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Epidemiologic Analysis of the Prevalence of Iron Deficiency Anemia in the Republic of Uzbekistan for 2007-2019

By Gavkhar J. Jarylkasinova & Iskandar. R. Mavlyanov
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Abstract- An epidemiological assessment of the structure and dynamics of the incidence of iron deficiency anemia in the Republic of Uzbekistan from 2007 to 2019 was carried out. The study showed that, according to WHO standards, in the Republic of Uzbekistan during the period under study, it was possible to achieve the transition of the category of significance of the Iron Deficiency Anemia (IDA) problem for public health from medium (prevalence 20.0–39.9 %) to moderate (5.0–19.9 %)... In some regions, where in 2007 the prevalence of anemia was more than 40 % for 12 years, it was possible to achieve a transition to the category of medium significance. However, the national average is still far from acceptable (4.9 %), which makes it necessary to continue and deepen preventive and health-improving measures.

Keywords: iron deficiency anemia; epidemiology; regional features of epidemiology.

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Epidemiologic Analysis of the Prevalence of Iron Deficiency Anemia in the Republic of Uzbekistan for 2007-2019

Gavkhar J. Jarylkasinova [α] & Iskandar. R. Mavlyanov [σ]

Abstract- **An epidemiological assessment of the structure and dynamics of the incidence of iron deficiency anemia in the Republic of Uzbekistan from 2007 to 2019 was carried out. The study showed that, according to WHO standards, in the Republic of Uzbekistan during the period under study, it was possible to achieve the transition of the category of significance of the Iron Deficiency Anemia (IDA) problem for public health from medium (prevalence 20.0–39.9 %) to moderate (5.0–19.9 %)... In some regions, where in 2007 the prevalence of anemia was more than 40 % for 12 years, it was possible to achieve a transition to the category of medium significance. However, the national average is still far from acceptable (4.9 %), which makes it necessary to continue and deepen preventive and health-improving measures.**

Keywords: iron deficiency anemia; epidemiology; regional features of epidemiology.

I. Introduction

Iron deficiency anemia (IDA) is a widespread pathology among population, according to data presented by World Health Organization (WHO) this disease has been ranked as one of the most common among the 38 most widespread human diseases [1, 4]. As you know, IDA is more common in developing countries than in developed ones. For example, in India, up to 88% of pregnant women and 74% of non-pregnant women suffer from anemia, in Africa - about 50% of pregnant women and 40% of non-pregnant women. In Latin America and the Caribbean, the prevalence of IDA in pregnant and non-pregnant women is about 40 % and 30%, respectively [7,13,18] .

The incidence of IDA is 20%, and iron deficiency (ID) exists in 50 % of the population in the population [2, 3]. ID is the most common malnutrition in the world affecting many children and women in developing countries, and the only type of nutritional deficiency that is also prevalent on a large scale in industrialized countries [8]. At the same time, according to statistics in the world, about 50% of preschool children and pregnant women suffer from IDA [10].

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ID and IDA reduce the labor productivity of the population, lead to serious economic consequences and create obstacles to the development of the country. Invisible but pervasive in many developing countries, the true consequences of ID and IDA are hidden behind statistics on overall mortality rates, maternal bleeding, poor school performance and reduced work ability. The health consequences are latent but destructive, imperceptibly weakening the potential for the development of people, society and the national economy [1,6,7,10] .

According to the grading of WHO experts, the prevalence of IDA in the population can be moderate - from 5 to 19.9%, average - from 20 to 39.9%, and significant - 40% or more [1, 7.18]. When the prevalence of anemia is more than 40%, the problem ceases to be only medical and requires measures at the state level. A similar situation was observed in the Republic of Uzbekistan, one of the developing countries of Central Asia, where in the mid-90s the incidence rate of IDA in some regions was much 40%. In this regard, the country began to carry out preventive and health-improving measures, the first results of which appeared already in 2006-2007 [5,9] .

Despite the fact that work in this direction began to give results, the incidence rate in some regions remained high and presented a significant problem for the country's health. The following years were characterized by significant changes in the structure and operation of the health care system, which became more focused on the prevention of diseases. In this regard, the main objective of this study was evaluation of the structure and dynamics of the incidence of IDA in the Republic of Uzbekistan from 2007 to 2019.

II. Materials and Research Methods

The study was performed in the department of Hematology of Bukhara branch of the Tashkent Medical Academy. The research materials were the data of official statistical reporting, accounting and reporting documentation, information and analytical materials collected for the period from 2007 to 2019. The material was collected as a result of work with the Ministry of Health of the Republic of Uzbekistan, as well as regional, city and district health departments in regions

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of the country. Particular emphasis was placed on the analysis of the epidemiological situation in the Kashkadarya, Bukhara and Navoi regions, as well as separately in the Republic of Karakalpakstan.

The study was comprehensive in nature using descriptive and analytical epidemiological techniques, retrospective epidemiological analysis, and medical statistics.

Statistical analysis included with the used of the district and merge data into a single computer database. During processing, we used the computer packages STATISTICA and BIOSTAT. For analysis were used both parametric and non-parametric methods. For quantitative indicators mean values, standard errors, and standard deviations were calculated. The trend lines were drawn to predict further morbidity with the calculation of the approximation reliability (R^2) .

III. Results

The considered time period was characterized by an increase in the total population from 26 million to 31 million inhabitants [14].

The dynamics of the absolute number of cases of anemia among the population was not so even during the first 3 years, only since 2010 a steady decline in the number of cases from 5.6 million to 4.1 million in 2017 began. At the same time, in the period from 2007 to 2018 in the country, the average annual population growth was equal to 1.45%, while the average annual regression rate of anemia in the entire population was 0.81% (Fig. 1).

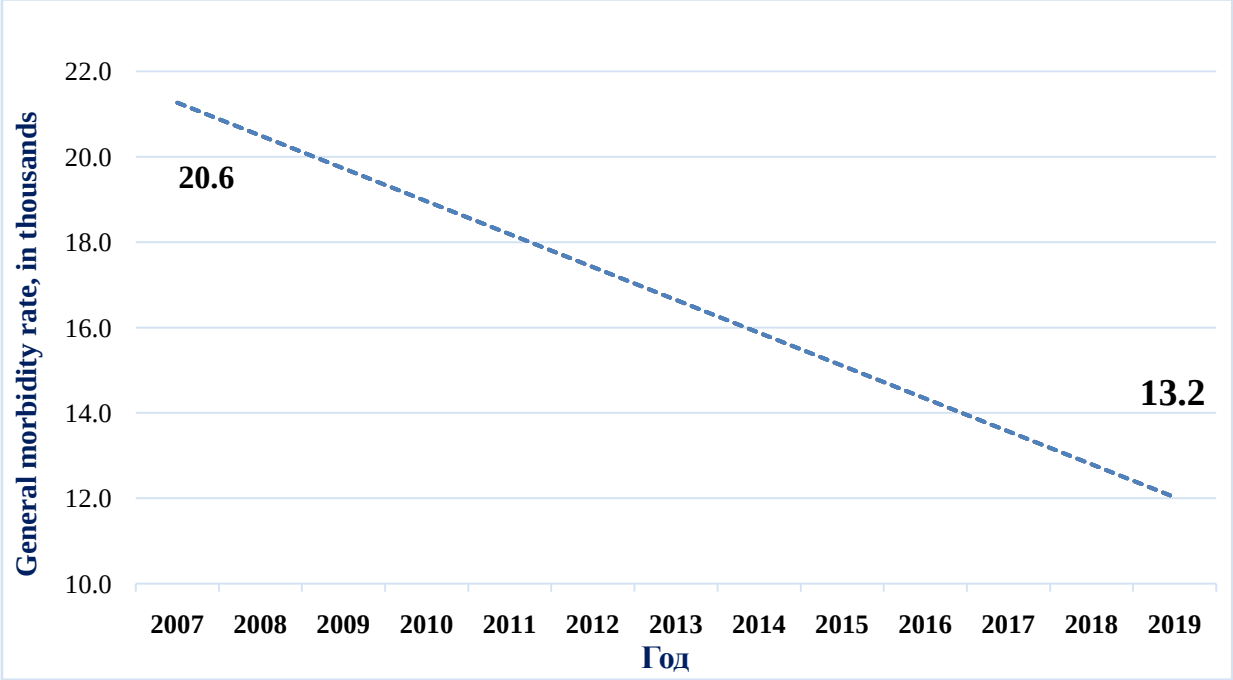


Figure 1: Dynamics of the overall incidence rate from 2007 to 2019.

