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Management of Covid-19

A Study of Pediatric Poisonings

Highlights

Diabetes Mellitus Type 2

Lebanese Population in Bekaa Valley

Discovering Thoughts, Inventing Future

VOLUME 20 ISSUE 8 VERSION 1.0

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The use of Antidepressants among Lebanese Population in Bekaa Valley: Knowledge and Perspective

By Mohamed Hendaus, Mahmoud Moussa, Samar Younes, Dalal Hammoudi, Mohamed Rahal & Nisreen Mourad
Lebanese International University

Abstract- *Objectives:* This study aims to evaluate the use of antidepressants among the Lebanese population, focusing on factors that may contribute to their use, and to assess the knowledge of antidepressants in patients recruited for this study.

Methods: This observational study was conducted over a period of one month in the Bekaa region. After taking their approval, a total number of 283Lebanese residents were interviewed and asked about the use, perspective and knowledge of antidepressants. A questionnaire was filled by pharmacists to gather information from the residents.

Results: Results showed that 61.1% of respondents took antidepressants in the 3 past months, 30.4% were university students ($p = 0.048$), among of which32.5% reported using social media many times per day. 83.2% of medications were prescribed by a physician, while 9.8% were prescribed by a pharmacist, among of which 48% didn't interrupt the treatment course on their own ($p=0.001$). Furthermore, 54.77% of respondents got scores of more than 4/6 when asked about their knowledge concerning antidepressants.

Keywords: *antidepressants, depression, Lebanese, community pharmacy, Lebanon.*

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The use of Antidepressants among Lebanese Population in Bekaa Valley: Knowledge and Perspective

Mohamed Hendaus [α], Mahmoud Moussa [σ], Samar Younes [ρ], Dalal Hammoudi [ω], Mohamed Rahal [¥] & Nisreen Mourad [§]

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Conclusion: High percentage of interviewed population were using or had already used antidepressants; social media and educational level may have significant relation. Despite the counseling provided mainly by physicians, a large percentage of users still had doubts about the use of antidepressants, especially in relation to compliance and interruption of therapy.

Keywords: antidepressants, depression, Lebanese, community pharmacy, Lebanon.

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I. Introduction

Major depressive disorder is a common and serious medical illness characterized by a period of at least two weeks when a person experienced a depressed mood or loss of interest or pleasure in daily activities, and had a majority of specified symptoms, such as problems with sleep, eating, energy, concentration, or self-worth. Depression is a common and serious medical condition. It can be minor causing minor functional impairment or major leading to suicide [1], causing an impact on one's social and economic status [2]. The treatment of depression varies in duration and type, usually a minimum of six months is needed for treatment. It consists of psychological interventions such as cognitive behavioral therapy (CBT) and interpersonal therapy [2], or psychotherapy using medications such as tricyclic antidepressants (TCAs) and selective serotonin reuptake inhibitors (SSRIs) [3]. In some instances, a combination of psychological interventions and psychotherapy is adopted [4]. In Lebanon drugs are easily accessible and some rely on family and friends for medical advice and thus are prone to maltreatment and misuse of their medication. The purpose of this study is to evaluate the use of antidepressants among a sample of the Lebanese population, focusing on factors that may contribute to their use, and to assess the knowledge of antidepressants in patients recruited for this study.

II. Methods

The study was conducted in pharmacies located in Bekaa region- Lebanon. Ethical approval was obtained from the School of Pharmacy at the Lebanese International University. The study was carried within one month (June 2019). This observational cross- sectional study was conducted using a questionnaire prepared by the research team of the Lebanese International University School of Pharmacy. The questionnaire was divided into 3 main sets: the first set included participants' socioeconomic information, while the second set included questions about the use and perspective towards antidepressants and instructions

provided. The third set included an assessment about their knowledge of antidepressants through a graded scale out of 6, presenting 6 questions that reflect facts about the course of treatment and medications. To ensure validity, the questionnaire was evaluated by academics possessing previous experience in clinical studies. Survey random sampling was used; the researcher approached random residents entering pharmacies in the Bekaa area. Responders were offered to participate in the study, and an information leaflet was provided upon acceptance. Verbal consent was taken from each participant before completing the survey.

Fourth year pharmacy student interns approached residents randomly in community pharmacies during their internship. To negate any bias, the pharmacy students didn't introduce themselves as pharmacy interns that can make decisions or changes. The community pharmacist was present upon interviewing. Participants provided informed oral consent after agreement. Collected data were gathered and then returned for data entry and analysis. A quantitative approach was used in this study; collected data were encoded and then analyzed using Statistical Package for the Social Sciences (SPSS, version 22). Descriptive analysis was carried out, and Chi square test was used to identify significant correlations between different variables, with significance defined as p value < 0.05.

III. Results

During the four-week study, 283participants completed the questionnaire. Average age was 36.9 ± 13.5 (range between 18 and85 years), 36.7% were less than 30 years old, and 61.5% were females. The participants' socioeconomic data are presented in [Table 1].Among participants, 61.1% took an antidepressant in the past 4 weeks (61.27% were females and 38.7% were males), and among them, 79.1% received instructions and enough counseling about the medication use. 54.1% of the participants were university students or having a university degree, and 35% were married.

The majority of prescribers were physicians, accounting for 83.2%, while pharmacists account for only 9.8%; the rest of prescribers were relatives and friends 7% [Figure 1]. Among patients who received instructions from physicians, 19.7% stated that they interrupted the treatment without referring to their physician, while 43.4% didn't ($p = 0.026$). Almost half of the patients believed that the instructions provided were beneficial (54.4%), and among them, 39.2% didn't change the treatment course without referral.

A high percentage of patients who took antidepressants had doubts about the treatment (54.8%), while 44.2% didn't ($p<0.001$). A high percentage of patients (48.0%) reported no interruption of the treatment course on their own, while 23.7% did ($p<0.001$).

There was a significant association between patients who received antidepressants and used social media, where 32.5%of patients reported using social media many times per day ($p =0.034$), 10.6% reported using it once per day, and 14.5% rarely used it. Another significant association was noted in patients who received antidepressants and their educational level, where 30.4% of them had at least a university degree, 13.8% had a secondary degree, 10.2% had a primary degree, and 6.7% were illiterate ($p = 0.048$). Knowledge regarding antidepressants use was also assessed: only 37 patients (13.0%) got a score of 6/6, 61 patients (21.5%) got a score of 5/6, and 57 (20.1%) got a score of 4/6. The rest of patients got scores of 3/6 and below [Table 2].

IV. Discussion

The results shown in this study were similar to other studies in terms of gender difference receiving antidepressant. Our study reveals that 61.27% of patients receiving antidepressants were females, and this was consistent with the American Psychological Association statistics, which revealed that women are more likely than men to take antidepressants in every age group (16.5% for women compared with 8.6% for men) [15].

The patient's cultural background and own beliefs are always thought to be an unprecedented factor in the treatment plan, and hence the overall outcome [5]. The World Organization of Family Doctors (WONCA) culturally sensitive depression guideline notes that 'The primary care physician needs to understand the cultural, religious and gender paradigm that the individual brings to the consultation in order to increase the chance of establishing a therapeutic alliance that reduces the personal distance between physician and patient. This will maximize the chance of therapeutic success" [7,8]. Many studies revealed that physicians must be aware of the cultural differences especially in countries with diverse ethnic and religious groups, which may affect the treatment plan, in order to minimize any therapeutic failure [6,8]. In Lebanon, the use of medications without prior prescription is customary. Our study showed that the majority of patients in the Lebanese community who are currently on antidepressants referred to physicians and had received instructions on how to use the medication, which is consistent with the fact that drugs acting on the psychology and mental health are taken with caution, where discussion between patients and physicians may help clarify mutual expectations and opinions [16]. Although depression and antidepressants in our community are often thought to be taboo and patients might not adhere to the dosage regimen due to the fear side effects, our findings show the contrary [9].

The majority of antidepressant prescriptions in this study were prescribed by physicians, while pharmacists account to a minimal percentage. This implies that patients prefer to be examined by a specialized physician when it comes to their mental health, unlike other conditions that in their opinion seem to be minor and need no intervention by physicians. This study also showed that healthcare professionals play a critical role in influencing patients to adhere to their treatment regimen, where the majority of antidepressants users didn't interrupt the treatment on their own and stating that the instructions were very beneficial. This reveals the trust the patients have in their treatment plan and in their health team, particularly pharmacists in assuring and reinforcing adherence [8,10].

