low-risk patients potential adverse events from therapy unlikely to influence their survival.Multigene panels can provide better risk discrimination relative to clinic-pathological factors. Unfortunately, all these tests are expensive.Given the potential savings in cost and resource utilization, several algorithms have been proposed to predict Oncotype DX recurrence score (ODX RS) using commonly acquired clinical and histopathologic variables designated as subrogate parameters (SP).

Purpose: We evaluate the possibility, in a MIC country such as Argentina, of having the data from the normally required clinical-pathological report of the BC, in order to apply 10 selected published algorithms that are offered as alternatives to ODX to predict the ODX RS specifically in patients with "*early-stage breast cancer*" cases.

Methods: From the total of 1832 (stage I to IV) BC cases reported, between 2012 and 2014, to PROYCAM2012 (www.cancerdemama2012.org.ar) a consortium (still in force) created for the study of BC in Argentina a subset of 706 (38,5%) "*early-stage breast cancer*", was identified and analyzed. An online search and selection of published scientific research on SP, (2010 onwards), was carried out. Ten publications were selected and analyzed and the SP used in them identified. The presence of the SP shared by the different studies selected on - line was analyzed in our series, namely: age, tumor size, histology, grade, Estrogen/ Progesterone receptor, Her2 / neu status and Ki-67.

Results: The subset of 706 (38,5%) showed the following characteristics: predominant in menopausal women (72%), average age of 61 years, 3.2% bilaterally and a personal (30,3%) and/or family history (9,3%) of BC. Pathologically, the average size of the tumors is between 1.8 -2.0, with predominance of infiltrating ductal lesions (67, 7%) grade2 (46,7%). From the total of 10 nomograms selected only in 1 our series can complete the required two SPs: HR (96, 6%) andHer2 / neu (100%). In a second nomogram our cases complete the three of the proposed SPs being: Grade (94 %), ER (100%) and PR (99.6%). In a third nomogram cases complete the required six SPs being these: tumor size (88.5%), patient age (100%), laterality (100%), ER receptor (100%), PR receptor (99.6%) and HER2 / neu (100%). In a fourth our cases nomogram completes the required six SPs, being these: size (88,5%), ER (100%), PR status (99,6%), HER2neu (100%), Nottingham (94%) and histomorphology (77,5%). In a fifth nomogram the cases complete the required five SPs: age (100%), tumor size (88.5%), grade (94), PR status (99,6) and histologic type (77,5). In the five remaining nomograms evaluated the percentage of cases that could complete the required SPs only reached 61.5% of the cases.

Conclusion: We demonstrate that, although there are gaps in the updated care process (for example: genetic profile) of BC, it is possible to use nomograms in our country through a comprehensive and complete collection and a careful subsequent analysis of the conventional parameters normally present in the diagnosis of BC. Special emphasis should be noted on the histopathological and immunohistochemical

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results, available almost routinely in our series, a fact that allows us to evaluate the RS and thus apply the corresponding therapy trying to achieve results similar to those that would be obtained with the use of GP.

I. Introduction

Breast Cancer (BC) is the most commonly diagnosed cancer amongst women worldwide [1] and is a leading cause of death and disability among women in low- and middle-income countries (MICs)among which is Argentina [2].

Nowadays in BC, beyond the standard determination of cancer stage according to the classic anatomical criteria of the TNM classification, expression of estrogen and progesterone receptors and HER2/neu receptor are required. The study of genic profile (GP) of cancer has also been encouraged although, for now, not in mandatory form [3]Implementation of the multigene panels assay has led to a change in the manner in which chemotherapy is utilized mainly in patients with,early stage, *estrogen receptor (ER)-positive, Her2-neu negative, lymph node-negative*[*ER (+) / HER2 (-) / lymph node-negative*], BC ensuring that patients at highest risk of recurrence are prescribed systemic treatment, while at the same time sparing low-risk patients potential adverse events from therapy unlikely to influence their survival [4,5].

Multigene panels can provide better risk discrimination relative to clinic-pathological factors, which are significantly superior to traditional prognostic factors in predicting clinical outcome and identifying patients who can be spared chemotherapy safely. There are several tests available at the moment. The Oncotype DX (ODX) BC recurrence test (ODXRS) is the one recommended based on the experience accumulated since its implementation in 2010 [6]

Unfortunately, all these tests are expensive. Oncotype DX (ODX) is expensive and is performed in only 1/3 of patients with BC positive for the estrogen receptor (ER) in developed countries [7,8]and are not affordable or available for the majority of the breast cancer patients globally [9]. The economic non-accessibility and / or technical availability are also the main reasons why in a middle-income country (MIC), such as Argentina, the study is only carried out in very few cases (0,23%) who fulfilled the established guidelines for gene-expression profile study and in a sporadic way [10].

Given the potential savings in cost and resource utilization, several algorithms have been proposed to predict Oncotype DX recurrence score (ODX RS) using commonly acquired clinical and histopathologic variables designated as subrogate parameters (SP). These studies reached different conclusions regarding which model demonstrated the best statistical discrimination power, mainly due to differences in clinical and pathologic variables used [11-20].

In this study we evaluate the possibility, in a MIC country like Argentina, of having the necessary data from the normally required clinical-pathological report of the BC, in order to apply some selected published algorithms that are offered as alternatives to ODX to predict the ODX RSspecifically in patients with "early-stage breast cancer".

II. Material and Methods

a) Data source

We retrospectively reviewed the pathology reports from successive incident BC cases reported, between 2012 and 2014, to PROYCAM2012 (www.cancerdemama2012.org.ar) a consortium (still in force) created for the study of BC in Argentina [10]. The PROYCAM2012 recruited a total of 1832 (stage I to IV) BC until the end of the period under study. From the total of cases reported a subset of 706 (38,5%) *"ER (+) / HER2 (-) / lymph node-negative"* BC, was identified and analyzed.

b) Surrogate parameters

An online search and selection of published scientific research on the same thematic from 2010 onwards, was carried out[11-20]. The presence of the SP shared by the different studies selected was analyzed in our series, namely: age, tumor size, histology, grade, Estrogen/Progesterone receptor, Her2 / neu status and Ki-67.

c) Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards, the National Law 25326 of Habeas Data Personal Data Protection and the National Patient Rights Act 26529. For retrospective studies (applies to our study): "for this type of study formal consent is not required''.

III. Results

a) Substitute parameters in selected publications

The selected 10 publications were analyzed and the SP used in them identified as shown in table 1.

Table 1: Publications on surrogate parameters published and selected. Characteristics of the selected series.