Analysis of indicators of general and primary illness rates per 100,000 population in the Republic of Uzbekistan for the period from 2007 to 2019 is shown in Figures 2 and 3 . The graphs show that there has been a significant decline in both indicators.

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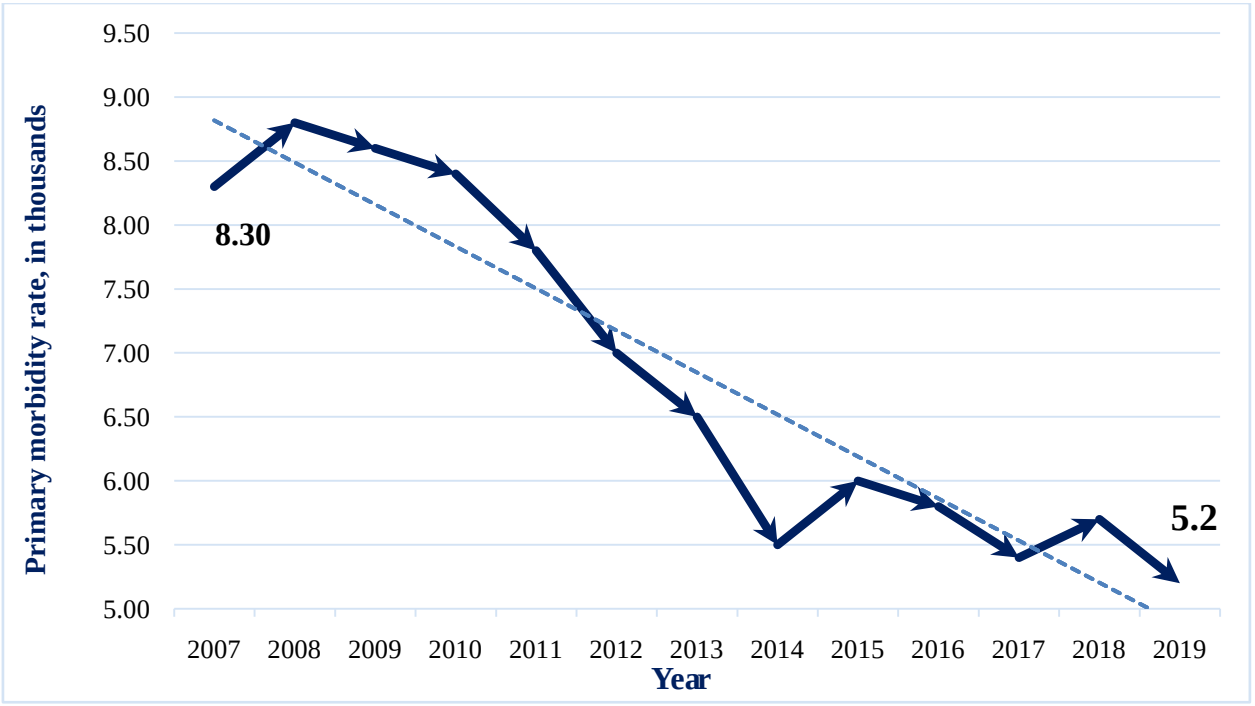


Figure 2: Dynamics of the primary incidence rate from 2007 to 2019.

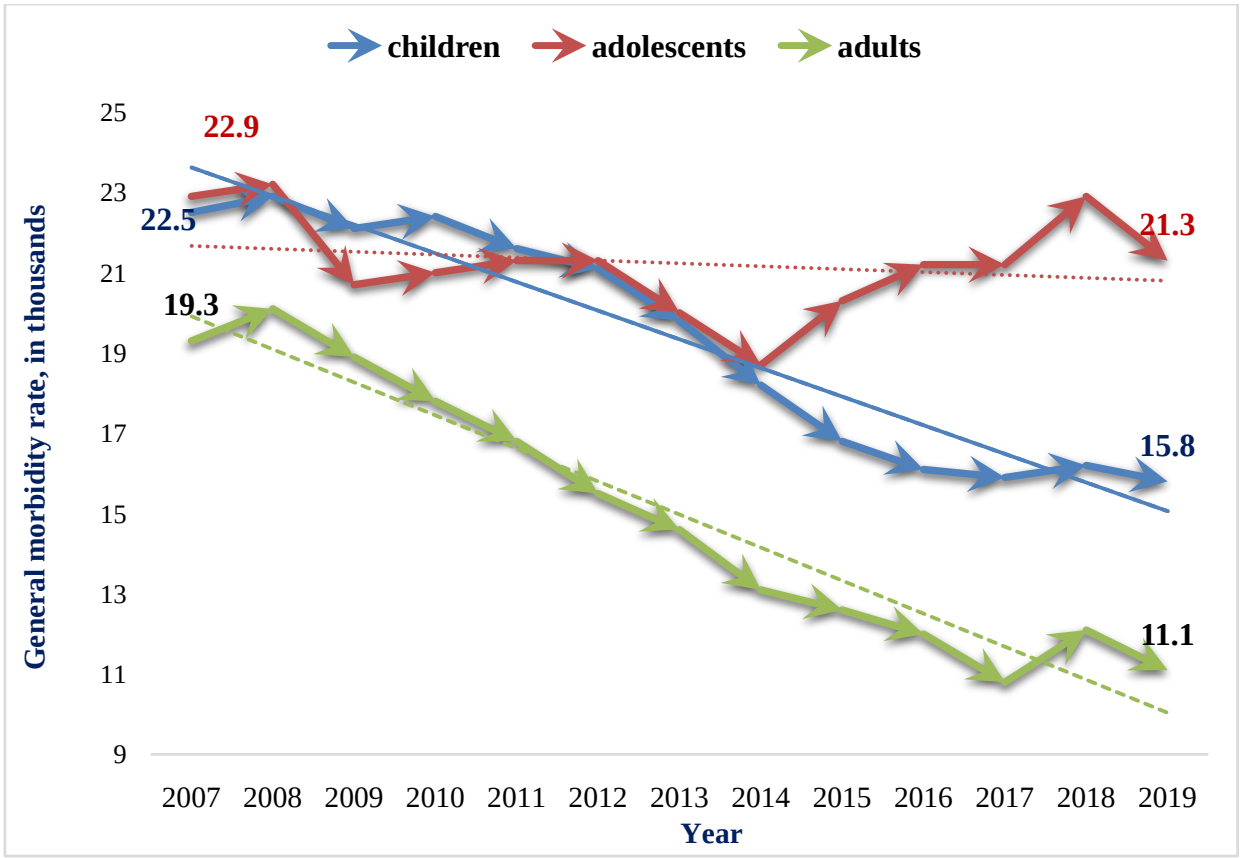


Figure 3: Dynamics of indicators of the general incidence of anemia per 100,000 in different age groups.

The overall incidence rate was 20,620 per 100 thousand population, after a slight increase in the rate in 2008, its stable decline began, which continued until 2017. In 2018, there was a slight increase in the overall incidence of up to 13,837 cases per 100 thousand population. Nevertheless, the graph shows that over 12 years there has been a decrease in the overall incidence rate by almost 33%. At the same time, on average, there

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was a decrease in the indicator by 816 cases per 100,000 population annually ($R^2 = 0.9517$).