Online social networking has changed the way people communicate and interact. However, it remains unclear, whether some of these changes can affect behaviors and mental health or not [11]. Many publications have shown that online social networking can be classified as a potential addiction disorder [12,13,14]. One observational study reported that sudden cessation of online social networking may cause signs and symptoms that at least resemble the ones seen during drug/alcohol/nicotine abstinence syndrome [11]. Our observational findings suggest that the use of antidepressants may be linked to the use of social media, and may be consistent with the previous studies in terms of relation between social networking and mental disorders.

This study has certain limitations in which was conducted for patients or customers presenting at community pharmacies located at Bekaa Valley, which is one of the Lebanese governorates, and thus this population may not be not reflect the whole Lebanese community perspective. Also, it is a descriptive cross-sectional study, and thus less significant correlations may be drawn. A large-scale nationwide study is needed to assess the whole population perspectives.

V. Conclusion

In total, 61% of the interviewed population were using or had already used antidepressants; social media and educational level may have significant relation. Prescribers were mostly physicians, with most of the antidepressant users believed that the instruction provided were beneficial. Despite the counseling provided, a large percentage of users still had doubts about the use of antidepressants, especially in relation to compliance and interruption of therapy. Future actions with a view to improve the knowledge and perspective seem to be particularly needed and relevant.

Conflicts of interest

The authors have no conflicts of interest to disclose

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None

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Table 1: Participants' socioeconomic data

Demographic	N=283	Percentage
Gender		
Female	174	61.5%
Male	109	38.5%
Marital status		
Married	99	35%
Single	146	31.6%
Widowed/divorced/	21	7.4%
In a relationship	17	6%
Education		
Illiterate	28	9.9%
Primary school	39	13.8%
Secondary school	63	22.3%
University and above	153	54.1%
Occupation		
Students	49	17.3%
Healthcare	34	12%
Nonhealthcare	99	35%
Unemployed	92	32.5%
retired	5	3.2%
Home		
Private	221	78.1%
Shared	17	6%
Rented	45	15.9%
Alcohol		
Yes	28	9.9%
No	255	90.1%
Nationality		
Lebanese	243	85.8
Non-Lebanese	20	7.1
Syrian Refugee	20	7.1
Smoker		
Yes	143	50.5
No	140	49.5
Income per month		
<500 $	30	10.6%
500-1500 $	158	55.8%
>=1500 $	95	33.6%
Health Insurance		
NSSF	67	23.7%
COOP	25	8.8%
Private	67	23.7%
None	124	43.8%

Use of social media		
Many times per day	164	58%
Once per day	46	16.25%
Every other day	16	5.7%
Rarely	57	20.1%

Table 2: Knowledge related questions and scoring

Questions related to knowledge (Yes, no, I don't know) 1. Do all antidepressants need prescription? 2. Do you know that antidepressants may cause side-effects? 3. Do you know that antidepressants may cause dependency? 4. Do you know that antidepressants may cause tolerance? 5. Do you know that the interruption at the end of treatment should be gradual? 6. Do you know that antidepressants can be used for other indications		
Number of patients	Score	Percentage
37	6/6	21.55477
61	5/6	13.0742
57	4/6	20.14134
50	3/6	17.66784
28	2/6	9.893993
40	1/6	14.13428
10	0/6	3.533569

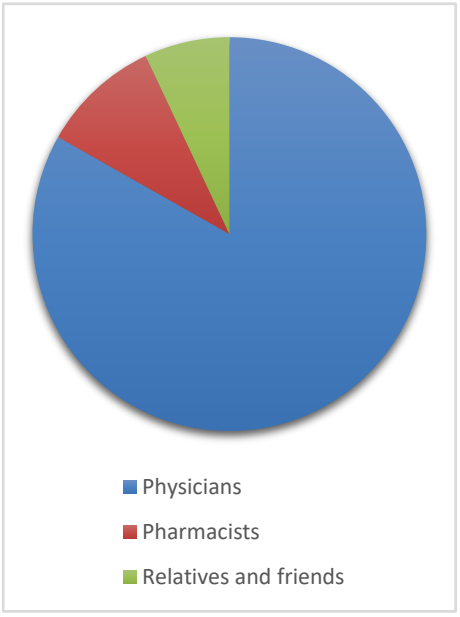

Figure 1: Prescribers

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A Review of Drug Therapy in the Management of Covid-19

By Dinesh Dhodi & Amitrajit Pal
Grant Medical College & Sir JJ Group of Hospitals

Abstract- The wrath of the COVID-19 pandemic has crippled the entire world in a state of a medical emergency. The number of cases has been increasing at an alarming and exponential rate and exhausting the medical resources vastly, at the same time questioning the future of such a deadly pandemic. An amalgamation of medical and non-medical knowledge is being followed globally to flatten the curve. However, without any proven cure at hand, several drugs are being researched into studies like Favipiravir, Remdesivir, Tocilizumab, Hydroxychloroquine, to gain substantial evidence of their use either individually or in combination, supplemented by supportive therapy, vitamins, and zinc, to effectively treat the patients and curb the mortality rate of the population.

Keywords: *COVID-19, Remdesivir, Favipiravir, Tocilizumab, Hydroxychloroquine, Vitamins, Zinc.*

GJMR-B Classification: *NLMC Code: WB 330*

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Keywords: COVID-19, Remdesivir, Favipiravir, Tocilizumab, Hydroxychloroquine, Vitamins, Zinc.

I. Introduction

The wrath of COVID-19 (Coronavirus disease) has gripped and crippled the entire nation and its effects worldwide on a global basis. The engorging pandemic has arisen to test the abilities of the medical fraternity and its arsenal. The current knowledge about COVID-19 is limited, but it is rapidly evolving with time. During this outbreak, the medical community has used evidence and experience from past upsurges of SARS-CoV and MERS-CoV to predict COVID-19's behavior, clinical presentation, and treatment. Also, coronaviruses (CoV) can cause signs and symptoms of multi-organ system damage, many of which can go unnoticed even by trained medical professionals.

CoVs (Coronavirus) are a large family of single-stranded RNA viruses that infect humans mainly through droplets and fomites[1]. Coronaviruses constitute the subfamily Orthocoronavirinae, within the family Coronaviridae, order Nidovirales. These are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry[2].

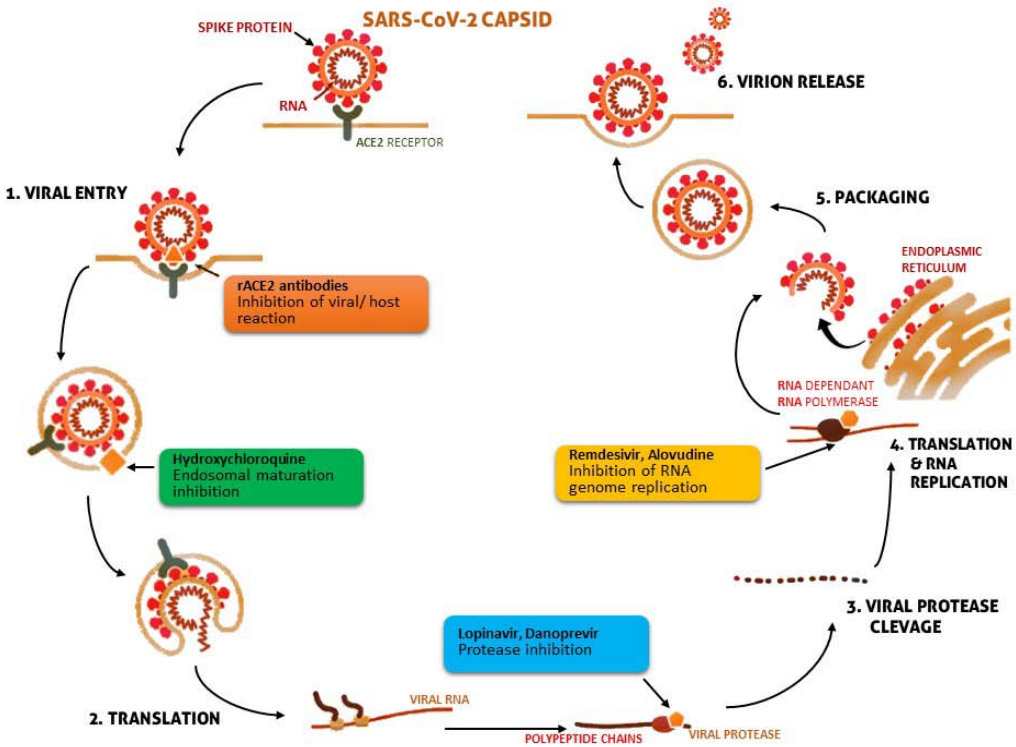

Figure 1: Life cycle of SARS[3]