Reference	Breast cancer cases (n, %) ER(+; HER2 (-);lymph node-negative/Total	Notification period (years). Country	Clinical and pathologic markers required as SP
Auerbach J et al., 2010 [11]	138 cases with available Oncotype DX recurrence scores	USA	Tumor size, patient age, laterality, ER receptor, PR receptor results and HER2/neu result
Dellapasqua S et al. 2012 [12]	378/1063 (35,5%)	1990-1999 Australia, Canada, Hungary, Italy, New Zealand, Slovenia, South Africa, Spain, Sweden, and Switzerland.	Age, Histotype, Tumor size, Grade, ER/PgR , Her2/neu status and Ki-67.
Rouanet R et al.,2013 [13]	714/1271 (56,1%)	1994-2004 France	HR and HER2 status.HER2-HR+; HER2-HR-; HER2+HR+; HER2+HR-
Turner B et al; 2015 [14]	299 cases with available Oncotype DX recurrence scores	2009-2013 USA	ER, PR, HER-2, and Ki-67, Nottingham score (NS) and tumor size.
Gage MM et al.2015 [15]	221ODX-tested ER(+)/HER2(-)/lymph node-negative	2006–2013 USA.	-Low grade and positive progesterone receptor tumors (LG+PR). -High grade or low estrogen receptor (ER) (ER < 20%) tumors (HG/ LER).
Özmen V et al., 2016 [16]	165 ODX-tested ER(+)/HER2(-) /lymph node-negative	Turkey	Age, LN Status, Grade, ER score ≤10%, PR score ≤20% and Ki67 score.
Harowicz MR et al., 2017 [17]	305ODX-tested ER (+) /HER2(-)/lymph node-negative	2000-2014 USA	Estrogen receptor status and progesterone receptor status along with different combinations of grade, proliferation indices (Ki-67, mitotic rate), HER2 status, and tumor size.
Farrugia DJ et al,2017 [17]	237/614 (38,5%)	2010-2014 USA	Magee Equation 3 test: ER, PR, HER2 status and Ki-67.
Hanna MG et al.2017 [19]	536 ODX-tested ER (+)/ lymph node-negative	2007-2013 USA	Size, ER, PR status, HER2neu, Nottingham and histomorphology.
Orucevic et al,2019.[20]	65,754 ODX-tested ER (+) /HER2 (-)/lymph node-negative	2010-2014USA	Age,tumour size, grade, PR status and histologic type.

b) Clinical-pathological characteristics

The subset of 706 (38,5%) "*ER (+) / HER2 (-) / lymph node-negative" cases* selected from a database of 1832 cases of BC (stages I-IV) showed the following clinic-pathological characteristics (Table 2). The main clinical characteristics that define this group are: predominant in menopausal women (72%), average age of 61 years, 3.2% bilaterally and a personal (30,3%) and/or family history (9,3%) of BC. Pathologically, the average size of the tumors is between 1.8 -2.0, cm according to the left and right side, with predominance of infiltrating ductal lesions (67, 7%) grade2 (46,7%).

c) Substitute parameters evaluated

The frequency of the presence, in the 706 cases of "ER (+) / HER2 (-) / negative lymph node" BC, of the selected SPs is shown in Table 3. Of the total of 8

parameters, 4 (50%) (Age, ER / PR and Her2 / neu) are present between 96 and 100% of cases.The next most frequently found SP were grade (94%) and size (88.5%). Finally, the least frequent were histology 77.5%) and Ki67 expression (61.5%).

d) Coincidence between substitute parameters

The percentages in which, in our series, each of the SPs required in the different nomograms is fulfilled and also according to the possibility of a complete application of all SP of each proposed nomogram are shown in table 4. From the total of 10 nomograms selected only in 1 [13] our series can, in the 99.6% of the cases, complete the required two SPs being them: HR (96, 6%) and the Her2 / neu (100%). In a second nomogram [15] at least 94% of our cases complete the three of the proposed SPs being these: Grade (94 %), ER (100%) and PR (99.6%). In a third nomogram [11] at least 88.5% of the cases complete the required six SPs being these: tumor size (88.5%), patient age (100%), laterality (100%), ER receptor (100%), PR receptor (99.6%) and HER2 / neu (100%). In a fourth nomogram [19] 77,5% of cases complete the required six SPs, being these: size (88,5%), ER (100%), PR status (99,6%), HER2neu (100%), Nottingham (94%) and histomorphology (77,5%). In a fifth nomogram [20] also a 77,5% of the cases complete the required five SPs: age (100%), tumor size (88.5%), grade (94), PR status (99,6) and histologic type (77,5).Finally, in the five remaining nomograms evaluated [12,14,16-18] the percentage of cases that could complete the required SPs only reached 61.5% of the cases in each of them because this was the percentage of cases in which the Ki67 status study was conducted to evaluate the rate of tumor proliferation.

IV. Discussion

BC in Argentina, as we reported earlier, has an epidemiological pattern and an incidence rate typical of a "western" and "developed" country [10] without major variations of both qualifiersin the BCover the last 40 years [21]We also report that, with the resources currently available, the BC can be staged properly, according to the latest version of the TNM, in 75% of cases [22]

That a subset of no more than 706 (38.5%) of "early" BC "*ER (+) / HER2 (-) / negative nodes*" come from a database of 1832 new cases of BC, (stages I-IV) recorded between 2012 and 2014, presents its logic. The highest incidence of the whole "early stages" BC in developed countries, due to a massive and continuous use of mammogram screening in these populations [23-25] entails a high frequency of "*ER (+) / HER2 (-) / negative nodes*" BC. On the contrary, in our population, although the mammography is known and applied, but not in a massive and systematic way the frequency of this kind of BC *("ER (+) / HER2 (-) / negative nodes")* is related to a lowest diagnosis of the whole types of "early stages BC" [10,22].

Genomic platform tests are now considered "standard of care" to maintain treatment decision-making for patients "*ER (+) / HER2 (-) / negative lymph node*" BC. Previous analyses of genomic platforms testing have assessed hypothetical cohorts under ideal conditions and concluded that testing had low costs relative to its benefits; the application of gene panels in clinical practice avoids overtreatment, with its possible adverse effects, in the short term and toxic in the longer term [26-28] as well as reducing treatment cost [29-31]

MIC countries, such as Argentina, where gross national income per capita is between US$9,950 and $12,055 per year [32] are mainly characterized by fragmented and poorly coordinated medical care, moderate or high levels of poverty and disparities to access a basic standard of care not only for cancer but also for other complex diseases beyond of being covered by law. Patients in the public environment cannot pay for targeted therapy, so there are currently no hospital laboratories offering genomic platforms.

OncotypeDx® is expensive [the current estimated cost is U$4000 [9]. The cost of the study is the main reason for the almost no realization in the past (2012-13) and nowadays in the MIC countries such as Argentina. None of the health sub-sectors recognizes this study (not included in the oncological diagnosis and treatment protocols accepted by law in our country) for which they do not reimburse their cost. The few cases performed were done privately, paid by the patients and performed abroad the country. For all the mentioned the current tendency, encouraged by research groups, is to use clinic pathologic variables for prediction of low-risk or high-risk OncotypeDx® Recurrence Score (ODXRS) using nomograms models.

Quality prediction models depends on the amount and quality of data derived. In some aspects of the diagnosis of BC our country performs better than expected due to its economic development level. For example, immunohistochemistry (IHC) for HR and Her2 / neu is performed routinely in a high percentage of cases, in almost most laboratories for at least more than a decade. As such, IHC is an accessible and relatively inexpensive test and one that can be performed quite quickly. This is in sharp contrast to genomic test that are routinely performed abroad the country resulting in a prolonged time of realization and increased costs. Having, in our series, the results of HR and Her2 / neu in almost all cases, this allows us to apply 5/10 of the selected nomograms in which these required SPs are available between 88.5% and 99.6% of the cases. On the contrary, when it is necessary to know the proliferation index studied by the Ki67 expression as SP to fulfill a nomogram, this data is only present in 61.5% of the cases in the remaining 5 nomograms.