Analysis of the primary incidence rate showed that in 2007 it was 8.3 thousand cases per 100 thousand population. In 2008, there was an increase in the rate to almost 9 thousand cases, after which over the next 6 years there was a decrease, which reached its lowest point in 2014 and amounted to 5.5 thousand cases. Over the next 4 years, periods of rise and decline alternated until in 2019 the primary incidence rate reached the final mark of 5.2 thousand cases. These graphs show that over 12 years there was a decrease in the indicator by more than 30% with an average annual regression equal to 343 cases ($R^2 = 0.8729$).

The analysis of dynamic changes in the incidence rate of IDA in individual age groups is presented in Figure 4.

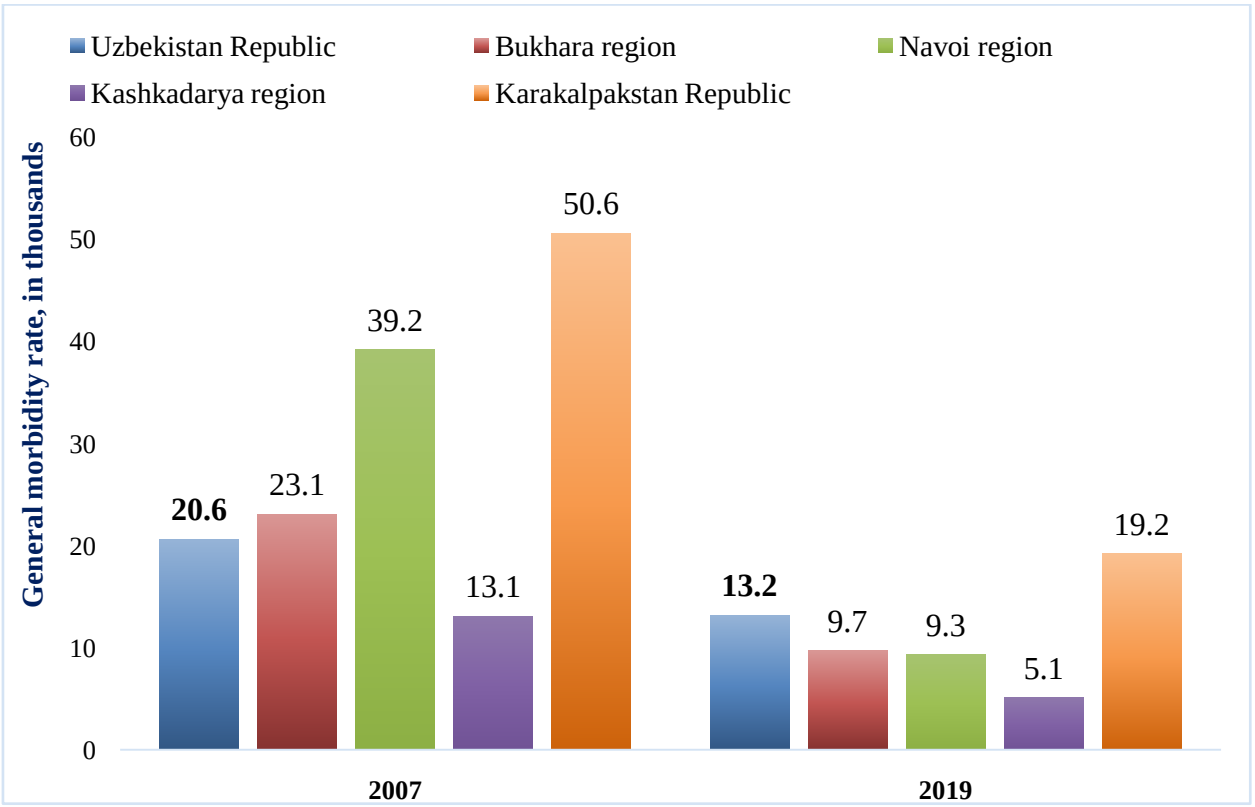


Figure 4: The indicator of the overall incidence of IDA per 100 thousand of the population in the most problematic regions and the whole Republic as a whole for 2007 and 2019.

It can be seen from the graph that consideration of the overall incidence rate per 100,000 population, depending on the age group, shows significantly higher numbers in children (under 14 years of age) and adolescents (15-17 years old) compared to the adult population. So in 2008, the total incidence of anemia was 22657 per 100,000 children, and 22,973 cases per 100,000 adolescents. In adults, this figure was 19347 cases. After increasing rates in 2008, the overall incidence in children and adults declined steadily over the next 9 years. In children, over the past period, there was a decrease in regression of the indicator by 28%, while in adults by 37%. At the same time, the average value of the annual regression was almost 750 cases in children ($R^2 = 0.9211$) and almost 870 cases ($R^2 = 0.947$) in adults per 100,000 population.

The dynamics of the general morbidity in the age group of adolescents during the specified period did not have a stable trend. The graph shows that during the first 3 years there was a significant decrease in incidence from 23% at the beginning to almost 20% in 2009. Over the next 3 years, there was a slight increase in the rate, which was replaced by a sharp decline over the next 2 years, when in 2014 the lowest rate was recorded equal to almost 19,000 cases per 100,000 adolescents. However, during the last 4 years of follow-up, there was a second increase in the rate, which in 2018 even surpassed the original rate of 2008 and amounted to 22,993 cases per 100,000 adolescents.

An analysis of the overall incidence rate per 100,000 population in the regional aspect is shown in Figure 4. Statistical data from Bukhara, Navoi and Kashkadarya regions, as well as the Republic of Karakalpakstan, were taken for the study, since these regions were considered the most problematic in terms of IDA prevalence for many years. The graph shows that in 2007 the overall incidence rate of IDA per 100,000 population in the Republic of Karakalpakstan was more

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than 2 times higher than the national average and amounted to 50.6 thousand cases. The indicators of the Navoi region were also almost 2 times higher than the national average, amounting to 39.2 thousand, while the incidence in the Bukhara region was only slightly higher, equal to 23.1 thousand. Only the indicators in the Kashkadarya region were 13 in 2007, 1 thousand, which was significantly lower than the national average of 20.6 thousand.

If we analyze similar data for 2019, it becomes clear that, like a decrease in the average indicator for the whole of Uzbekistan as a whole, there has also been a significant decrease in these regions. In all 4 regions, over the past 12 years, there was a decrease in the overall morbidity rate by more than 2 times compared to 2007. At the same time, in the Republic of Karakalpakstan and Navoi region, a regression occurred by 57% and 75 %, respectively. The data for 2019 suggests that only the indicators of the Republic of Karakalpakstan (21.6 thousand) significantly exceed the national average (13.8 thousand), while in other regions they are lower.

IV. Discussion

The prevalence of IDA among the population is an indicator that largely depends on socio-economic factors, since its development is associated with a lack of iron and other important nutrients in the body, that is, the quality of nutrition [8]. In this regard, the analysis of its dynamics makes it possible to understand the vector of development not only of health care, but also of other aspects of state life. The Republic of Uzbekistan is a developing state, in which a demographic growth of about 20% was observed over the 12 years studied. However, despite a significant increase in the population, the absolute number of IDA cases among the country's population over the past period has decreased by more than 26%. This regression shows that, in general, there has been significant progress in the country, associated not only with the improvement of methods of treatment and prevention of IDA, but also with a number of socio-economic changes in the life of the country.

The dynamics of the most important epidemiological indicators, indicators of general and primary morbidity showed that over the past period they decreased by 33% and 30%, respectively, while the value of the approximation reliability (R^2) in both cases was quite high, which provides a basis for statistics to expect further continuation of the regression of morbidity.