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The recently identified COVID-19 is a beta-CoV that infects both humans and animals. All 3 of the novel viruses (SARS-CoV, MERS-CoV, and COVID-19) originate from zoonotic transmissions. Bats may be the source of SARS-CoV and COVID-19 based on sequence similarity with bat CoVs. It is believed that the virus has originated from the Hubei region of Wuhan in China[4].There is no standard care at present, for the prevention or treatment of the jeopardized respiratory system in COVID-19 as of now. Medications including glucocorticoids, IL-6 antagonists, Janus kinase inhibitors, antivirals, and chloroquine and hydroxychloroquine are currently been studied as possible therapeutic options for the ongoing pandemic[5]. The following are an overview of the various pharmacotherapeutic aspects utilized in the management of Covid-19 globally.

a) Favipiravir

It has currently been incorporated in the management protocol of COVID-19. Its mechanism of action is to selectively inhibit RNA dependant RNA polymerase (RdRP), an enzyme that is essential for RNA viral replication within human cells. It operates as a purine analog and is incorporated instead of guanine and adenine. The incorporation of a single molecule of Favipiravir causes the termination of the elongation of viral RNA. The drug is converted intracellularly into its active phosphorylated form and is recognized as a substrate by viral RdRP. It has a broad spectrum of activity against RNA viruses (Influenza, Rhino, and Respiratory Syncytial Virus, etc.) but not much against DNA viruses[6].

It has an excellent bioavailability (~94%), 54% protein binding, and a low volume of distribution (10–20 L) to the tissues. It reaches C_{max} within two hours after a single dose. Both T_{max} and half-life increase after multiple amounts of dosage. Favipiravir has a very short half-life (2.5–5 h), thus leading to rapid renal excretion in its hydroxylated form. Elimination is been mediated by aldehyde oxidase and marginally by xanthine oxidase. Favipiravir shows bothdose-dependent and time-dependent pharmacokinetics. It has not been metabolized by the cytochrome P450 systembut inhibits one of its components (CYP2C8)[7].

The recommended dosage of Favipiravir for adults for treatment in COVID-19 positive patients is 1800 mg orally twice daily on 1st day, followed by 800 mg orally twice daily, up to a maximum of 14 days.

The safety profile of the drug also seems acceptable, with asymptomatic hyperuricemia and mild, reversible increase in transaminases being the most frequently reported adverse effects. In the Indian trials conducted, no special safety signal has been elicited. It is, however teratogenic and not to be used in pregnant women. The main disadvantage is a high pill burden, which works out to a loading dose of 18 tablets on the first day and then eight tablets a day for the rest of the course[8].

b) Remdesivir

Remdesivir is a prodrug of a nucleotide analog that is intracellularly metabolized to an analog of adenosine triphosphate, thus inhibiting viral RNA polymerases. It has broad-spectrum activity against several virus families, including filoviruses (e.g., Ebola) and coronaviruses (e.g., SARS-CoV and MERS-CoV). It has prophylactic and therapeutic efficacy in nonclinical models of these various coronavirus[9-12].

Based on its physicochemical properties, instability in tissues, and pharmacokinetic properties, Remdesivir has low tissue distribution and penetration, especially into the lung. In monkey studies, Remdesivir was not detectable in the lung[13].

The drug has to be administered via an intravenous route (IV) with a loading dose on day 1 (200 mg in adults, adjusted for body weight in pediatric patients) followed by a daily maintenance dose (100 mg in adults) for up to 10 days. In non-human primates, regular administration of 10 mg/kg of Remdesivir generated a short plasma half-life of the prodrug (t1/2= 0.39 h) but maintained intracellular levels of the triphosphate form[14].

Adverse effects of hepatotoxicity, gastrointestinal symptoms, nephrotoxicity, cardiotoxicity have been observed in several studies, and it is complex to distinguish the underlying causes of adverse events during Remdesivir treatment.

The drug has been made available by the Food and Drug Administration to be used under emergency circumstances. It has also been authorized for the management of adults and children with severe Covid-19 disease.

Research studies being currently done at present support the use of Remdesivir in hospitalized patients with Covid-19 and require supplemental oxygen therapy.

c) Tocilizumab

Tocilizumab is an IL-6 receptor-blocking agent, and is currently been used for the treatment of severe COVID-19 patients. It is a humanized monoclonal antibody capable of interfering with the IL-6 soluble and membrane binding site of the receptor (IL-6R), thereby disrupting the integrity of the activated complex with the transmembrane protein (gp130-IL-6-sILr). It is also able to obstruct IL-6 trans-signalling, which is strongly related to the pro-inflammatory effects of IL-6 (e.g., release of acute-phase proteins). Tocilizumab has a non-linear pharmacokinetic profile, with a dose-response curve that plateaus at an approximate dosage of 800 mg[15].High levels of IL-6 are being observed among the main features of cytokine storm and cytokine release syndrome (CRS) in Covid-19 patients, both of which are characterized by an exaggerated release of pro-

inflammatory cytokines and potentially life-threatening multiorgan damage[16].

Moreover, elevated levels of IL-6 are linked with a hypercoagulable state in both animals and humans, and coagulopathy is another characteristic feature of patients with COVID-19 at high risk of death[17].

Adverse reactions of secondary infections, skin and subcutaneous infections, elevated liver enzymes, and gastrointestinal disorders are most commonly observed in the case of Tocilizumab[18]. The effects of tocilizumab against IL-6 related pro-inflammatory and pro-coagulant status partially explain its possible role in COVID-19. It has to be kept in mind that currently, there is yet no evidence that subduing the physiological inflammatory response to the virus is indeed advantageous[19].

d) Hydroxychloroquine

It is an anti-malarial drug, and has found its way in the management and prevention of Covid-19. It has similar effects to Chloroquine in interfering with the glycosylation of ACE2, blocking virus/cell fusion, and inhibiting lysosomal activity by increasing the pH. Hydroxychloroquine can also inhibit major histocompatibility complex (MCH) class II expression, which in turn inhibits T cell activation, expression of CD145, and cytokines release[20-22].

Furthermore, it has shown to impair Toll-like receptors (TLRs) signaling through increasing endosomal pH and interfering with TLR7 and TLR9 binding to their DNA/RNA ligands, thereby inhibiting the transcription of pro-inflammatory genes.

The long half-life of both Chloroquine and Hydroxychloroquine could range from 30 to 60 days, is likely attributed to their large volume of distribution (200–800 L/kg) and extensive tissue uptake.

Chloroquine and hydroxychloroquine both have unusual pharmacokinetic properties with enormous apparent volumes of distribution (chloroquine > hydroxychloroquine) and very slow elimination from the body (terminal elimination half-lives > 1 month).

Dosage is 800 mg on the first day, followed by 400 mg weekly for the next seven weeks on a prophylactic basis for those with a high risk of exposure to the virus.

The most common Chloroquine and Hydroxychloroquine adverse effects are gastrointestinal symptoms such as nausea, vomiting, and abdominal discomfort[23],and uncommonly worrisome fulminant hepatic failure[24], toxic epidermal necrolysis (TEN)[25], and cardiotoxicity that could manifest with QT abnormality.

Both Chloroquine and Hydroxychloroquine have demonstrated promising in vitro results; however, such data have not been translated yet, into meaningful in vivo studies.

FDA has determined that Chloroquine and Hydroxychloroquine are unlikely to be effective in treating COVID-19 at present for the emergency purpose. Additionally, in light of ongoing severe cardiac adverse events like PR interval prolongation, arrhythmia and other serious side effects, the known and potential benefits of Chloroquine and Hydroxychloroquine no longer outweigh the known and potential risks for the authorized use[26].

e) Ivermectin

Ivermectin is a known anti-helminthic drug that causes stimulation of gamma amino butyric acid (GABA)-gated-chloridechannels, thus leading to hyperpolarizationand resulting in paralysis of the causative organism. Another mechanism has been postulated for the same effect which speculates upon the immunomodulation of host response, attained by the activation of neutrophils, an increase in the levels of C-reactive protein, and interleukin-6[27].