V. Conclusion

Despite the fact that MIC oncologists are theoretically well informed in the use of genomic platforms [8,33-36] they are far away from developed in the real-world a practice based in precision oncology; this kind of practice is a great challenge for themand frequently limited, when it is possible, to private practice. Our study, despite its limitations, provides some evidence for the design and orientation in our country of health policies and diagnostic interventions such as nomograms in the treatment of BC cancer, especially in early stages. These nomograms are useful tools to help to decide whether further OncotypeDx® testing is necessary and are excellent surrogates for patients for which OncotypeDx® testing is not affordable or even available. We demonstrate that, although there are gaps in the updated care process (for example: genetic profile) of BC, it is possible to use nomograms in our country through a comprehensive and complete collection and a careful subsequent analysis of the conventional parameters present in the diagnosis of BC. Special emphasis should be noted on the histopathological and immunohistochemical results, available almost routinely in our series, a fact that allows us to evaluate the RS and thus apply the corresponding therapy trying to achieve results similar to those that would be obtained with the use of GP.

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Seroprevalence of HIV, HBV and HCV Infectivity among Blood Donors in Sudan

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Abstarct- *Objective:* Numerous infectious diseases are spread by blood transfusion, particularly viral infections. The hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and other pathogenic organisms are transmitted through inappropriate screening of blood products (Nilima Sawke, et al., 2013).

These infected blood products are causing fatal, persistent and life frightening disorders (WHO, 2012). Aim of the current study was to estimate a statistical of the incidence of HBV, HCV, and HIV among blood donors in Sudan.

Results: In the blood supplies system in Sudan the total average of voluntary blood donors (VBD) was10.1%, whereas the family replacement donation (FBD) was 89.9% (3), the total incidence in blood donors was 3.2%.

Keywords: *human immunodeficiency virus, hepatitis b&c virus, seroprevalence, blood donors.*

GJMR-F Classification: *DDC Code: 615.39 LCC Code: RM171*

Strictly as per the compliance and regulations of:

Seroprevalence of HIV, HBV and HCV Infectivity among Blood Donors in Sudan

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Abstract- Objective: Numerous infectious diseases are spread by blood transfusion, particularly viral infections. The hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), and other pathogenic organisms are transmitted through inappropriate screening of blood products (Nilima Sawke, et al., 2013).

These infected blood products are causing fatal, persistent and life frightening disorders (WHO, 2012). Aim of the current study was to estimate a statistical of the incidence of HBV, HCV, and HIV among blood donors in Sudan.

Results: In the blood supplies system in Sudan the total average of voluntary blood donors (VBD) was10.1%, whereas the family replacement donation (FBD) was 89.9% (3), the total incidence in blood donors was 3.2%. The seroprevalence of hepatitis B was uppermost 1.6%, followed by HCV 1.6%, and seroprevalence of HIV was nil among family replacement donation (FBD) whereas the total incidence was nil among voluntary blood donors.

Keywords: human immunodeficiency virus, hepatitis b&c virus, seroprevalence, blood donors.

I. Introduction

Blood transfusion transfers of blood and its components such as red blood cells, platelets, and plasma from donor to the recipient (WHO, 2011). The donation of the blood saves the lives of millions of people universally, and it is essential to the helpfulness of the health system by supporting current transfusions worldwide (WHO, GDB, 2011).The following tests were mandatory performed in Sudan, at all blood centers at all levels following WHO, international organizations and regulatory bodies for blood safety: Hepatitis B surface antigen (HBsAg), anti-HIV1, HIV2, and an approved test for anti-HCV. All three tests have to be negative. (Roger Y. Dodd, 2001). All reactive results of blood donor's samples for infectious transmitted disease were should be retested in duplicate by the same assay. (WHO, 2012). All confirmed contaminated blood components units by TTI through repeatedly testing samples were not used for therapeutic applications and should normally be destroyed unless useful for non-therapeutic purposes or investigations. All blood donors have reactive testing results should be evaluated by a confirmatory tests and there should be a mechanism to inform blood donors the positive testing results. (WHO, Geneva, 2013). It is recommended that national testing algorithms for TTI shall be developed and used to enable consistent resolution of discordant indeterminate or unconfirmed results. (Jain C,. et al, 2011). In some African countries, in addition to TTI markers other serological tests were performed, for instance, anti-HBC testing may be performed on whole blood donations to further reduce the risk of exposure of recipients to HBV by contaminated blood or blood components to supply of safe blood products for transfusion, it's compulsory to introduce an advanced technology like a nucleic acid test (NAT) because of excellent clinical sensitivity and good specificity to detect infected blood components as it identified pathogens prior in the 'window period' than enzymes immune assay (Gerard C,, . et al , 1995). Even though, it has some margin in blood components with a lesser range of viremia, which can even free quantifiable by NAT (WHO, Geneva, 2012). Even with this margin, the grouping of both enzymes immune assay and NAT has notably condensed the hazard of pathogen spread during transfusion (11). Also, many scientific research data showed that the comparison between p24 antigen detection or conventional serological testing, it is estimated that the use of NAT reduces the detection time from 22 to 11 days for HIV; from 70 to 10 days for HCV, and from 60 to 30 days for HBV infection (H.Sheikholeslami,. et al, 2010). Additional testing for other agents or markers such as anti-HTLV I, II, anti-T.cruzi, or West Nile virus (WNV) may be taking into account the epidemiological situation in any given region or country or the frequency of donating blood (H.W.Reesink, 2000). In addition to testing TTI markers serologically, Nucleic Acid Testing (NAT) testing of blood donations for the virus genomes has been introduced in some countries to increase the chance of identifying infected blood donors. Testing for the presence of nucleic acid may be performed for viruses such as HCV, HBV, HIV, HTLV, and WNV and or Parvovirus B19, and the application of this technology may be extended to other transmissible microbes (M.M.E Nageh,. et al, 1994). Nucleic Acid Testing (NAT) require a sophisticated laboratory environment, special equipment, and specially trained laboratory personnel. To supply of safe blood products for transfusion, it's compulsory to introduce an advanced technology like a

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nucleic acid test (NAT) because of excellent clinical sensitivity and good specificity to detect infected blood components as it identified pathogens prior in the 'window period' than enzymes immune assay to supply of safe blood product for transfusion, it's compulsory to introduce an advanced technology like a nucleic acid test (NAT) because of excellent clinical sensitivity and good specificity to detect infected blood components as it identified pathogens prior in the 'window period' than enzymes immune assay (WHO, GDB,2011).Even though, it has some margin in blood components with a lesser range of viremia, which can even free quantifiable by NAT. Even with this margin, the grouping of both enzymes immune assay and NAT has notably condensed the hazard of pathogen spread during transfusion (WHO, Geneva, 2002).Even though, it has some margin in blood components with a lesser range of viremia, which can even free quantifiable by NAT(WHO, Geneva,2012). Even with this margin, the grouping of both enzymes immune assay and NAT reduced the hazard of pathogen spread through blood (Widman FK, 1985). Mainly because of an extraordinary risk of false-positive testing results due to contamination when NATs were performed to donor samples, therefore very stringent handling and logistics are mandatory. (WHO, 2008–2015). In contrast to testing of individual blood donor specimen's serologically for TTI markers, NAT testing can be performed following assembling various samples in mini-pools . (WHO, Geneva , 2014). However, this requires thoroughly validated laboratory systems including samples labeling, a validated strategy and pooling process, a validated algorithm to resolve pool results to individual donors. Hence, specific logistics systems shall be established at all laboratory and blood transfusion services process to collect suitably label samples. (WHO, Geneva, 2011). Contiguously tracing blood samples through the whole process from blood donation, through pooling samples, testing, and release of the testing results may present a particularly demanding challenge. A system should exist in the country or region for approval of laboratory testing systems, such as accredited laboratory or council. (WHO. GDB, 1998 – 1999).The blood transfusion department contains clinical methods and guidelines for blood screening before transfusion. If the screening procedure and other regulations are not followed well, there is a possibility to carry the risk of spreading blood transfusion contagious pathogens like HIV, HBV, HCV, Bacteria (syphilis), and others (WHO Geneva, 2012). Also, there is a 1% of chance of transfusion - related infection in each unit of blood even if the procedure is followed well (WHO, 2002) .Therefore, the risk of blood transfusion - transmitted infection today is minimized than constantly, the delivery of safe blood products stays behind inquiry to infection with accepted and until now to be predictable human pathogens (WHO, June 2011).