However, it should be noted that consideration of the dynamics of morbidity in separate age groups showed that adolescents (15-17 years old) did not show a general trend towards a stable regression over the studied time interval, and in 2018 the indicator turned out to be slightly higher than the initial one. Earlier in Exposure to extreme th incidence of IDA adolescents may be due to several reasons. Earlier it was shown that among the factors contributing to the development of IDA, in this age group are "growth spurt " , chronic blood loss (prolonged and abundant menstruation) and inappropriate nutrition [11, 12, 15, 16] .

Regional features of IDA prevalence were represented by higher morbidity rates in Navoi region and the Republic of Karakalpakstan, where in 2007 this pathology was found in almost every second inhabitant. Over the past 12 years, in these regions, a significant decrease in incidence rates has been achieved, however, in the Republic of Karakalpakstan, the rates are still almost 2 times higher than the average rates throughout the country.

In general, if we turn to the recommendations of the WHO [1 7,18], in the Republic of Uzbekistan for the period from 2007 to 2019 it was possible to achieve the transition of the category of importance of the IDA problem for public health from the average (prevalence 20.0-39.9 %) moderate (5.0–19.9 %). In some regions, where in 2007 the category of the problem was significant (≥40 %), over 12 years it was possible to achieve a transition to the category of medium importance. Nevertheless, the national average is still far from normal (4.9 %), which necessitates the continuation and deepening of preventive and health-improving measures.

V. Conclusion

Thus, the conducted epidemiological study showed that in the period from 2007 to 2019 in the Republic of Uzbekistan it was possible to achieve a significant regression of the incidence rates of iron deficiency anemia. However, in certain age groups, in particular among adolescents, the prevalence of the disease remains high, which requires the development of a new approach to treatment and prevention measures in them. Also, the analysis of regional features of the incidence of iron deficiency anemia shows that in some regions it is much higher than in the country as a whole, which requires a deeper study of pathology in a given area, the dynamics of its growth and factors that contribute to it.

Conflict of Interest

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

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The Indian Strategy of One Health Concept

By Sreeja Nair

Introduction- In nature, every microenvironment is provided with the resources necessary for the health care needs of the organisms living in. It is a widely accepted fact that the Indian Traditional Knowledge plays a key role in the pluralistic health care system concept. People believe that many of the health care questions arising in developing countries can be answered by this pluralistic approach. The "One Health Concept" is grabbing attention worldwide where the concept of health care is addressed to all living beings in the environment- human beings, animals and plants. An embracing approach towards Traditional system of medicine is getting due attention regarding the safety and efficacy of the products used. The techniques to learn these non-codified knowledge systems are refined and reoriented. One such technique is a Trans-disciplinary approach where the learning starts with an intradisciplinary analysis for understanding all the dimensions of a particular discipline. It would always be speculative to trace lines of congruence between kingdoms and species, from the platform of modern medicine. On the other hand, there are some systems of medicines where life is always perceived akin. Hence, in those systems, health care is pertinent with one another and so is the treatment schedule.

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Introduction

In nature, every microenvironment is provided with the resources necessary for the health care needs of the organisms living in. It is a widely accepted fact that the Indian Traditional Knowledge plays a key role in the pluralistic health care system concept. People believe that many of the health care questions arising in developing countries can be answered by this pluralistic approach. The "One Health Concept" is grabbing attention worldwide where the concept of health care is addressed to all living beings in the environment-human beings, animals and plants. An embracing approach towards Traditional system of medicine is getting due attention regarding the safety and efficacy of the products used. The techniques to learn these non-codified knowledge systems are refined and reoriented. One such technique is a Trans-disciplinary approach where the learning starts with an intradisciplinary analysis for understanding all the dimensions of a particular discipline. It would always be speculative to trace lines of congruence between kingdoms and species, from the platform of modern medicine. On the other hand, there are some systems of medicines where life is always perceived akin. Hence, in those systems, health care is pertinent with one another and so is the treatment schedule. Most of such systems study the pattern of life in all living beings, then the health status and finally intervene through a more or less analogous treatment method for all living beings. There might be difference in dose, administration or combinations based on the species, body weight, digestion pattern or habitat but the family of medicines are mostly the same.

The thought of one treatment can be further cemented based on the ancient and traditional system of treatment, which is now named as 'Ethnomedicine'. Traditional health care practices are in effect from centuries and have been passed down orally through generations (Martin et al., 2001). Livestock keepers relied on traditional practices even before the Modern medicine broke in. The scientific study of people-plant relationship with the usage of plants for health and wellbeing is termed 'Ethno botany' (Mathias, 2004). The term was firstcoined by the American botanist Dr. John William Harshberger, in 1895, in a lecture at Philadelphiato describe his field of inquiry. In his words, Ethnobotany is the study of "plants used by primitive and aboriginal people." In 1896, Harshberger published the term and suggested 'Ethnobotany' as a field which can throw some light on the 'cultural position of the tribes who depended on plants for food, shelter and clothing'.

A further nomenclature as 'Ethno Veterinary Medicine' and much more diplomatically as 'Ethno Veterinary Practices' is also in use for Traditional Animal Health Care Practices contemporarily. Ethno Veterinary Practices(EVP) are bunches of non-documented practical experiences on animal health care, which are transmitted through generations orally, with its origin back in 1800 B.C. during the reign of King Hamurabi of Babylon who formulated laws on veterinary fees and charged for treating cattle and donkeys (Van Veen, 1996). EVP often provides cheaper and easier options andas a result, many parts of the world are interested in the field of Ethno Veterinary research and development (Zschocke et al., 2000; Masika et al., 2000; Kone and Atindehou, 2008;Raikwar and Maurya, 2015). 80% of the world depends of such traditional practices for health care as per the World Health Organisation.

In cases where all other documented systems of treatment flounder, these non-documented medicines play wonders. In certain other cases, a balanced implementation of all the systems work well, which proves that all the systems consider life as a whole for all living beings. Though a modern intervention is very much necessary in certain acute and emergency cases, a follow up with any alternative technique can cure the condition to the hilt.

Ethno Veterinary Practices can mostly be related to Ayurveda, the ancient and holistic Indian system of medicine from 6000 B.C. Ayurvedic medical textbooks are written in Sanskrit, one of the oldest recorded languages of the world. The word 'Ayurveda' means "science (ved) of life (ayur)" in Sanskrit.

Indian medicine adopted an observational and rational procedure by the end of the Vedic period and emerged as Ayurveda, which gave the basic model of animal health care. Most of the documents of Ayurveda are in the ancient Indian language called Sanskrit, written by Palakapya, the father of Indian surgery (Palakapya, 1894; Mukhopadhyaya, 1926).

Gau-ayurveda (cows), Hastyayurveda (elephants), Ashvaayurveda (horses), Mrig-Ayurveda (animals), Vriksha-ayurveda (plants) etc are the various Ayurvedic text books written and followed by Indians during ancient eras. In the Indian epic Mahabharatham, it is mentioned that the two Pandavas, Nakula and Sahdeva were experts in veterinary medicine who

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mastered the use of plants for animal welfare (NakulaSamhita). Majority of the plants used by them are extinct already due to climatic drift and global warming. Most of the Ayurvedic herbs are unique, and used to grow in the exceptionally diverse panoply of ecosystems found only in India, supported by the more tropical climate and richly volcanic soil specific to the Himalayas and other mountain ranges (Boswellia serrate, Shilajeet). Hence preserving medicinal flora grabs equal importance in the current scenario.

Mahabharatam (~3000 bc) even introduces an animal trainer and a caretaker. Somavanshi has reviewed the ethnoveterinary resources in ancient India (Somavanshi, 1998). Chapters describing animal health care practices are there in Indian text books like SkandaPurana and Devi Purana.

Mrig Ayurveda or Animal Ayurveda is quoted from Rig Veda, the ancient religious text book of India (2000 to 4000 BC) where the practices are focused on animal welfare, treatment, management and surgery which were safe and effective and even with the backup of clinical trials. Ayurvedic Materia Medica, Mrig Ayurveda, Aswa Ayurveda (horse Ayurveda) and Hasti Ayurveda (elephant ayurveda) are the first text books in Veterinary Practices written by Salihotra. The first Veterinary Hospital was started by King Oshika in 1463 BC, and they depended exclusively onAyurvedic Botanicals.