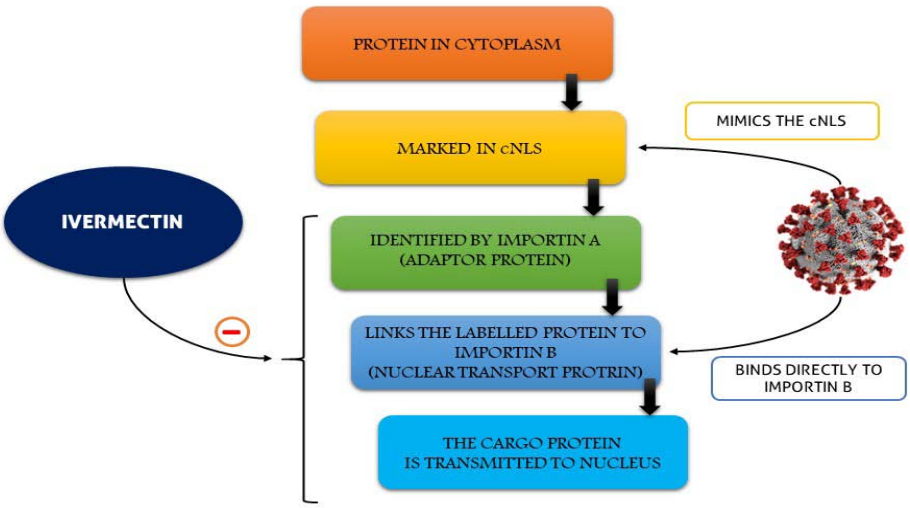

Figure 2: Mechanism of ivermectin induced inhibition of importin α/β mediated coronavirus proteins transport[28]. cNLS: classical Nuclear Localization Signal.

The drug is absorbed after oral administration, and due to its high lipid solubility, it is highly distributed in the body and it's extensively bound to the plasma proteins. It is extensively metabolized by cytochrome P450 enzymes. It is excreted mainly in feces with only 1% in urine[29].

Current clinical trials have used Ivermectin in a dose ranging from 200 to 1200 mcg/kg body weight, for a duration of 3–7 days, showing promising results both in terms of symptomatology and viral load reduction[30].

Ivermectin causes tiredness, loss of energy, stomach pain, vomiting, diarrhea, dizziness, drowsiness, and itchiness. It may lead to joint pain and swelling, swollen and tender lymph nodes, itching, rashes, fever, and eye problems.

Some of the serious adverse effects include low blood pressure, inability to breathe, and can also lead to liver damage.

f) Arbidol

Arbidol, also known as Umifenovir, is a broad-spectrum antiviral drug. It has been licensed for the prophylaxis and treatment of influenza and other viral respiratory infections. Its mechanism of action includes interactions with amino acid residues to form a hydrophobic aromatic assembled structure and interactions with aromatic residues of the viral glycoproteins involved in fusion and cellular recognition[31].

Some studies have observed anti- COVID-19 potential of Arbidol in vitro and clinic[32].

A retrospective study showed that Arbidol might not be efficacious enough to improve the prognosis or accelerate SARS-CoV-2 clearance in non-ICU patients[33].

g) Role of Corticosteroids

Corticosteroids have primarily been introduced in COVID-19 patients as a prior means to stave off the cytokine storm and its consequences like ARDS, disseminated intravascular coagulation, hypotension, shock, and death.

World Health Organization (WHO) and The Centre for Disease Control and Prevention (CDC), USA advises against the use of corticosteroids in COVID-19 for the prior purpose of immune modulation[34].

In sharp contrast, the recent multinational Surviving Sepsis Guideline in COVID-19 recommends to giving steroids in patients with severe COVID-19 on mechanical ventilation with ARDS (Acute Respiratory Distress Syndrome) to reduce the destructive inflammatory immune response and to treat suspected adrenal insufficiency associated with sepsis, particularly in those with refractory shock. However, this guideline advises against the use of corticosteroids in COVID patients in non-ARDS respiratory failure on mechanical ventilation[35].

Nevertheless, the Randomized Evaluation of COVid-19 therapy (RECOVERY Trial) conducted in patients with COVID-19 has shown significant improvement in the outcome with dexamethasone, a corticosteroid, used in the treatment of severe COVID-19 requiring oxygen therapy or on mechanical ventilator[36].

Methylprednisolone has the least mineralocorticoid activity, while dexamethasone has the highest glucocorticoid activity. Theoretically, methylprednisolone (0.5–2 μg/kg/day) has the advantage of parenteral administration, a quicker onset of action, and a shorter duration of action than dexamethasone[37].

Potential aftermath of corticosteroid therapy might be the worsening of dysglycemia/unmasking of latent diabetes. It causes increased lipolysis, increased hepatic glucose output, and can increase the insulin resistance by up to 60–80% by directly interfering with the signaling cascade of the GLUT-4 receptors[38].

h) Role of Low Molecular Weight Heparin

Recent studies have described the presence of a hypercoagulable state in COVID-19-affected patients[39], primarily due to secondary lymphohistiocytosis.

Lin et al., in a study, has asserted that the rise of inflammatory factors and D-dimer on days 7–14 of the disease could be supported by anticoagulation with low molecular weight heparin (LMWH) as a therapeutic strategy. The risk of sepsis-induced disseminated intravascular coagulation (DIC) induces recommendation for anticoagulation in COVID-19 patients with D-Dimer levels above four times the upper limit of normal (ULN), except for those with contraindications to anticoagulation. A subcutaneous dose of 100 IU/kg of LMWH twice a day is recommended, for at least 3–5 days[40].

i) Role of Zinc

Zinc is involved in various cellular pathways and has a variety of direct and indirect antiviral properties. Zinc deficiency is associated with decreased antibody production. It has affected the function of the innate immune system (e.g., low natural killer cell activity), reduced cytokine production by monocytes, and the chemotaxis and oxidative burst of neutrophil granulocytes[41].Antiviral properties of Zinc against several viral species are mainly been realized through the physical processes, such as virus attachment, infection, and uncoating, and through inhibition of viral protease and polymerase enzymatic processes[42].

Zinc supplementation alone or in combination with hydroxychloroquine for prevention and treatment of COVID-19 is currently under evaluation in clinical trials. The optimal dose of zinc for the treatment of COVID-19 has not been established as of now. The recommended dosage for elemental zinc is 11 mg daily for men and 8 mg for non-pregnant women. The quantities used in registered clinical trials for COVID-19 vary between

studies, with a maximum amount of zinc sulfate 220 mg (50 mg of elemental zinc) being given twice daily[43].

Zinc supplementation possesses a variety of direct and indirect antiviral properties, which may be beneficial in the COVID-19 pandemic.

j) Role of Vitamin C & Vitamin D

Vitamin C is also considered as one of the possible therapeutic agents for COVID-19 because it has a promising role in maintaining proper bodily functions and also helps in removing damaged reactive oxygen species and thus protects the cell from oxidative damage. Vitamin C is needed in much larger quantities for proper immune functioning. The beneficial role in SARS-Cov-2 and other viral infections is evident from the fact the level of vitamin C decreases during infection, and the body needs more of it to fight against the illness[44]. Vitamin C is a suggested therapy in COVID-19 because it minimizes the effect of oxidative stress and cytokine and. This promising role has also been observed in 146 COVID-19 patients in a study done by Hemila H[45]. Dosage recommendations are 1000 mg daily.

On the other hand, Vitamin D supplementation helps to reduce many complications associated with pneumonia and also decreases the cytokine stormin many of SARS-Cov-2 infections[46-47].

It also helps to modulate the rennin- angiotensin system which in turn regulates the expression of the ACE2 receptor, a common binding site for SARS-Cov-2.The activity of the DPP-4/CD26 receptor is decreased significantly in vivo upon the correctness of vitamin D insufficiency[48].