II. Main Text

In the present study were incorporated 500 blood donors. All the donors have been screened with a medical consultant before donation, who attended as voluntary and replacement in blood transfusion centers in all states from January 2014 to December 2015.

III. Sample Collection

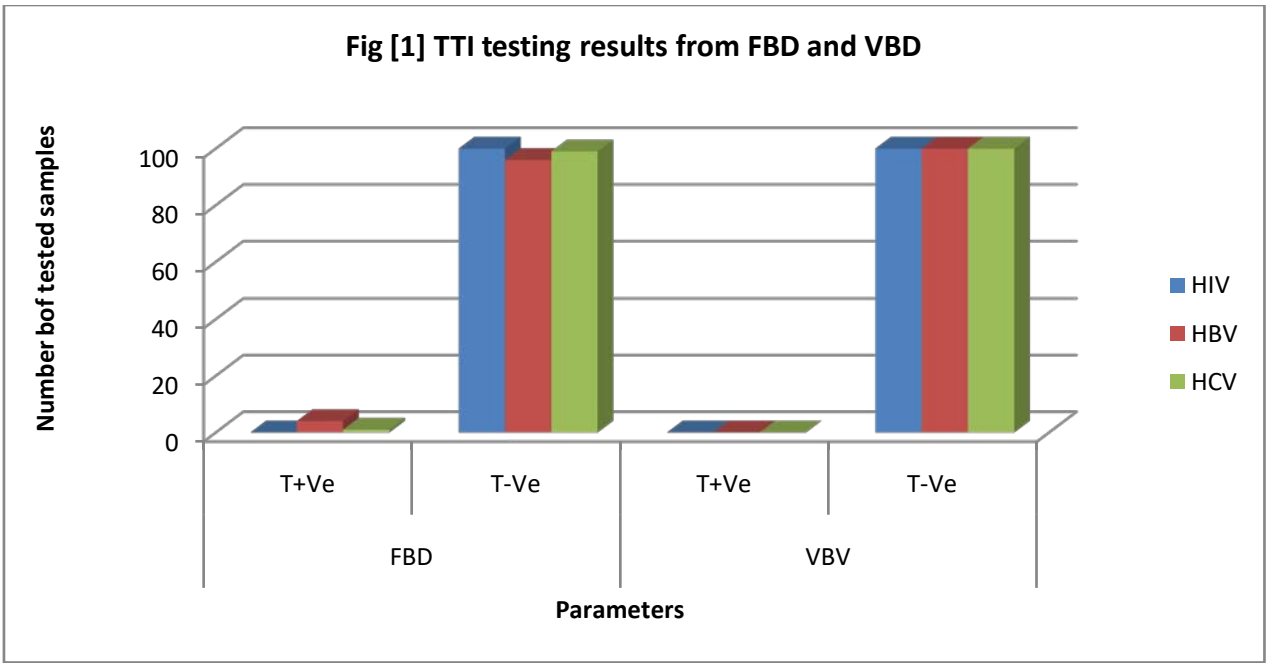
Five milliliters (5ml) of venous blood were collected from each donor after taking history and clinical examination using plain vacationer tubes during donated blood. All samples were allowed to clot formation and then were centrifuged at 3000 rpm for 10 minutes. All serum samples were separated into sterile 2ml cry vial containers and stored at -20°C until used. All serum samples were shipped and transported from the states to the national blood directorate in the Khartoum within the acceptable period, and temperature using cool boxes containing ice bags, temperature - controlled in each cool box using thermostats.

IV. Serology

All donors samples were screened by ELISA kits from fortress diagnostic Unit 2C Antrim technology park, Antrim BT41 IQS (United Kingdom): the least most negligible (cut off) was considered as per company guidelines for reporting positive and negative outcomes. Actual positive and negative samples were used subjectively as an outside run in each screening for our laboratory intention. The donated blood was discarded if the serum sample was positive for any infectivity. The statistical analysis was done using Microsoft ware office excel 2007.

V. Results

Two hundred samples were collected from blood donors for TTI markers (HIV, HBV, and HCV) testing. One hundred samples were collected from family replacement blood donors and another one hundred samples were collected from voluntary blood donors. All models were tested for HIV, HBV, and HCV using the ELISA technique. 4 models have positive results for HBV and one model had positive effects for HCV from the FBD group, in contrast all models from VBD were negative for TTI markers as presented in fig 1.



VI. Discussion

Overall average laboratory testing principle in the blood transfusion services in Sudan was found to be 54.18 % The world health organization (WHO) recommends that all donated blood be screened for HIV1&11, HBV, HCV, and syphilis (WHO, 2009) .The lowest incidence and prevalence of transfusion-transmissible infections is generally found among regular voluntary non-remunerated donors rather than first-time or occasional donors and family replacement blood donors (WHO, GDB reports, 2001–2002).The tested results of samples from family replacement blood donors (FRBD) show that there are 5.6% seropositive for HBV was found in family replacement blood donors while in contrast the number of representatives from voluntary blood donors (VBD) was found free of viral transfusion transmissible inactions such as HIV, HBV and HCV. The obtained results by this study was in high agreement With results done in the African countries, and the results shows that the prevalence of hepatitis B among blood donors in WHO African Region countries were 5-15% and the prevalence of hepatitis C among blood donors in Cameroon 8.8% , in Tanzania and Africa 5-15% (DR Neelam, June 2006).HIV causes significant health problems in sub -Saharan Africa where the prevalence of HIV among blood donors ranges between 2-20% similarly: the prevalence of HCV was 4.8% in Cameron,1.5% in Tanzania (WHO, 2013). And high in Egypt 13.6 % (Martin, H and Jeffery's, 2011). Hepatitis B prevalence was 2.1% and Hepatitis C, 13.6% among blood donors in Egypt (Egypt, 2016).

VII. Conclusion

Comparison of seroprevalence of (TTI) between family replacement and voluntary blood donors shows that there are 5.6% of family replacement blood donors has positive HBV results, which increase the risk of transfusion of infected blood in contrast all voluntary blood donors show that the testing result for (TTI) markers are negative which that the blood supply through voluntary blood donors is safest than family replacement blood donation system. The seroprevalence rate was low in voluntary blood donors compared to family replacement blood donors because regularly voluntary blood donors are safe and recommended by WHO.

VIII. Limitation of the Study

In this study, rapid and ELISA techniques were used to diagnose the infection. Although it has a specific accuracy, it is currently used to diagnose diseases. Also no previous studies data in Sudan were used for comparison.

List of abbreviations
Not applicable

Declarations

Ethical approval and consent to participant

Approval of conducting this study was obtained from the National public health laboratory, Khartoum, Sudan. Written consent was taken from each member of the study.

Approval of this study was obtained from the National public health laboratory, Khartoum, Sudan. Written consent was taken from each member of the study.

Consent for publication
Not applicable.

Availability of data and materials

The datasets generated during and/or analyzed in this study are not publicly available due to the National public health laboratory, Khartoum, Sudan, ethical policy to protect participant confidentiality.

Competing interest

The authors declare that they have no competing interests.