Veterinary Ayurvedic text books explain a variety of edible products with indication of the different properties suitable for animals of a given temperament, comportment and health status, living in a particular climate and at a particular time of the day. A feed which is considered safe for a healthy animal may complicate another with a disease. Horses were never fed with grass, as it was said to weaken the vitality. Barley, beans and butter were considered good for pregnant mares. Sea salt is said to cure gastric disturbances, venous diseases and horses with sleeping difficulties, but it was not recommended for very old or very young horses. (Blondeau, 1972; Mazars, 1994).

In addition to medicines, Ayurveda also supports the administration of tonics and stimulants (rasayana), and aphrodisiacs (vajikarana) for enhancing general health. There were rasayana elixirs prescribed to strengthen animals and also for disease prevention.

A mixture of Asparagus racemosus, Emblicaofficinalis, Terminaliabellerica, Terminaliachebula, Tinosporacordifolia and Zingiberofficinale and a piece of buffalo horn based on aconite and three peppers was widely in use for extending the life span of horses.

Charaka Samhita (Siddhisthana, XI, 20-26) gives the formula for an enema mixture which can be used in elephants, camels, cattle, horses and sheep. The basic mixture contains a combination of Acoruscalamus, Glycyrrhizaglabra, Piper longum, Randaspinosa and Saussurealappa. A dozen of other plants are to be added to the basic ingredients for elephant enemas. For cattle, Buteamonosperma, Cedrusdeodara and Terminaliachebula should be added to the basic mixture. For Horses, Baliospermummontanum or Croton tiglium (Sharma, 1983) should be the addition to the base.

There are Traditional Ayurvedic alternatives to tonics, fortifiers and digestives, as well as anti-parasitic and antifungal products, most of which are polyvalent due to the multiplicity of ingredients in them. A stomachic and tonic containing 59 ingredients is manufactured by a company in Bangaluru, India, which is recommended for digestive disorders in animals. The main ingredients are Aeglemarmelos, Aquilariaagallocha, Buteamonosperma, Centratherumanthelminticum, Curcuma longa, Ferula narthex, Moringaoleifera, Piper longum, Punicagranatum, Terminaliabellerica, Terminaliachebula, Tinosporacordifolia, Trachyspermumammi and Zingiberofficinale, all of which are aperitive, digestive, stomachic and anthelmintic as perAyurvedic text books (Mazars, 1994). An ointment for sprains and sores is prepared from a mixture of Abrusprecatorius, Acoruscalamus, Celastruspaniculatus, Hyoscyamusniger, Moringaoleifera, Nardostachysjatamansi, Ocimum sanctum, Saussurealappa and Vitexnegundo. The combination is mixed with extracts of Anacyclus pyrethrum, Colchicum luteum, Curcuma amada, Gloriosasuperba, Litseasebifera, Myricanagi and Neriumodorum. (Chopra et al., 1956; Ambasta, 1986).

Nardostachysjatamansi mixed with the oil of Hyoscyamusnigercan be used as an antineuritic.

Ocimumtenuiflorum and Vitexnegundo can be used for wound dressing.

Curcuma amada root can be used to cure contusions and sprains.

Colchicum luteum extract can be used as an analgesic.

The evidence of health care provided for animals as mentioned in Ayurvedic text books states that veterinary medicine was so advanced from years aback. Documents with emphasis on the safety, efficacy, and dosing of medicinal herbs are available in Ayurvedic text books, that can guide a veterinarian in following Ethno Veterinary Practices

It is more like giving a wide angle to our belief of healthcareand wellbeing. A holistic approach towards animal health care can join hands with human health care, concluding that there is only 'one form of life, one pattern of health status and one line of treatment'.

In order to revitalize traditional practices, they have to be documented, assessed and promoted for community usage. Research and development can strengthen the local health traditions and bring scientific reasoning to the plant bases used in traditional treatment. Ethno Veterinary Practices need to be

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understood in all possible dimensions and all necessary worldviews so that they can be assessed in a way that is universally acceptable. Ethno Veterinary practices need to be mainstreamed for the use of field veterinarians through veterinary education and research.

The Indian Government has given a new impetus to these practices recently. Study and practice of traditional medicine has been regulated, and training is provided by various hospitals and care centres. Traditional practices got revised and revived as a result of plentiful movements. There are certain Indian laboratories where these ancestral recipes are followed for animal health care product manufacture. Hopefully, the campaign gets more recognition and acquiescence universally, setting the scene for a better health of all living beings by virtue of the solidarity of all the health care systems followed ubiquitously.

Glossary of Terms

1. Non-codified/Non-documented– Without the support of any written documents or language codes
2. Trans disciplinary– Relating to more than one discipline of knowledge
3. Intradisciplinary– Relation within the same discipline of knowledge
4. Ethno– A particular society and it's culture in the purest form
5. Ayurveda– The traditional Indian system of medicine based on the balance between bodily systems and their functions
6. Sanskrit– Ancient classical South Asian language
7. Mahabharatham- One of the two major Sanskrit epics of ancient India
8. Pandavas– Five brothers who are the main characters in Mahabharatham
9. Rig Veda– Oldest known Indian sacred canonical text with a collection of Sanskrit hymns

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Prevalence and Risk Factors for the Formation of Bronchial Asthma

By Naima N. Ubaydullaeva, Nematjon S. Mamasoliev & Bakhtiyor S. Ganiev

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Abstract- Bronchial asthma is a multifactorial disease. Industrial chemical compounds are also included in the list of causative factors of bronchial asthma. The contribution of industrial allergens to the formation of bronchial asthma is undeniable. In studies carried out in conjunction with professional pathologists, children were found to be sensitized to industrial allergens (nickel, chromium, formaldehyde, etc.), which contribute to the formation of bronchial asthma. However, determining factor, is the presence of atopy.

Keywords: *respiratory diseases, bronchial asthma, prevalence, risk factors.*

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Prevalence and Risk Factors for the Formation of Bronchial Asthma

Naima N. Ubaydullaeva [α], Nematjon S. Mamasoliev [σ] & Bakhtiyor S. Ganiev [ρ]

Abstract- Bronchial asthma is a multifactorial disease. Industrial chemical compounds are also included in the list of causative factors of bronchial asthma. The contribution of industrial allergens to the formation of bronchial asthma is undeniable. In studies carried out in conjunction with professional pathologists, children were found to be sensitized to industrial allergens (nickel, chromium, formaldehyde, etc.), which contribute to the formation of bronchial asthma. However, determining factor, is the presence of atopy.

Until now, bronchial asthma is sometimes considered as a condition of the respiratory tract, and not as a disease, as a heterogeneous syndrome, which can only be given a descriptive definition. Such conclusions lead to clinical uncertainty, erasure of nosological boundaries, and therefore to disorientation of the doctor.

Keywords: respiratory diseases, bronchial asthma, prevalence, risk factors.

I. Introduction

In the previous versions of the National Program (1997, 2006 - 2008), it is rightly indicated that bronchial asthma is an independent nosological form characterized by a complex pathogenesis. In children, the immunological mechanism of the development of the disease is the leading and decisive one. The question of non-immunological forms of bronchial asthma in children, as before, is the subject of scientific discussions. According to most researchers, nonspecific factors provoking bronchial asthma in children are secondary, and their effects are preceded by body sensitization and the development of allergic inflammation of the bronchi.

Modern genetic studies have proven the role of hereditary predisposition to the development of bronchial asthma; however, the phenotypic realization of the genotype is determined by the influence of environmental factors.

The key role in the development of bronchial asthma in children belongs to the IgE-dependent type of allergic reaction. Sensitization to allergens and their repeated exposure leads to asthma manifestations as a result of airway inflammation, reversible obstruction and increased bronchial reactivity. However, it is possible to involve non-allergic mechanisms of airway inflammation, which are not well understood in our time.