It is worth suggesting take up to 250 μg/day for a month, which is productive in increasing the serum levels of 25(OH)D into the optimal range between 75 and 125 nmol/L. The dosage amount can be reduced to 100 μg/day after one month to maintain the concentrations of 25(OH)D in the circulation[49-50].

k) Role of Plasma Therapy

Plasma therapy is an upcoming and promising mode of treatment in the recent COVID infection. According to WHO, management of COVID-19 has mainly detailed prevention, early case detection and monitoring, and supportive care along with symptomatic and conservative treatment of the positive cases. However, there is no specific recommended anti-SARS-CoV-2 treatment, due to the lack of proper evidence. Most importantly, the current guidelines dictate that systematic corticosteroids should not be given on a routine basis to treat COVID-19. Evidence at present shows that convalescent plasma (from patients who have recovered from viral infections), can be used as a treatment without the occurrence of severe adverse events in them. Therefore, it might be worthwhile and fruitful to test the safety and efficacy of convalescent plasma transfusions in SARS-CoV-2-infected patients[51]. Trials and studies regarding plasma therapy are currently being conducted on a larger scale in India. Plasmapheresis programmes have also been developed to combat the infection.

l) Role of Supportive Therapy

Coronavirus disease-19 (COVID-19) pandemic has caused a global crisis, where old age, comorbid conditions, end-stage organ impairment, and advanced cancer aggravate the risk of mortality in critical COVID-19 patients. Early warning scores (EWS), oxygen saturation, and respiratory rate can aid in categorizing COVID-19 patients as stable, unstable, and end of life. Breathlessness, respiratory secretions, delirium are the main symptoms that need to be identified, analyzed, assessed, and palliated. Palliative sedation measures are instrumental in managing intractable symptoms. Goals of care are to be discussed, and an advance care plan to be made in patients who are not likely to benefit from aggressive ICU measures and ventilation. For patients who are already in an ICU, either ventilated or needing ventilation, a futility assessment is to be made for future purposes. The concerned family has to be communicated sensitively about the futility of ICU measures and ongoing life-sustaining treatment. Family meeting outcomes are to be documented, and consent for ongoing life-sustaining treatment has to be obtained. Appropriate symptomatic management enables comfort at the end of life to all critically ill COVID-19 patients who are not receiving or not eligible to receive ICU measures and ventilation[52].

II. Discussion

As we move gradually towards the end of the year, we are more knowledgeable in fighting the pandemic and preventing its occurrence. Medical & non-medical approaches, be it as it may, are being applied in supplementation to each other in combating the deadly virus. The medical arsenal composes the backbone of treating the patient to curb the mortality rate of the population. Several drugs have been used in the management protocol to save the patient. It has to be kept in mind that since there is no proven evidence for a drug that can cure the patient from the disease, depending solely on a single drug to work the miracle is not to be expected. The virus manifests itself in many pathophysiological mechanisms to elicit different conditions, which are counteracted by drugs like Favipiravir, Remdesivir, Tocilizumab. Ivermectin may be beneficial in treating the patients. In addition to a different mechanism of action, there are other aspects in which the drug usage may be considered to be advantageous. For instance, the adverse effects associated with hydroxychloroquine (irreversible retinal damage, prolonged QT interval, myopathy, neuropathy) or with lopinavir & ritonavir combination (hypertriglyceridemia, hypercholesterolemia) have not

been reported in patients who are on ivermectin therapy. Future strategies have to be designed by incorporating antiviral agents with other therapeutic approaches or combinations of antiviral agents to continue to improve patient outcomes in Covid-19 and supplement in the treatment regimes.

Retrospectively speaking, the ongoing pandemic could have been prevented or delayed worldwide by early preparedness, and active participation in initiating the social distancing and rapid case diagnosis and treatment could have paved the way for a better future. The main challenge lies in the future that speaks of a suppressed fear that lingers on in the minds of the people regarding the persistence of the infection in the community and the environment. Every step in the ladder of science have to be used, as the entire world looks forward to researchers as they toil to find a cure, their hopes high, their heads tired, but firm in their resolve.

Ethical considerations – Not required

Conflict of interest - None

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Insulin Resistance and Pharmacotherapy Effectiveness in Patients with Long – Term Diabetes Mellitus Type 2

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Abstract- *Introduction:* With the development of the availability of genetic research, a multiplex approach to determining the pharmacotherapy tactics has become possible, taking into account the individual characteristics of the patient. Nevertheless, the modern tactics of pharmacotherapy "to failure" has been adopted, which over time leads to the intensification of therapy. A personalized approach to the pharmacotherapy of type 2 diabetes mellitus by determining the genotype of endothelial synthase of nitric oxide will predict the effectiveness of metformin monotherapy in the debut of the disease and reduce the risk of decompensation and complications with long-term type 2 diabetes mellitus.

The aim of the study was to monitor the effectiveness of metformin pharmacotherapy for long-term type 2 DM, depending on the patient's genotype.

Keywords: *type 2 diabetes mellitus, monotherapy, methformin, eNOS3 gene polymorphism, insulin resistance.*

GJMR-B Classification: *NLMC Code: WB 330*

Strictly as per the compliance and regulations of:

Insulin Resistance and Pharmacotherapy Effectiveness in Patients with Long – Term Diabetes Mellitus Type 2

Индивидуальные показатели инсулинорезистентности и эффективности фармакотерапии при длительно текущем СД 2 типа

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Резюме- ***Введение:*** **С развитием доступности генетических исследований стал возможным мультиплексный подход к определению тактики фармакотерапии с учетом индивидуальных особенностей пациента. Тем не менее, принята современная тактика фармакотерапии «до неудачи», что с течением времени приводит к интенсификации терапии. Персонализированный подход к фармакотерапии сахарного диабета 2 типа при помощи определения генотипа эндотелиальной синтазы оксида азота позволит спрогнозировать эффективность монотерапии метформином в дебюте заболевания и снизить риск декомпенсации и осложнений при длительно текущем сахарном диабете 2 типа.**

Целью исследования стал мониторинг эффективности фармакотерапии метформином длительно текущего СД 2 типа в зависимости от генотипа пациента.

Материалы и методы: **одноцентровое рандомизированное проспективное исследование 200 пациентов, направленных на плановую госпитализацию. Определяли однонуклеотидный полиморфизм гена (ОНП) *eNOS3*, уровень гликированного гемоглобина. Для оценки инсулинорезистентности применялась гомеостатическая модель 2 (HOMA2) с использованием уровня С-пептида. По результатам генетического исследования пациенты разделены на три группы: с генотипами CC, TC и TT.**

Результаты и обсуждение: **Пациенты группы с генотипом CC достигли и удерживали уровень гликированного гемоглобина ниже целевого в 80% случаев при применении метформина в дозе 1700 мг в сутки. Ни один из представителей генотипов TC и TT не достиг целевых значений гликированного гемоглобина. Таким образом, применения метформина в качестве монотерапии для компенсации углеводного обмена недостаточно при TC и TT генотипах, т.е. требуется комбинированная сахароснижающая фармакотерапия, в том числе инсулинотерапия.**

Заключение: **Выявление наличия того или иного аллеля гена *eNOS3* предоставляет возможность более раннего назначения соответствующих препаратов в индивидуальной дозе для снижения инсулинорезистентности и вероятного ограничения прогрессирования сахарного диабета, а также увеличения степени компенсации углеводного обмена.**

Ключевые слова: сахарный диабет 2 типа, эндотелиальная синтаза, метформин, полиморфизм гена eNOS3, инсулинорезистентность.

Abstract- Introduction: With the development of the availability of genetic research, a multiplex approach to determining the pharmacotherapy tactics has become possible, taking into account the individual characteristics of the patient. Nevertheless, the modern tactics of pharmacotherapy "to failure" has been adopted, which over time leads to the intensification of therapy. A personalized approach to the pharmacotherapy of type 2 diabetes mellitus by determining the genotype of endothelial synthase of nitric oxide will predict the effectiveness of metformin monotherapy in the debut of the disease and reduce the risk of decompensation and complications with long-term type 2 diabetes mellitus.

The aim of the study was to monitor the effectiveness of metformin pharmacotherapy for long-term type 2 DM, depending on the patient's genotype.

Materials and methods: A single-center, randomized, prospective study of 200 patients referred for planned hospitalization. The single nucleotide polymorphism of the gene eNOS3, the level of glycated hemoglobin. Homeostatic model 2 (HOMA 2) was applied to evaluate insulin resistance in patients. In consistency with the results, patients were divided into three groups: with the CC, TC and TT genotype.