Funding

No funding was obtained for this study

Authors contributions

KM and AA contributed to literature search and manuscript writing. KM had the main idea of the study and contributed to manuscript writing; EW contributed to clinic work; AH contributed to statistical analysis. A supervised the study and critically reviewed the manuscript .All authors read and approved the final draft of the manuscript.

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Systematic Review of Clinical and Economic Evidence for Primary Open-Angle Glaucoma Therapy with Tafluprost vs Travoprost

By Shoyusuf F. Shodmanov, Shakhnoza Z. Umarova & Zoya R. Usmanova

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Abstarct- *Background:* According to WHO, the number of patients with glaucoma in the world ranges from 60.5 to 105 million people, and the number of such patients is also predicted to increase to 80 million. Out of 28 million blind people in the world almost one in five lost their sight due to glaucoma. The aim of this research is to conduct a systematic review of the clinical and economic evidence for the treatment of primary open-angle glaucoma with Tafluprost vs Travoprost.

Methods: PubMed interface, MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, NICE databases were used as main searching sources of this study.

Keywords: *primary open-angle glaucoma, systematic review, clinical efficacy, economic efficiency, PubMed.*

GJMR-F Classification: *DDC Code: 617.741 LCC Code: RE871*

Strictly as per the compliance and regulations of:

Systematic Review of Clinical and Economic Evidence for Primary Open-Angle Glaucoma Therapy with Tafluprost vs Travoprost

Shoyusuf F. Shodmanov [α], Shakhnoza Z. Umarova [σ] & Zoya R. Usmanova [ρ]

Abstract- Background: According to WHO, the number of patients with glaucoma in the world ranges from 60.5 to 105 million people, and the number of such patients is also predicted to increase to 80 million. Out of 28 million blind people in the world almost one in five lost their sight due to glaucoma. The aim of this research is to conduct a systematic review of the clinical and economic evidence for the treatment of primary open-angle glaucoma with Tafluprost vsTravoprost.

Methods: PubMed interface, MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, NICE databases were used as main searching sources of this study. Reviews of clinical studies have shown that using prostaglandin analogues has significant clinical efficacy in glaucoma. Travoprost has the most significant antihypertensive effect, Tafluprost shows slightly less or approximately the same hypotensive effect. Reviews of sources of economy about treatment of primary open-angle demonstrated that evidences supported efficiency of Tafluprost compared with Travoprost.

Keywords: primary open-angle glaucoma, systematic review, clinical efficacy, economic efficiency, PubMed.

I. Introduction

Glaucoma is one of the leading causes of blindness, it is a chronic disease that visual area is reduced permanently because of optic nerve damage.

According to the World Health Organization, total number of patients with glaucoma in the world ranges from 60.5 to 105 million people, and increasing this number is predicted to 80 million. There is significant an increase the role of glaucoma among primary disability causes, the nosological structure increased up to 20% in the last decade. According to the statistics of WHO, more than 28 million people in the world faced to the blindness, it means almost one in five has lost sight cause of glaucoma.

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In majority of patients (about 86%) suffer from glaucoma for a long time, the disease passes into a more severe stage. In this regard, this disease is not only purely medical issue, but also it is social problems.

The research questions were asked in discussions with healthcare providers, clinical professionals, and other healthcare stakeholders.

The aim of the study was to conduct a systematic review of the clinical and economic evidence for the therapy of primary open-angle glaucoma (POAG) with Tafluprost vsTravoprost.

II. Materials and Methods

A literature search was performed on PubMed interface and used for the MEDLINE database, in addition, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and NICE were used to search for relevant literature. As an input of medical librarians, search strategy was developed by using appropriate keywords and control variables. In order to obtain relevant information on the prevalence of glaucoma and other important evidence, we searched the gray literature on various health websites. The formulation of the PICO concept is very critical because it facilitates the therapeutic question and directly addresses the relevant issues, defining the key concepts that should be the focus of our economic analysis of health care.

The acronym PICO is presented in the following table 1 below:

Table 1: PICO formulation for literature search

Acronym	General definition	Acceptance of the model
P	Population (patients)	Patients over 40 with open-angle glaucoma
I	Intervention (Intervention - an alternative method of treatment (relatively new)	Tafluprost is a prostaglandin analogue eye drops used to prevent the progression of open-angle glaucoma by lowering intraocular pressure(IOP).
C	Comparator (Comparator - traditional treatment)	Travoprost is a prostaglandin analogue eye drops used to prevent the progression of open-angle glaucoma by lowering IOP.
O	Outcome of economic efficiency (The result is profitability)	Lowering IOP and delaying the progression of glaucoma

In order to evaluate clinical outcomes feedback was requested from several associations involved in glaucoma therapy in Tashkent city. We turned to an ophthalmologist, nurses who regularly diagnose glaucoma in patients. The role of the clinical expert was to critique our requests, provide information regarding the patient management algorithm, review the clinical review plan and medical technology assessment.

Economic literature search was conducted to cover studies conducted from inception to the date of the search. PubMed interface was used for the Medline database, and the Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and NICE were used to search relevant literature. By input from medical librarians, a search strategy was developed with relevant keywords and control variables, with an economic filter set. In order to obtain relevant information on the current prevalence of glaucoma and other important evidence, we conducted a gray literature search on various health websites.

Titles and abstracts of the papers were carefully reviewed, for those studies that should meet the eligibility criteria, we purchased articles with full content and completed further evaluation for eligibility.

a) Inclusion Criteria

– Full content publications in English;
– Studies have been carried out from the moment of creation to the present day;
– Studies comparing Tafluprost with Travoprost in patients with open-angle glaucoma;
– Profitability analysis;

b) Exclusion Criteria

– Reviews, polls, edited compositions, notifications, letters, case studies and articles;
– An economic evaluation of laser treatment of open-angle glaucoma and eye drops was carried out;

c) Outcomes of concern

– Quality-adjusted life years (QALY);
– Expenses;
– Additional costs or additional efficiency;
– Average cost utility ratios and costs from different points of view;

d) Data Extraction

The data was obtained under the following conditions:

– Source (for example: country, year of publication and title);
– Sample set and comparator;
– Intervention;
– Outcomes (costs, incremental economic effectiveness ratios, side-effects and well-being outcomes);

III. Results and Discussions

A clinical efficacy literature search identified 434 studies, including those obtained from database searches and additional sources. After removing duplicates and irrelevant studies assessed by title selection, 285 citations remained. Finally, only 2 articles meet the inclusion criteria. To report the studies, we found in systematic reviews, we developed the PRISMA Chart (Preferred Reporting Items for systematic reviews and meta-analyses) (Figure 1).