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II. Materials and Methods

The understanding of the immunological mechanisms of bronchial asthma is constantly deepening, new and new aspects of them are being discovered not only at the cellular, but also at the molecular level. The combination of various inflammatory mediators causes the whole complex of clinical manifestations characteristic of bronchial asthma. Bronchoconstriction, mucus hypersecretion, edema of the bronchial mucosa develop, bronchial hyperreactivity is formed. The dynamics of various immunological parameters correlates to a certain extent with the activity of inflammation and clinical symptoms.

Currently, the important role of infection, primarily viral, as a triggering factor in the development of bronchial asthma and the main trigger mechanism has been shown.

As clinical experience shows, typical for the overwhelming number of sick children are attacks of bronchial asthma, occurring in the form of difficulty breathing, paroxysms of expiratory suffocation. Atypical manifestations of bronchial asthma in children are sometimes expressed by attacks of persistent spasmodic cough.

Treatment approaches are determined by the severity and control of the disease. The development of severe exacerbations of bronchial asthma can pose a threat to the patient's life, and a severe exacerbation can develop with any severity of the course of the disease.

Bronchial asthma is a real life-threatening disease, which makes it necessary to pay special attention to the organization of medical care and social support for patients. Only under the influence of adequate and systematic pathogenetic therapy in children with bronchial asthma, a stable remission can be achieved.

Taking into account the above fundamental provisions, the following definition of bronchial asthma in children has been adopted:

Bronchial asthma in children is a disease based on chronic allergic inflammation of the bronchi, involving a number of cells, including eosinophils, neutrophils, mast cells, lymphocytes. This is accompanied by airway hyperresponsiveness, bouts of shortness of breath or

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suffocation as a result of widespread bronchial obstruction caused by bronchoconstriction, mucus hypersecretion, edema of the bronchial wall. Bronchial obstruction (under the influence of treatment or spontaneously) is reversible. The impact of allergens and various nonspecific factors on the respiratory tract provokes the development of acute reactions in the sensitized organism in the form of bronchospasm, edema of the bronchial wall, obturation of their lumen with mucus. Chronic allergic inflammation leads over time to structural changes in the bronchial wall (remodeling).The clinical manifestations of bronchial asthma in children depend on age. This is especially true for children in the first five years of life, which suggests appropriate approaches to diagnosis and treatment. In clinical practice, until now, bronchial asthma in children is often not diagnosed, the diagnosis is replaced by the concept of "obstructive syndrome", "obstructive bronchitis", "asthmatic component in 17 respiratory viral infections", etc. Episodes of recurrent cough and / or obstruction in 60–70% of children in the first six years of life are transient. Bronchial asthma (BA) is a heterogeneous disease (a disease characterized by chronic inflammation of the respiratory tract and diagnosed by respiratory symptoms such as wheezing, shortness of breath, tightness in the chest or coughing, variable in duration and intensity, combined with reversible obstruction. Chronic inflammation, respiratory hyperactivity and remodeling, which are at the heart of BA, are implemented with the participation of a large number of different types of cells and mediators, which determines the pathogenesis, phenotypes and endotypes of the disease. The cytokine cascade of an allergic reaction, which develops in a sensitized organism through repeated contact with an allergen, causes allergic inflammation, tissue damage, and contributes to narrowing and hyperreactivity of the respiratory tract [4]. In terms of frequency, current severity, disability and danger to life (especially in teenagers), BA is one of the most important problems in modern paediatrics (3). According to ISAAC, the true prevalence of BA in different regions of our country is 7-8 times higher than official statistics [1,2]. In the structure of hospital morbidity of the Uzbekistan, children with AD make up 33%, specialized children's pulmonary sanatorium - 45%, among patients with diseases of the bronchopulmonary system the level of disability from AD is 70%, which indicates the socio-economic importance of this problem for the region under consideration.

III. Results and Discussion

In recent years, allergic diseases have been increasingly referred to as the "global problem of our time" because of their high prevalence in children and adults (S.Yu. Kaganov, 1997; Patterson R., Gryammer L.K., 2000; Holgate S.T., Arshad S.H., 2004). A special place among allergic diseases belongs to bronchial asthma as one of the most significant and widespread diseases of childhood. The social significance of the disease and the impact of its nature on the state of the labor force in present and future society have necessitated large-scale epidemiological studies.

Epidemiological studies in recent years indicate that at least 5-10% of the child population and 5% of adults suffer from bronchial asthma (Chuchalin A.G. 2000; National Programme "Bronchial Asthma in Children. Treatment and Prevention Strategy "2006). At the same time, data on disease prevalence based on medical statistics is much lower, and there is also a discrepancy between the distribution of patients by the severity of bronchial asthma. Thus, according to official statistics, severe and severe forms of the disease are much more common in children than mild asthma, which differs significantly from the prevalence structure revealed by epidemiological methods, where mild asthma prevails (MizernitskyYu.L., Rosinova H.H. and others 2004; Geppe H.A., Mokina H.A., 2007). Thus, a significant proportion of children with a mild course of the disease are practically not diagnosed.

The published results of epidemiological studies conducted both in our country and abroad mainly concern the prevalence of bronchial asthma in large industrial centres, while the overall incidence of bronchial asthma in children living in rural areas has not been studied (E.G. Kondyurina, Elkina T.N., 1998; Petrova T.I. 2004; Chernyak B.A., Tyarenkova C.B., 2004; Asher M.I., Weiland S.K., 1998). In addition, there are practically no data on the prevalence of the disease in children of different age groups living in urban and rural areas, and the structure of the disease by severity depending on age is not described.

The State Programme for Staged Implementation of a Set of Measures for Early Detection and Treatment of Bronchial Asthma, Complication Prevention and Disability Development is a priority in the modern concept of health care development (V.A. Revyakina, 2005). This determines the importance of epidemiological research to obtain reliable data on the prevalence of the disease in various climatological and geographical regions, independent of the quality and level of health care development. However, the medical and social significance of such studies also lies in their ability to better understand the role of exogenous and endogenous factors in the development of such a multifactorial disease as bronchial asthma (Baranov A.A., 1999). Determining the ratio of internal factors to environmental factors in the prevalence of this disease in children, especially in connection with the growth of negative trends in the population health of children and various environmental problems, is a difficult but promising trend in pulmonology (VeltishchevYu.E., Fokeeva V.V., 1996). Such information allows us to

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expand our understanding of factors predisposing to the disease, and thus to make individual medical forecasts and, consequently, make the right decisions in planning both therapeutic and preventive work.

Thus, conducting transverse single-stage studies to examine the true prevalence or prevalence of bronchial asthma, in accordance with international recommendations, using a representative sample and a validated questionnaire followed by clinical, instrumental and immunological examination seems to be a relevant and up-to-date task.

Conflict of Interests

The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article and report on the contribution of each author.

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Ethical Approval

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Optimizing the Combination of Different Pulsed Nd: YAG Laser Beam Welding Process Parameters to Attain Minimum HAZ for Thin Cp.Ti with Ti-6Al-7Nb Sheets using Response Surface Methodology (RSM) Method

By Weaam Mohammed Moslim

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Abstract- The objectives of this study were to test the effect of Nd: YAG Laser welding parameters (WP, PE, Ton and WS) on the HAZ of C.P Ti and T-6Al-7Nb alloys. The chosen Nd: YAG Laser welding parameters were three levels and CCD was selected to design the experiments. A 2nd regression equation relating to outputs and Nd: YAG Laser welding parameters was developed by using RSM. The result conducted that all the main effects of input parameters, i.e., WP, PE, Ton, and WS were found to be highly significant in affecting the HAZ.

Keywords: Nd: YAG laser welding, Cp. Ti alloy, Ti-6Al-7Nb alloy, Heat affected zone(HAZ), RSM Technique.