Results and discussion: Patients of the CC genotype group achieved and kept glycated hemoglobin below the target level in 80% of cases, when metformin was used at a dose of 1700 mg per day. No one of the patients, who representatives of the TC and TT genotypes reached the target values of glycated hemoglobin. Thus, the use of metformin as monotherapy to compensate for carbohydrate metabolism is not enough for TC and TT genotypes, and combination hypoglycemic pharmacotherapy, including insulin therapy, is required.

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Conclusion: Identification of the presence of a particular eNOS3 gene allele provides the possibility of earlier prescribing appropriate drugs in an individual dose to reduce insulin resistance and likely limit the progression of diabetes mellitus, as well as increase the degree of compensation for carbohydrate metabolism.

Keywords: type 2 diabetes mellitus, monotherapy, methformin, eNOS3 gene polymorphism, insulin resistance.

I. Введение

Общеизвестно, что сахарный диабет (СД) приобрел статус неинфекционной эпидемии. Согласно данным международной федерации диабета, более 415 млн. человек во всем мире страдают СД 2 типа, а по предварительным подсчетам к 2040 г. это число достигнет 642 млн. При этом, на данный момент 320,5 млн. пациентов с СД 2 типа относятся к группе трудоспособного населения от 20 до 64 лет [1].

Фармакотерапия занимает основное место в лечении СД. Сахароснижающие лекарственные средства назначаются с момента диагностирования СД и на всю последующую жизнь пациента. Основными принципами фармакотерапии СД являются: патогенетический подход, учет сопутствующих заболеваний, максимальная эффективность при максимальной безопасности. С внедрением современных методов диагностики СД при условии доступности методов генетических исследований стал возможным мультиплексный подход к определению тактики фармакотерапии с учетом индивидуальных особенностей пациента (рисунок 1) [2].

В отличие от моногенных форм диабета (MODY, неонатальный диабет и некоторые другие), СД 2 типа характеризуется множеством вариаций и модификаций генов, которые определяют не только развитие и тяжесть течения заболевания, но и ответ на фармакотерапию, формируя «портрет пациента» [3].

На данный момент активно проводятся исследования эффективности и безопасности сахароснижающих препаратов в зависимости от мутации генов, связанных с развитием СД 2 типа (*PPARG, DIPOR2, ADAMTS9, IRS1, GCKR, KLF14, ADIPOQ*), связанных с мишенью лекарственных препаратов (*SUR1, GLPR-1*), а также влияющих на фармакокинетику препарата (*MATE и OCT*). Особый интерес представляют мутации генов, вовлеченных в фармакодинамику сахароснижающих средств опосредованным образом. Например, вариации гена карбоксипептидазы и гена, отвечающего за развитие пигментного ретинита [4].

На фоне стремительного роста заболеваемости СД 2 типа проведение многоцентровых исследований позволяет получать объективную информацию об эпидемиологической ситуации в отношении СД и его осложнений, оценивать эффективность различных схем проводимой терапии и диагностических стратегий, направленных на выявление системных сосудистых осложнений заболевания. Фармакоэпидемиологическими исследованиями было доказано, что самым назначаемым препаратом является метформин, как в монотерапии, так и в комбинации с другими препаратами. При этом у трети пациентов отмечен неадекватный гликемический контроль ($HbA_1c>8\%$), у большинства больных было выявлено наличие от двух до шести хронических осложнений СД [5]. Большую часть затрат составляют потери внутреннего валового продукта вследствие нетрудоспособности пациентов. На лечение осложнений СД приходится 57% прямых медицинских затрат, тогда как на долю сахароснижающей терапии – всего 10% [6].

Такой традиционный подход к фармакотерапии можно описать как стратегию лечения «до неудачи». То есть, в соответствии с рекомендациями, в зависимости от исходного уровня показателя компенсации углеводного обмена подбирается та или иная фармакотерапия с последующим контролем не реже 1 раза в месяц и с принятием решения об интенсификации не позднее, чем через 6 месяцев. И даже при таком графике коррекции фармакотерапии СД 2 типа, который часто не соблюдается пациентами, как показали результаты исследования ФОРСАЙТ, коррекция гипергликемии и других нарушений при СД происходит постфактум [7].

В связи с этим, особое значение приобретает прогнозирование эффективности фармакотерапии СД 2 типа ещё на этапе определения ее тактики.

С этой целью был разработан способ прогнозирования эффективности терапии больных СД 2 типа метформином в стандартной дозе 1700 мг в сутки при назначении его в качестве монотерапии, который основан на определении генотипа эндотелиальной синтазы оксида азота (*eNOS3*) у пациентов в дебюте заболевания с удовлетворительным контролем гликемии с целью прогноза эффективности. Выбор гена был обоснован тем, что метформин является донатором оксида азота (NO) [8] и улучшает NO-зависимую утилизацию глюкозы [9].

Установлено, что через три месяца применения метформина в дозе 1700 мг/сутки у всех пациентов с генотипом CC наблюдается эффективное снижение гликогемоглобина на 1% и достижение его целевых значений [10]. У пациентов с генотипами TC и TT за три месяца фармакотерапии метформином динамика снижения уровня гликемии и гликированного гемоглобина несущественна, и при прогнозировании на 6 месяцев может не достичь требуемой удовлетворительной динамики снижения HbA1c на 0,5-1% [11].

Следует отметить, что для большинства пациентов среднего возраста при удовлетворительной компенсации целевое значение гликированного гемоглобина составляет менее 7%. Если исходный показатель HbA1c находится в целевом диапазоне или

превышает индивидуальный целевой уровень менее чем на 1,0 %, то лечение можно начинать с монотерапии (приоритетным препаратом является метформин при отсутствии противопоказаний). При этом эффективным считается темп снижения HbA1c ≥ 0,5 % за 6 месяцев наблюдения [11]. Однако с течением времени многим пациентам требуется интенсификация терапии вследствие того, что достижение целевых показателей гликированного гемоглобина при традиционной тактике становится невозможным. В связи с этим, целью исследования стал мониторинг эффективности фармакотерапии метформином длительно текущего СД 2 типа в зависимости от генотипа пациента.

II. Материалы и Методы

Дизайн исследования: одноцентровое проспективное рандомизированное исследование. Проводилось наблюдение за динамикой эффективности фармакотерапии в прогрессе заболевания в зависимости от генотипа пациента при поступлении в порядке плановой госпитализации (200 пациентов). Однонуклеотидный полиморфизм гена (ОНП) *eNOS3* (rs 2070744) определяли методом полимеразной цепной реакции в реальном времени при использовании стандартных наборов (НПФ «Литех», Россия). Гликированный гемоглобин определяли на жидкостном хроматографе Bio-Rad со стандартными наборами (Франция). Уровень С-пептида, используемого для расчета показателей HOMA 2-IR, HOMA 2-B и HOMA 2-IS гомеостатической модели, оценивали с помощью диагностических иммуноферментных тест-систем «Mercodia C-peptide ELISA specific». При статистической обработке полученных данных применялись непараметрические методы анализа. Различия между независимыми группами оценивали с помощью U критерия Манна-Уитни. Различия между зависимыми группами оценивались с помощью критерия Вилкоксона. Показатели представлены в виде: Медиана [25% квартиль;75% квартиль]. Расчет показателей гомеостатической модели 2 (HOMA2) проводили с помощью специализированного приложения, разработанного Оксфордским Университетом, версия 2.2.3 [12].

III. Результаты и Обсуждение

Группы пациентов с генотипами ОНП *eNOS3* CC, TC и TT были сопоставимы по полу, возрасту, длительности СД 2 типа, наличию сопутствующих заболеваний и диабетических осложнений, сопутствующей фармакотерапии. При средней длительности СД 2 типа 10 лет у обследованных пациентов целевой показатель гликированного гемоглобина составил 7,5%. При этом среди пациентов с генотипом CC достигли и удерживали уровень гликированного гемоглобина даже ниже целевого 80% больных при применении метформина в дозе 1700 мг в сутки в течение указанной длительности заболевания и соответствующей длительности его терапии. Исключение составили пациенты с глубокой декомпенсацией, нуждающиеся в инсулинотерапии, которые не соблюдали в течение всего периода лечения врачебные предписания о приеме метформина (таблица 1).