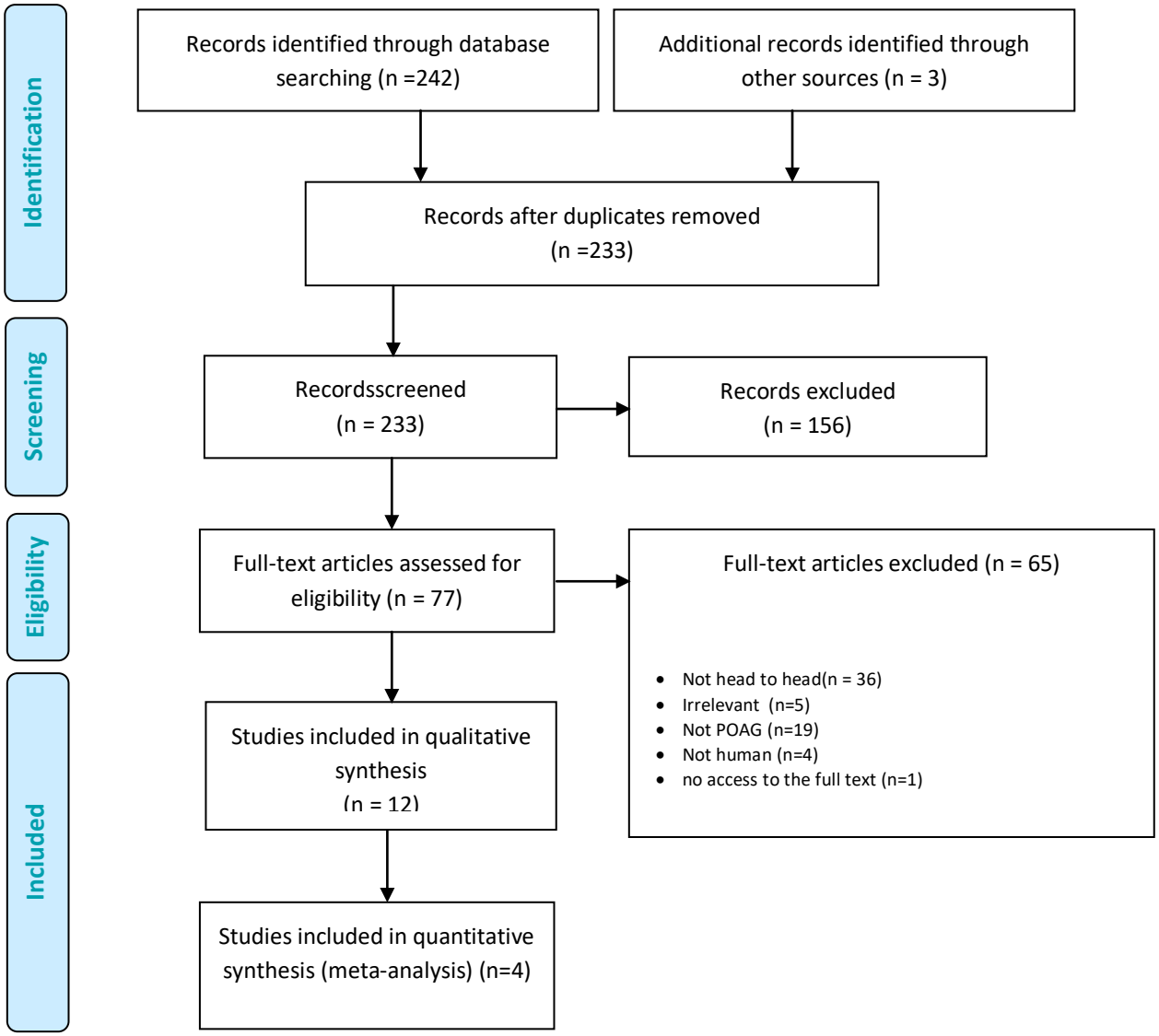

Fig. 1: PRISMA diagram - results of clinical effectiveness

Literature search about economic effectiveness identified 50 studies, including those obtained from database searches and additional sources after deduplication. After eliminating duplicates and irrelevant studies assessed by title checking 10 citations remained for full-text citation. Finally, after reviewing full-text articles, one study was selected that met the inclusion criteria. Figure 2 is a PRISMA chart for the results of an economic search strategy.

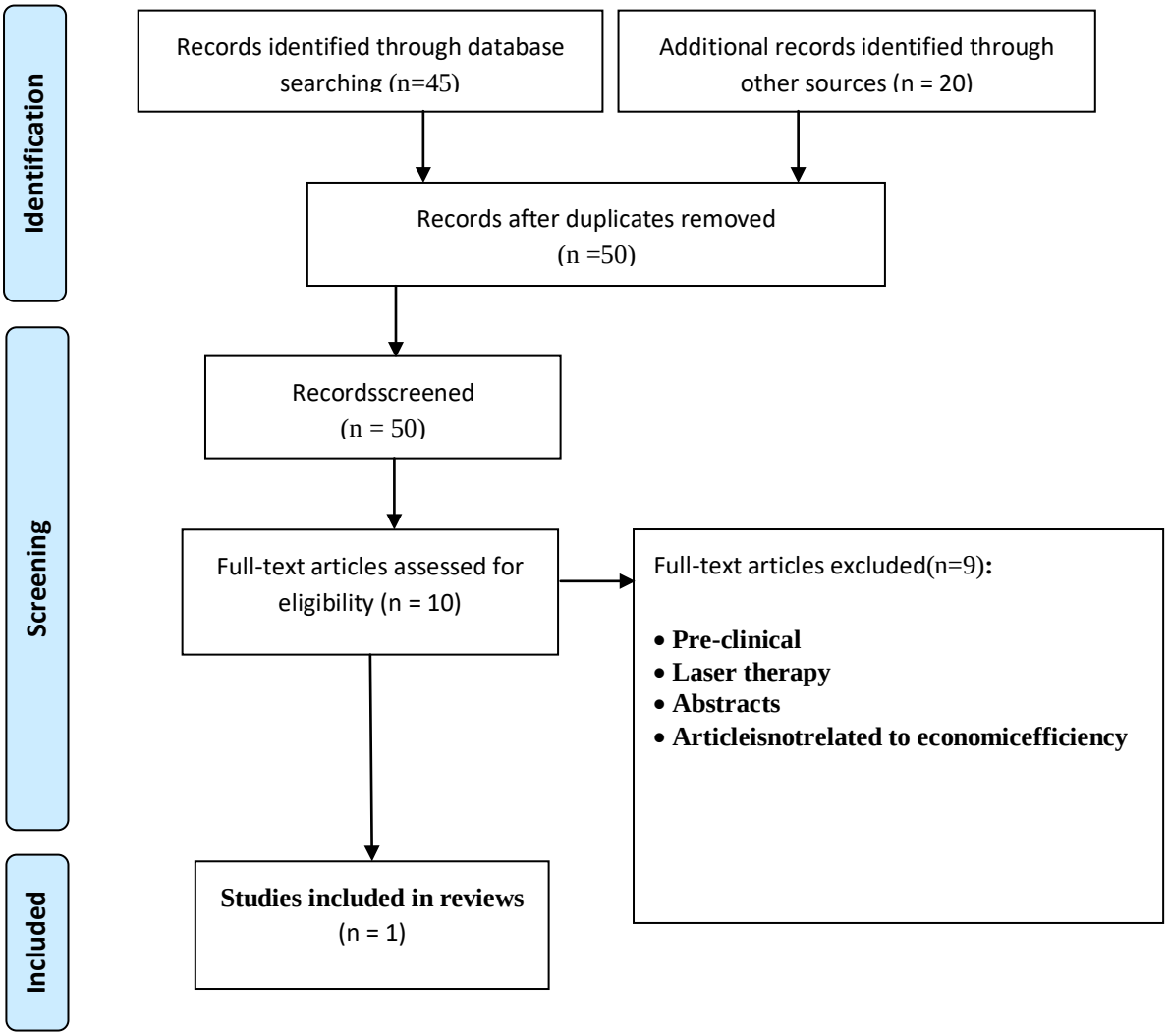

Fig. 2: PRISMA chart - economic search results

Two single arm cohort studies were selected because they met the inclusion criteria. The first study examined IOP adjustment and visual area imperfection movement over a 3-year period while adjusting Travoprost eye drops monotherapy in patients with POAG [2]. A second cohort study examined the effects of Tafluprost eye drops on IOP changes, visual area progression, safety, and side effects in patients with POAG [3].