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Keywords: Nd: YAG laser welding, Cp. Ti alloy, Ti-6Al-7Nb alloy, Heat affected zone(HAZ), RSM Technique.

I. Introduction

In the recent decade, commercially pure titanium (CP Ti) and titanium alloys have expanded in their range of dental applications- dental implants, crowns, and fixed/removable partial dentures, due to its superior biocompatibility. However, disadvantages of CP. Ti have also been pointed out, such as lake of mechanical strength for some dental applications and poor wear resistance. There is also a concern about the cytotoxicity of vanadium in Ti6Al-4V alloy, With high mechanical properties and biocompatibility, Ti-6Al-7Nb alloy was consequently introduced to be an alternative to CP.Ti or Ti-6Al-4V alloy as a dental casting alloy.

Soldering is a common method that joins dental alloy prostheses for clinical use although the corrosion resistance of the soldered materials is a concern. However, soldering is not suitable for joining CP.Ti or titanium alloys because of the decrease in corrosion resistance and biocompatibility due to the contact of different types of metal. Other methods for joining CP.Ti or titanium alloys have been introduced, such as plasma welding, tungsten inert gas (TIG) welding and infrared brazing, but the disadvantage of large heat affected zone created by plasma welding, TIG and infrared brazing was also reported, In addition, these methods require filler metals that could potentially reduce corrosion resistance. Against these disadvantages, laser welding has become a preferred method to join metals in dentistry, especially for CP. Ti and titanium alloys. As most of the studies focused mainly on CP. Ti, laser welding on titanium alloys, especially Ti-6Al-7Nb alloy, has not yet been sufficiently investigated[1].

Laser-beam welding has been emonstrated to be an effective technique for dental laboratory work[2,3]. In general, laser welding has some advantages compared with conventional dental soldering:

1. With the use of laser welding, it is easier and more simple to connect dental alloys because no further materials, such as investment or gas torches, are needed, and welding can be performed directly on the model[4,5].
2. Laser-welded pieces may have higher corrosion resistance because laser welding can weld parent metals without solder or with solder consisting of the same metal.
3. Because laser energy can be concentrated in small area, there is a smaller heat-affected zone.
4. Oxidation on the area surrounding the spot is minimal, because laser welding is performed in argon atmosphere.

Laser welding might be suitable for joining dental prostheses made of titanium because of its high reactivity to oxygen at high temperature[6-8].

Pulsed Nd: YAG laser welding is one of the few techniques suitable for joining thin sheet metals. Small heat affected zone (HAZ), low heat input periuniti volume, high degree of automation and high welding speed are the merits of laser welding technology[9]. Titanium alloys can be welded using a pulsed mode laser. In pulsed laser applications, a small molten pool is formed by each laser pulse and within a few milliseconds it resolidifies[10]. But the control of the Nd: YAG laser welding parameters to attain small HAZ in the CP. Ti and/or Ti6Al7Nb welding process remain huge

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problem in relation to their microstructure. Depending on the method, the weld could result in a very narrow or fairly wide fusion zone (FZ) and heat affected zone (HAZ) due to the heat input experienced by the work piece[11].

II. Materials and Methods

Experimental was carried out on commercial purity titanium (Ti) and Ti-6Al-7Nb with 100 × 50 mm and 1.5 mm thickness. The major chemical composition and mechanical/physical properties of this alloys are listed in Table 1. In the present investigation, all the experiments were performed on Pulse Nd-YAG laser welding as a source of laser (model Haas HL3006D), accompanied with high speed imaging (HIS), this laser is able to radiate a continuous wave mode (this mode was actually used in the experiments) with upto 3KW and predetermined were recorded using a high speed imaging system. Fig.1 is how the employed laser system. A coaxial nozzle is used purging pure argon gas (purity 99.998) with the laser beam. The pulsed Nd: YAG laser has adjustable pulse shape which offers high flexibility in optimizing the weld parameters to achieve defect free joints.

Table 1: Chemical composition of Ti and Ti -6Al-7Nb alloy used

Element	Ti	Ti-6Al-7Nb
Al	<0.005	7.0
V	0.011	<0.01
Cr	<0.005	<0.005
Cu	0.005	0.01
Fe	0.15	0.06
Mn	<0.005	0.02
Mo	<0.01	0.03
Nb	0.01	4.46
Sn	<0.02	<0.02
Ni	<0.005	0.005
Si	0.01	0.03
Zr	0.02	0.04
Pd	<0.01	<0.01
Ru	<0.01	0.01
Ti	Base	Base



Fig.1: Show the Pulse Nd: YAG laser welding system, (a) laser welding machine ; (b) laser generating device and (c) argon gas tube

III. Response Surface Methodology

Response surface methodology(RSM) is a combination of mathematical, statistical method and it can be used to develop the regression model and optimization of engineering problems [12]. It is one of the design of experiments method used to approximate an unknown function for which only a few values are computed. These relations are then modeled by using least square error fitting of the response surface. A Central Composite Design (CCD) is used since it gives a comparatively accurate prediction of all response variable averages related to quantities measured during experimentation[13]. CCD offers the advantage that certain level adjustments are acceptable and can be applied in the two-step chronological RSM. In these methods, there is a possibility that the experiments will stop with a few runs and decide that the prediction model is satisfactory. In CCD, the limits of the experimental domain to be explored are defined and are made as wide as possible to obtain a clear response from the model. The WP, PE, Ton, and WS are the welding variables selected for this investigation. The different levels taken for this study are depicted in Table

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2. The arrangement to conduct the experiments using a CCD with four variables, the cardinal points used are sixteen cube points, eight axial points and six center point, in total of 30 runs in three blocks[14]. The values of DOP and BW are shown in Table 3. The second order model is normally used when the response function is not known or nonlinear. In the present study, a second order model has been utilize. The experimental values are analyzed and the mathematical model is then developed that illustrate the relationship between the process variable and response. The second order model in equation (1) explains the behavior of the system[15].

$$Y = b_o + \sum_{i=1}^{k} b_i x_i + \sum_{i=1}^{k} b_{ii} x_i^2 + \sum_{i<j=2}^{2} b_{ij} x_i x_j \pm \varepsilon \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where Y is the corresponding response, X_i is the input variables, X^2_{ii} and X_iX_j are the squares and interaction terms, respectively, of these input variables. The unknown regression coefficients are β_o, β_i, β_{ij} and β_{ii} and the error in the model is depicted as ε.

Table 2: Input Variables used in the experiment and their levels

Coded Factors	Actual Factors	Parameters	Unit	Coded /Actual levels		
				-1	0	1
A	WP	workpieces type	-	AA	AB	BB
B	PE	pulse energy	J	9	12	15
C	Ton	pulse duration	μsec	4	6	8
D	WS	welding speed	mm /sec	3	5	7

NOTE:
A: C.P Ti
B: Ti-6Al-7Nbi
AA: C.P Ti + C.P Ti (similar)
BB: Ti-6Al-7Nb + Ti-6Al-7Nb (similar)
AB: C.P Ti+ Ti-6Al-7Nb (dissimilar)

Table 3: Design layout & experimental results (CCD)

Run Order	Pt Type	Blocks	WP ---	PE J	Ton μsec .	WS mm /s	HAZ μm
1	1	1	-1	-1	-1	1	2893
2	1	1	1	-1	-1	-1	1377
3	1	1	-1	-1	1	-1	3472
4	1	1	-1	1	-1	-1	3568
5	1	1	1	1	-1	1	1653
6	0	1	1	-1	1	1	1488
7	1	1	0	0	0	0	2382
8	0	1	0	0	0	0	2379
9	1	1	-1	1	1	1	3468
10	1	1	1	1	1	-1	1835
11	0	2	0	-1	0	0	2268
12	1	2	0	0	0	0	2382
13	1	2	0	0	0	1	2257
14	0	2	0	0	0	-1	2507
15	1	2	0	0	-1	0	2290

Table 3: Design layout & experimental results (CCD) (Contd.)