Таблица 1: Характеристика групп и уровень гликированного гемоглобина в зависимости от генотипа пациентов при длительном СД 2 типа и монотерапии метформином (Me [25p;75p])

Показатель	Генотип (частота встречаемости)		
	CC (0,14)	TC (0,45)	TT (0,41)
Возраст, лет	60,00 [55,00;64,00]	59,50 [55,00;66,00]	65,50 [58,00;69,00]
Длительность СД 2 типа, лет	9,5 [6,0;10,25]	10,2 [10,0;13,25]	10,0 [5,0;14,5]
Целевой HbA_1c, %	7,5		
Достигнутый HbA_1c,	6,90 [5,9;7,8] *p=0,029	8,61 [8,0;9,5]	8,5 [7,6;10,20]
Рекомендованная фармакотерапия	Метформин Инсулин длительного действия Ингибитор ДПП-4	Метформин Ингибиторы натрий глюкозного котранспортера-2 Инсулин длительного и короткого действия Ингибитор ДПП-4	Метформин Ингибиторы натрий глюкозного котранспортера-2 Инсулин длительного и короткого действия Ингибитор ДПП-4

Примечания: HbA_1 - гликированный гемоглобин; P - уровень статистической значимости; ДПП – дипептидилпептидаза.

Ни один из представителей генотипов ТС и ТТ не достиг целевых значений гликированного гемоглобина. При этом HbA1c в указанных группах превышал целевые значения. Полученные данные свидетельствуют о том, что при ТС и ТТ генотипах применения метформина в качестве монотерапии для компенсации углеводного обмена недостаточно. Этот факт обусловливает необходимость интенсификации фармакотерапии СД путем применения комбинированной сахароснижающей фармакотерапии, в том числе инсулинотерапии.

У носителей СС генотипа метформин нормализует углеводно-липидный обмен и способен снизить глюколипотоксичность и инсулинорезистентность (ИР), защитить бета-клетку от интенсивного повреждения [13], но этот факт не отменяет прогрессирования периферической ИР, что находит отражение в показателе HOMA2, и возможного истощения имеющихся запасов бета-клетки. В то время как у носителей Т аллеля, вероятно, плейотропный эффект метформина на глюколипотоксичность не реализуется в полной мере из-за особенностей функционирования гена *eNOS3*, несмотря на возможное устранение гипергликемии в первое время после назначения. Таким пациентам изначально необходима корригирующая терапия ИР, желательно без использования стратегии лечения «до провала».

Примененная нами гомеостатическая модель оценки 2 (HOMA2), оценивает установившееся состояние функции бета-клеток (%B) и чувствительность к инсулину (%S), в процентах от нормальной контрольной популяции, а также уровень периферической инсулинорезистентности (ИР). У пациентов с СС генотипом, несмотря на высокие показатели функционирования бета-клеток, индекс периферической ИР (HOMA2-IR) сравним с таковым у представителей других генотипов. Это может свидетельствовать о том, что, несмотря на достаточную компенсацию углеводного обмена, истощение бета-клеток у пациентов с СС генотипом медленно, но прогрессирует (таблица 2).

Таблица 2: Показатели инсулинорезистентности у пациентов с различными генотипами при длительном СД 2 типа и монотерапии метформином (Me [25p;75p])

Показатель	Генотип (частота встречаемости)		
	CC (0,14)	TC (0,45)	TT (0,41)
HOMA 2-IR (уровень периферической ИР)	3,5 [1,86;3,64]	3,79 [1,13;4,14]	4,47 [2,34;5,25]
HOMA 2-B (установившееся состояние функции бета-клеток, % от нормального)	93,2 [67, 88;177,2] *p=0,0078	54,3 [35,7;65,5]	46,9 [29,7;74,85]
HOMA 2-IS (чувствительность к инсулину, % от нормальной)	34,7333 [27,5;53,8]	26,4 [24,1;88,8]	31,45[19,05;42,65]

Примечание. P - уровень статистической значимости.

IV. Заключение.

Таким образом, не только гипергликемия, невозможность достижения целевых суточных колебаний гликемии, но и нарастающая инсулинорезистентность является важным звеном патогенеза СД 2 типа и обязательной мишенью фармакологической коррекции, а перспективным направлением персонализации фармакотерапии – изучение подходов к коррекции инсулинорезистентности. Отправным пунктом для интенсификации фармакотерапии при этом должен стать не уже возросший гликированный гемоглобин, как следствие персистирующей гипергликемии, а прогнозируемое нарастание инсулинорезистентности, в том числе вследствие полиморфизма гена *eNOS3*.

Выявление наличия того или иного аллеля данного полиморфного гена предоставляет возможность более раннего назначения соответствующих препаратов в индивидуальной дозе для снижения инсулинорезистентности и вероятного ограничения прогрессирования сахарного диабета, а также увеличения степени компенсации углеводного обмена [14].

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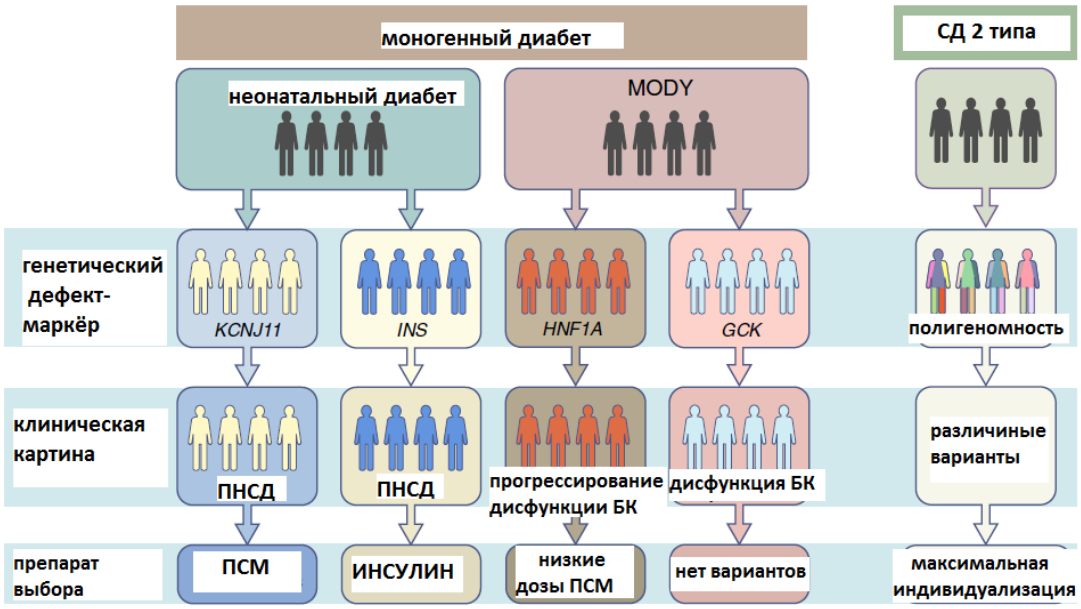

Рисунок 1: Современные тактики фармакотерапии. Адаптировано из A. T. Hattersle, K. A. Patel [2].

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A Study of Pediatric Poisonings in a Tertiary Care Hospital in Jammu and Kashmir in India

By Dr. ZulEidain Hassan, Dr. Sajad Ahmad & Dr. Bushra Shakil

Abstract- *Background:* Acute pediatric poisoning is a major health concern causing significant morbidity and mortality in pediatric practice in the critical care setting. Majority of poisonings are accidental and unintentional and occur in the toddlers and preschool age children. The objectives of this study were to assess the pattern of pediatric poisoning and its outcomes in a tertiary care setting.

Methods: Prospective observational study conducted in the Department of Pediatrics, Maternity and Child Care Hospital Anantnag over a study period of one year extending from April 2019 to April 2020.204 patients were enrolled in the study. Prevalence of admissions was 2.40%. More males were admitted compared to females. (1.42:1). Majority of patients belonged to rural background (n = 114,55.88%).

Keywords: *poisoning, organophosphates, hydrocarbons.*

GJMR-B Classification: *NLMC Code: WS 205*

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Conclusions: Acute poisoning is a common cause of mortality and morbidity and is a leading cause of children seeking critical care in a hospital setting especially in infancy and preschool age group. Prevention by proper disposal of household poisonous substances, health education, keeping household poisons and drug containers away from reach of children in sealed containers and avoidance of keeping of liquid household poisons or drugs in empty containers meant for food are key strategies to prevent poisoning related mortality and morbidity.

Keywords: poisoning, organophosphates, hydrocarbons.