We were unable to find studies examining mortality due to glaucoma. In addition, there is no any research conducted to investigate patients with advanced and end-stage glaucoma treated with our interventions.

Table 2: Research, patients and intervention features

Authors, year	Country	Purpose of the study	Randomized groups	Basic mean deviation(MD)	Patients(men /women)	Average age Years (SD)	Result
Inoue, Iwasa, Wakakura and Tomita, 2012	Japan	To study the efficiency of long-term Travoprost monotherapy without (BAC) on IOP and visual area efficiency.	Mean IOP at switch on 16.8±2.6 mmHg.	-5.4±4.7dB	76:33/43	54.8±13.9	Decreased intraocular pressure (IOP)

Inoue, Tanaka and Tomita, 2013	Japan	Calculate the effect of Tafluprost treatment for 3 years on visual area and intraocular pressure.	Initial IOP 15.7±2.2 mmHg.	-6.75±5.5dB	55:32/23	56.1±11.2	Decreased intraocular pressure (IOP)

Table 3: Decrease in IOP and progression of the visual area

Author s, year	Level of IOP reduction	Progression field of view
Inoue, Iwasa, Wakakura and Tomita (2012)	When treated with Travoprost	2.8%–13.9%
	14.1±2.4 mmHg (Before treatment: 16.8±2.6 mmHg)	
Innoue, Tanaka and Tomita (2013)	When treated with Tafluprost	10.3%–13.8%
	12.8±2.8 mmHg Art. (before therapy: 15.7±2.2 mmHg)	

Overall, both Travoprost and Tafluprost were found to be effective interventions for lowering intraocular pressure in patients with POAG. Innoueetal. (2012) in their randomized control trial showed the effectiveness of Travoprosteye drops in reducing IOP, which in the long term was 16.1-36.6%, while the reduction in IOP by 21.9±14.0% with the introduction of Tafluprost in patients with POAG. There have been no reports of visual area impairment due to long-term use of Tafluprost and Travoprost eye drops. Significant differences in average and standard deviation of the model were not observed before and after treatment with follow-up 3 years in both analyzed studies. It can be seen that when comparing the efficacy of the two interventions, Travoprost had a slightly higher efficacy in lowering IOP than Tafluprost among patients with POAG [2, 3].

A systematic review identified one study evaluating the economic effectiveness of Travoprost and Tafluprost in the treatment of pre-intervention open-angle glaucoma in previously untreated 65-year-old patients. Intraocular pressure, visual area characteristics, and patient value of drugs are derived from published retrospective clinical reviews and randomized control trials with a follow-up period of 20 years. Average wholesale prices were taken to calculate drug price data for both social and direct eye care costs. As recommended by the Health and Medicine Cost Efficiency Panel, all costs and benefits assessed by the patient were discounted annually at a rate of 3%.

Table 4: Economic indicators of Tafluprost and Travoprost

Author, year	Study type	Population	Intervention/ Control (Comparator)	Results			Research period
				health outcomes	Expenses	Economic Efficiency	
Brown 2019	Cost-utility analysis	Patients over 40 years of age	Tafluprost	1.99 QALY (17.9%)	$1,925 cost/year	ICER is missing	3 months a
			Travoprost	I.92 QALY (17.2%)	$944 cost/year		

QALY- Quality Adjusted Life Years (Additional Years of Quality Life)

The results showed that each anti-intervention drug has demonstrated clinical and economic effectiveness. Travoprost scored 1.92 QALYs (15% improvement in quality of life) over a 20-year period, and Tafluprost scored a slightly higher score of 1.99 QALYs (14.2% improvement in quality of life). The median ophthalmic costs for Tafluprost and Travoprost were 38,607 USD and 23,569 USD respectively. The authors concluded that Tafluprost is clinically effective for the treatment of patients with open-angle glaucoma, but is not cost effective compared to Travoprost. Moreover, sensitivity analyzes were also performed with upper and lower IOP limits at 95% confidence intervals. Tafluprost remained with the best QALY scores among other interventions.

A study by Brown et al. (2019) showed that even though Travoprost is cheaper than Tafluprost, Tafluprost saves more social costs due to greater IOP lowering effect and more years of good vision. The main limitation of the study conducted by Brown is the lack of calculation of comparative economic efficiency (Incremental Cost Effectiveness Ratio, ICER) [4].

So, according to Brown et al. (2019), there is no calculation of the ICER indicator. In this regard, we calculated the ICER indicator and obtained:

ICER=Cost(1)-Cost(2)/Ef(1)-Ef(2)=1925-944/1.99-1.92 = 14014 cost/QALY

IV. Conclusions

1. A review of clinical studies showed that the use of drugs from the group of prostaglandin analogues has a pronounced clinical efficacy. Travoprost has the most significant antihypertensive effect, Tafluprost show slightly less or approximately the same hypotensive activity.
2. Side effects from prescribing drugs - prostaglandin analogues do not have a significant impact on the quality of life of patients and their attitude to treatment. Tafluprost has the least side effects compared to Travoprost. The results of the review show that there is no significant statistical difference in the cost and effectiveness of treating POAG with both drugs.
3. A review of the economic literature on the treatment of primary open-angle glaucoma showed a paucity of economic evidence supporting the efficacy of treating POAG with Tafluprost compared with Travoprost.

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Introduction

FMRC/AMRC is the most prestigious membership of Global Journals accredited by Open Association of Research Society, U.S.A (OARS). The credentials of Fellow and Associate designations signify that the researcher has gained the knowledge of the fundamental and high-level concepts, and is a subject matter expert, proficient in an expertise course covering the professional code of conduct, and follows recognized standards of practice. The credentials are designated only to the researchers, scientists, and professionals that have been selected by a rigorous process by our Editorial Board and Management Board.

Associates of FMRC/AMRC are scientists and researchers from around the world are working on projects/researches that have huge potentials. Members support Global Journals' mission to advance technology for humanity and the profession.

FMRC

Fellow of Medical Research Council

FELLOW OF MEDICAL RESEARCH COUNCIL is the most prestigious membership of Global Journals. It is an award and membership granted to individuals that the Open Association of Research Society judges to have made a 'substantial contribution to the improvement of computer science, technology, and electronics engineering.

The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Fellows are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Fellow Members.

To the institution

Get letter of appreciation

Global Journals sends a letter of appreciation of author to the Dean or CEO of the University or Company of which author is a part, signed by editor in chief or chief author.

Exclusive Network

Get access to a closed network

A FMRC member gets access to a closed network of Tier 1 researchers and scientists with direct communication channel through our website. Fellows can reach out to other members or researchers directly. They should also be open to reaching out by other.

Career | Credibility | Exclusive | Reputation

Certificate

Certificate, LoR and Laser-Momento

Fellows receive a printed copy of a certificate signed by our Chief Author that may be used for academic purposes and a personal recommendation letter to the dean of member's university.

Career | Credibility | Exclusive | Reputation

Designation

Get honored title of membership

Fellows can use the honored title of membership. The “FMRC” is an honored title which is accorded to a person’s name viz. Dr. John E. Hall, Ph.D., FMRC or William Walldroff, M.S., FMRC.

Career | Credibility | Exclusive | Reputation

Recognition on the Platform

Better visibility and citation

All the Fellow members of FMRC get a badge of "Leading Member of Global Journals" on the Research Community that distinguishes them from others. Additionally, the profile is also partially maintained by our team for better visibility and citation. All fellows get a dedicated page on the website with their biography.

Career | Credibility | Reputation

Future Work

Get discounts on the future publications

Fellows receive discounts on the future publications with Global Journals up to 60%. Through our recommendation programs, members also receive discounts on publications made with OARS affiliated organizations.