I. Introduction

Acute poisoning is one of the commonest encountered emergencies in critical care setting in children and is one of the commonest reasons of children seeking specialized care and admission to the hospital. Poison is a substance which when inhaled, ingested or absorbed is injurious to human health either by causing direct injury to the human body or reaction of body to the toxic substance[1]. Poisoning can be accidental or deliberate with accidental poisoning being the more common in pediatric practice [2]. Most cases of pediatric poisoning are unintentional as young children are not mature enough to understand the consequences of ingestion of intoxicants [3]. Intentional poisoning becomes increasingly common in adolescents [4]. The type of poison consumed varies and depends upon the racial, ethnic, social, cultural, economic and educational backgrounds.[5,6]

As children acquire the ability to walk, reach out for things and explore surroundings and their immediate environment, they can easily fall prey to accidental ingestion of certain substances which are within their reach. It is a common practice by parents to keep household poisons in beverage bottles and empty cans of edible food materials. Such containers if within the reach of children can be easily mistaken for an edible substance and consumed by the child. This is also true of certain liquid medications and drugs which if not left properly sealed can also be mistakenly consumed [7]. The risk is especially increased if the substance is odorless, colorless and not obnoxious to taste. Such substances can be consumed in large quantities without apparent immediate manifestations and can lead to more worse consequences. [8,9]

Household poisonous products constitute the bulk of poisonous products in developing countries and drugs and pharmaceutical products are more commonly encountered in developed countries[10,11]. There is a considerable underreporting of poisoning cases as most mild cases are managed at local subcenters and primary health centers and are not referred to subdistrict and district hospitals. As such the data available in a tertiary care center significantly underestimates the actual magnitude of poisoning and hence the data available in tertiary care hospitals can't be extrapolated to get an idea about the actual magnitude of the poisoning problem in our state in particular and country in general.

In the present study we aimed to study the clinical, epidemiological profile and outcomes of poisonings in pediatric age group presenting to a tertiary care hospital in Kashmir Valley of India.

II. Material and Methods

The study was a prospective observational study conducted at Maternity and Child Care Hospital Anantnag, which is an affiliated hospital of Government Medical college Anantnag. It is a tertiary care referral

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center and caters to the whole pediatric population of South Kashmir seeking health care. All children <15 years of age presenting to hospital on OPD basis or IPD basis and patients who were referred from other peripheral health centers were included in the study. Patients with suspected food poisoning, animal envenomation and drug reactions were excluded from the study. The study period comprised one year from April 2019 to April 2020.

Clinical and demographic profile, type of ingestion, quantity of ingestion, time since ingestion, background of patients, gender, age group, nature of poisonous compound, presenting symptoms and outcome were recorded and details entered in a predesigned proforma. Results were compiled and entered in MS Excel spreadsheet. Data was expressed as frequency and percentage. Standard statistical analysis was used.

III. Results

A total of 204 patients were admitted during the study period of one year. Total admissions in the calendar year was 8513.The prevalence of admissions was 2.40%.

More males were admitted compared to females. Male to female ratio was 1.43 as shown in table 1

Table 1

Gender	Number	Percentage
Males	120	55.82 %
Females	84	41.18%

Patients were divided into 4 age groups. And the commonest age group observed to be involved was 1 to 5 years old as shown in table 2

Table 2

Age group	Frequency	Percentage
<1 year	46	22.55%
1-5 years	100	49.02%
6-10 years	30	14.71%
10-15 years	28	13.72%

More patients were admitted from rural background as shown in table 3

Table 3

Background	Frequency	Percentage
Rural	114	55.88%
Urban	90	44.12%

Indoor poisoning was found in majority of cases (n=178,87.25%)

Table 4

Nature of poisoning	Frequency	Percentage
Indoor	178	87.25%
Outdoor	26	12.75%

Accidental poisoning was the commonest type of poisoning followed by suicidal poisoning and homicidal poisoning as shown in table 5

Table 5

Type of poisoning	Frequency	Percentage
Accidental	170	83.33
Suicidal	28	13.73
Homicidal	6	2.94

Agents responsible for poisoning are summarized in table 6. Organophosphate compounds were the commonest compounds encountered in pediatric poisoning followed by kerosene and drug and pharmaceutical ingestion in that order. Less common causes of poisoning were corrosive ingestion, turpentine ingestion, thinner ingestion phenol ingestion etc. as shown in table 6.

Table 6

Nature of poison	Frequency	Percentage
Organophosphate	67	32.85%
Kerosene	41	20.10%
Drugs and pharmaceuticals	21	10.29%
Corrosives	19	9.32%
Turpentine	15	7.35%
Thinner	10	4.90%
Phenol	10	4.90%
Gasoline	9	4.41%
Datura	8	3.92%
Mosquito Repellant	4	1.96%

14 patients died during hospital stay. The case fatality rate was 6.68%.

IV. Discussion

Acute poisoning is one of the commonest encountered emergencies in pediatric practice and one of the commonest reasons of children seeking specialized care in a critical care unit. In the United States poisoning has surpassed even motor vehicle accidents to become the leading cause of injury related death. Poisoning in infants, toddlers and early preschool age children is mostly accidental and unintentional whereas in preadolescents and adolescents poisoning is mostly intentional and with either suicidal or homicidal intent.[3,4]

Our aim was to study the clinical and demographic profile of common pediatric poisonings in our set up which is a tertiary care referral center for southern part of the union territory of Jammu and Kashmir.

We encountered a total of 204 patients in our study during the study period from April 2019 to April 2020.there were a total of 8513 admissions during the calendar year. The cases comprised 2.40% of the total admissions; the values were comparable to studies conducted by Kariyappa M et al [12] and Shashidhar V et al [13] who reported a prevalence of 1.54% of total admissions.

Male to female ratio was 1.42:1. Male preponderance is in agreement with studies conducted by Shashidhar V et al [13] and Budhathoki S et al [14] as against female preponderance noted by Kariyappa M et al [12]. Majority of patients belonged to rural backgrounds (n=120,58.82%). Similar findings were observed by Shashidhar V et al[13].

Majority of patients were in the age group of 1-5 years (n=100,49.02%); similar to the study findings conducted by Kariyappa M et al [12] and Budhathoki S E et al [14]. The predominance of this age group can be explained by their inability to understand the consequence and nature of common household poisons, drugs and pharmaceutical ingestion. Such children have exploratory nature coupled with inherent tendency to put everything in mouth. As children grow older the tendency to mouthing decreases and the awareness about common household poisons increases. Hence unintentional poisoning becomes increasingly uncommon and suicidal rates increase.

Organophosphate poisoning was the commonest poisoning noted in our study (n=64;32.89%), followed by kerosene poisoning, drug intoxication, corrosive ingestion, turpentine ingestion, thinner ingestion, phenol ingestion, gasoline ingestion, Datura ingestion and mosquito repellant ingestion in that order. The study conducted by Kariyappa M et al [12] showed kerosene to be the commonest agent incriminated in pediatric poisoning cases whereas the study conducted by Shashidhar V et al[13] showed pesticides to be the commonest agent agreeing with our findings. The higher incidence of organophosphate poisoning in our study can be explained by the fact that a major proportion of business undertaking in the valley of Kashmir is comprised of fruit cultivation and a large proportion of cultivable land is composed of apple and pear orchards. Pesticides are extensively used and so is the availability ample in homes especially in rural and sub urban areas. People keep pesticides in fairly accessible sites leading to accidental consumption by children and poisoning. Kerosene is also widely used as a means to light firewood for bathing places called Hammams in Kashmir in harsh winter; as such kerosene is also found in ample quantities in Kashmiri homes.

14 patients died during hospital stay. The case fatality rate was 6.86%. This was more than the values reported by Kariyappa M et al (2.14%) [12]and much lower than values reported by Buddhathoki et al [14]. The case fatality rate was apparently higher because relatively more patients were admitted in the adolescent age group who had intentionally consumed a large amount of poisonous substance and were brought in a very critical condition.

V. Conclusion

Acute poisoning is a common cause of mortality and morbidity and a common reason to seek medical care especially in the under 5 age group. Organophosphate compounds, kerosene and drugs were the commonest substances to be ingested. The

measures to reduce acute poisoning include keeping constant vigil on toddlers and preschool children, keeping household poisons in tight containers, keeping household poisons properly labelled and out of reach of children., avoid keeping poisons in empty fluid/beverage bottles to avoid being confused with edible items.

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Associates 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

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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

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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.

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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.

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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.

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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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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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