Career | Financial

GJ Internal Account

Unlimited forward of Emails

Fellows get secure and fast GJ work emails with unlimited storage of emails that they may use them as their primary email. For example,
john [AT] globaljournals [DOT] org.

Career | Credibility | Reputation

Premium Tools

Access to all the premium tools

To take future researches to the zenith, fellows receive access to all the premium tools that Global Journals have to offer along with the partnership with some of the best marketing leading tools out there.

Financial

Conferences & Events

Organize seminar/conference

Fellows are authorized to organize symposium/seminar/conference on behalf of Global Journal Incorporation (USA). They can also participate in the same organized by another institution as representative of Global Journal. In both the cases, it is mandatory for him to discuss with us and obtain our consent. Additionally, they get free research conferences (and others) alerts.

Career | Credibility | Financial

Early Invitations

Early invitations to all the symposiums, seminars, conferences

All fellows receive the early invitations to all the symposiums, seminars, conferences and webinars hosted by Global Journals in their subject.

Exclusive

Publishing Articles & Books

Earn 60% of sales proceeds

Fellows can publish articles (limited) without any fees. Also, they can earn up to 70% of sales proceeds from the sale of reference/review books/literature/publishing of research paper. The FMRC member can decide its price and we can help in making the right decision.

Exclusive | Financial

Reviewers

Get a remuneration of 15% of author fees

Fellow members are eligible to join as a paid peer reviewer at Global Journals Incorporation (USA) and can get a remuneration of 15% of author fees, taken from the author of a respective paper.

Financial

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Become a member of the Editorial Board

Fellows and Associates may join as a member of the Editorial Board of Global Journals Incorporation (USA) after successful completion of three years as Fellow and as Peer Reviewer.

Career | Credibility | Exclusive | Reputation

And Much More

Get access to scientific museums and observatories across the globe

All members get access to 5 selected scientific museums and observatories across the globe. All researches published with Global Journals will be kept under deep archival facilities across regions for future protections and disaster recovery. They get 10 GB free secure cloud access for storing research files.

ASSOCIATE OF MEDICAL RESEARCH COUNCIL

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The primary objective is to recognize the leaders in research and scientific fields of the current era with a global perspective and to create a channel between them and other researchers for better exposure and knowledge sharing. Members are most eminent scientists, engineers, and technologists from all across the world. Associate membership can later be promoted to Fellow Membership. Associates are elected for life through a peer review process on the basis of excellence in the respective domain. There is no limit on the number of new nominations made in any year. Each year, the Open Association of Research Society elect up to 12 new Associate Members.

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Earn 60% of sales proceeds

Associates can publish articles (limited) without any fees. Also, they can earn up to 30-40% of sales proceeds from the sale of reference/review books/literature/publishing of research paper

Exclusive | Financial

Reviewers

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Financial

And Much More

Get access to scientific museums and observatories across the globe

All members get access to 2 selected scientific museums and observatories across the globe. All researches published with Global Journals will be kept under deep archival facilities across regions for future protections and disaster recovery. They get 5 GB free secure cloud access for storing research files.

Associate	Fellow	Research Group	Basic
$4800 **lifetime designation**	$6800 **lifetime designation**	$12500.00 **organizational**	APC **per article**
Certificate, LoR and Momento **2** discounted publishing/year **Gradation** of Research **10** research contacts/day **1 GB** Cloud Storage **GJ** Community Access	**Certificate,** LoR and Momento **Unlimited** discounted publishing/year **Gradation** of Research **Unlimited** research contacts/day **5 GB** Cloud Storage **Online Presense** Assistance **GJ** Community Access	**Certificates,** LoRs and Momentos **Unlimited** free publishing/year **Gradation** of Research **Unlimited** research contacts/day **Unlimited** Cloud Storage **Online Presense** Assistance **GJ** Community Access	**GJ** Community Access

Preferred Author Guidelines

We accept the manuscript submissions in any standard (generic) format.

We typeset manuscripts using advanced typesetting tools like Adobe In Design, CorelDraw, TeXnicCenter, and TeXStudio. We usually recommend authors submit their research using any standard format they are comfortable with, and let Global Journals do the rest.

Alternatively, you can download our basic template from https://globaljournals.org/Template

Authors should submit their complete paper/article, including text illustrations, graphics, conclusions, artwork, and tables. Authors who are not able to submit manuscript using the form above can email the manuscript department at submit@globaljournals.org or get in touch with chiefeditor@globaljournals.org if they wish to send the abstract before submission.

Before and during Submission

Authors must ensure the information provided during the submission of a paper is authentic. Please go through the following checklist before submitting:

1. Authors must go through the complete author guideline and understand and *agree to Global Journals' ethics and code of conduct,* along with author responsibilities.
2. Authors must accept the privacy policy, terms, and conditions of Global Journals.
3. Ensure corresponding author's email address and postal address are accurate and reachable.
4. Manuscript to be submitted must include keywords, an abstract, a paper title, co-author(s') names and details (email address, name, phone number, and institution), figures and illustrations in vector format including appropriate captions, tables, including titles and footnotes, a conclusion, results, acknowledgments and references.
5. Authors should submit paper in a ZIP archive if any supplementary files are required along with the paper.
6. Proper permissions must be acquired for the use of any copyrighted material.
7. Manuscript submitted *must not have been submitted or published elsewhere* and all authors must be aware of the submission.

Declaration of Conflicts of Interest

It is required for authors to declare all financial, institutional, and personal relationships with other individuals and organizations that could influence (bias) their research.

Policy on Plagiarism

Plagiarism is not acceptable in Global Journals submissions at all.

Plagiarized content will not be considered for publication. We reserve the right to inform authors' institutions about plagiarism detected either before or after publication. If plagiarism is identified, we will follow COPE guidelines:

Authors are solely responsible for all the plagiarism that is found. The author must not fabricate, falsify or plagiarize existing research data. The following, if copied, will be considered plagiarism:

- Words (language)
- Ideas
- Findings
- Writings
- Diagrams
- Graphs
- Illustrations
- Lectures

- Printed material
- Graphic representations
- Computer programs
- Electronic material
- Any other original work

Authorship Policies

Global Journals follows the definition of authorship set up by the Open Association of Research Society, USA. According to its guidelines, authorship criteria must be based on:

1. Substantial contributions to the conception and acquisition of data, analysis, and interpretation of findings.
2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

Changes in Authorship

The corresponding author should mention the name and complete details of all co-authors during submission and in manuscript. We support addition, rearrangement, manipulation, and deletions in authors list till the early view publication of the journal. We expect that corresponding author will notify all co-authors of submission. We follow COPE guidelines for changes in authorship.

Copyright

During submission of the manuscript, the author is confirming an exclusive license agreement with Global Journals which gives Global Journals the authority to reproduce, reuse, and republish authors' research. We also believe in flexible copyright terms where copyright may remain with authors/employers/institutions as well. Contact your editor after acceptance to choose your copyright policy. You may follow this form for copyright transfers.

Appealing Decisions

Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

Declaration of funding sources

Global Journals is in partnership with various universities, laboratories, and other institutions worldwide in the research domain. Authors are requested to disclose their source of funding during every stage of their research, such as making analysis, performing laboratory operations, computing data, and using institutional resources, from writing an article to its submission. This will also help authors to get reimbursements by requesting an open access publication letter from Global Journals and submitting to the respective funding source.

Preparing your Manuscript

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.

Format Structure

It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

Title

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

Tips for writing a good quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.

Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

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	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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