Run Order	Pt Type	Blocks	WP ---	PE J	Ton μsec .	WS mm /s	HAZ μm
16	1	2	1	0	0	0	1588
17	1	2	-1	0	0	0	3335
18	1	2	0	0	1	0	2474
19	1	2	0	0	0	0	2380
20	1	2	0	1	0	0	2518
21	0	3	-1	1	-1	1	3211

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22	-1	3	-1	-1	1	1	3125
23	-1	3	0	0	0	0	2378
24	0	3	-1	-1	-1	-1	3215
25	-1	3	-1	1	1	-1	3854
26	-1	3	1	-1	1	-1	1653
27	-1	3	1	1	1	1	1651
28	-1	3	1	1	-1	-1	1837
29	-1	3	1	-1	-1	1	1377
30	-1	3	0	0	0	0	2384

PtType 1 indicates a cube point of the design ;
PtType 0 indicates a center point ;
PtType -1 indicates an axial point ;

The unknown coefficients are determined from the experimental data as presented in Table 4. The standard errors in the estimation of the coefficients are tabulated in the column 'SE cofi.'. The F ratios are calculated for 95% level of confidence and the factors having p value more than 0.05 are considered in significant (shown with * in p column). For the appropriate fitting of HAZ, the non significant terms are eliminated by the backward elimination process. The regression model is re evaluated by determining the unknown coefficients, which are tabulated in Table 5. The model made to represent HAZ depicts that the pure quadratic effect of workpiece type (WP2) as well as the two way interactions of workpiece type with pulse energy (WP×PE), workpiece type with pulse duration (WP×Ton), workpiece type with welding speed (WP× WS) pulse energy with pulse-on time (PE×Ton) and pulse energy with pulse duration (PE×Ton) were also found to be extremely important terms influencing HAZ. The final response equations for HAZ are given in equations(2).

$$HAZ = 2383.3 - 871.22 \times WP + 151.50 \times PE + 88.83 \times Ton - 121.94 \times WS + 94.5 \times WP^2 - 19.69 \times WP \times PE - 40.56 \times WP \times Ton + 54.94 \times WP \times WS - 21.06 \times PE \times Ton \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

Table 4: Regression Coefficients for HAZ Model Parameters (before Elimination)

Term	HAZ model		
	Coef.	T-value	P-value
Constant	2380.3	213.87	0.000
WP	-871.22	-103.16	0.000
PE	151.50	17.94	0.000
Ton	88.83	10.52	0.000
WS	-121.94	-14.44	0.000
WP × WP	81.7	3.67	0.002
PE ×PE	13.2	0.59	0.561*
Ton × Ton	2.2	0.10	0.921*
WS × WS	2.2	0.10	0.922*
WP × PE	-19.69	-2.20	0.044
WP × Ton	-40.56	-4.53	0.000
WP × WS	54.94	6.13	0.000
PE × Ton	-21.06	-2.35	0.033
PE × WS	-17.31	-1.93	0.072*
Ton × WS	-13.69	-1.53	0.147*
R^2	99.87		
$R^2_{adj.}$	99.75		
$R^2_{pred.}$	98.92		

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Table 5: Finalized Regression Coefficients for the Individual HAZ Model Parameters (after Backward Elimination)(Contd.)

Term	HAZ model		
	Coef.	T-value	P-value
Constant	2383.3	221.15	0.000
WP	-871.22	-99.01	0.000
PE	151.50	17.22	0.000
Ton	88.83	10.10	0.000
WS	-121.94	-13.86	0.000
WP × WP	94.5	6.79	0.000
PE × PE	–	–	–
Ton × Ton	–	–	–
WS × WS	–	–	–
WP × PE	-19.69	-2.11	0.048
WP × Ton	-40.56	-4.35	0.000
WP × WS	54.94	5.89	0.000
PE × Ton	-21.06	-2.26	0.035
PE × WS	–	–	–
Ton × WS	–	–	–
R^2 (%)	98.38		
$R^2_{Adj.}$ (%)	97.87		
$R^2_{Pred.}$ (%)	96.62		

Since, YAG laser welding process is non linear in nature, a linear polynomial will be not able to predict the response accurately, and therefore the second order model (quadratic model) is found to be adequately modeled the process. The ANOVA table for the curtailed quadratic model Table 6, depicts the value of the coefficient of determination, R^2 as 99.93% and 99.96%, which signifies that how much variation in the response is explained by the model. The higher of R^2, indicates the best fitting of the model with the data. The model adequacy checking includes the test for significance of the regression model, model coefficients, and lack of fit, which is carried out subsequently using ANOVA on the curtailed model Table 6. The total error of regression is the sum of errors in linear, square, and interaction terms.

Table 6: ANOVA Table for the Trimmed HAZ

Source	DF	Adj SS	Adj MS	F	P
For HAZ					
Regression	9	14637610	1626401	1167.02	0.000
Linear	4	14485360	3621340	2598.49	0.000
WP	1	13662507	13662507	9803.52	0.000
PE	1	413140	413140	296.45	0.000
Ton	1	142045	142045	101.92	0.000
WS	1	267668	267668	192.06	0.000
Square	1	64336	64336	46.16	0.000
WP × WP	1	64336	64336	46.16	0.000
Interaction	4	87915	21979	15.77	0.000
WP*PE	1	6202	6202	4.45	0.048
WP ×Ton	1	26325	26325	18.89	0.000
WP ×WS	1	48290	48290	34.65	0.000
PE ×Ton	1	7098	7098	5.09	0.035
Error	20	27873	1394		
Lack-of-Fit	15	27848	1857	373.80	0.000
Pure Error	5	25	5		
Total	29	14665483			

Table 7 presents the Nd: YAG Laser welding parameters for each run order, along with the experimental results (expt.), the predicted response (Pred.) and the residues (Res.). Where the residues are the difference between the experimentally observed data and the model predictions. The predicted values of HAZ achieved using Equation 4. 4 is close to the experimental values confirming the sufficiency of the model and the residues are further analyzed in the following section.

A complete residual analysis has also been done for every developed response and the graph is

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shown in Fig.2. The normal probability plot is a graphical technique for evaluating whether a data set is approximately normally distributed. Normal probability plot of residual reveals that experimental data are spread approximately along a straight line, confirming a good correlation between experimental and predicted values for the response (Fig.2(a)) In graph of residual versus fitted values(Fig.2(b)) only small variation can be seen. The histogram of residuals (Fig.2(c)) also show Gaussian distribution which is desirable, and finally, in residual against the order of experimentationsv in Fig.2(d) both negative and positive residual are apparent indicating no special trend which is worthy from statistical point of view. As a whole, all the yielded models do not show any inadequacy.

Table 7: Comparison between Experimental and Model Prediction Results for HAZ

Run Order	WP ---	PE J	Ton μsec .	WS mm /s	Average HAZ (μm)		
					Expt.	Pred.	Resi.
1	-1	-1	-1	1	2893	2883.44	9.5599
2	1	-1	-1	-1	1377	1443.38	-66.3845
3	-1	-1	1	-1	3472	3503.50	-31.4956
4	-1	1	-1	-1	3568	3594.33	-26.3289
5	1	1	-1	1	1653	1642.50	10.5044
6	1	-1	1	1	1488	1482.66	5.3377
7	0	0	0	0	2382	2380.30	1.7018
8	0	0	0	0	2379	2380.30	-1.2982
9	-1	1	1	1	3468	3422.61	45.3933
10	1	1	1	-1	1835	1865.55	-30.5512
11	0	-1	0	0	2268	2242.04	25.9649
12	0	0	0	0	2382	2380.30	1.7018
13	0	0	0	1	2257	2260.59	-3.5906
14	0	0	0	-1	2507	2504.48	2.5205
15	0	0	-1	0	2290	2293.70	-3.7018

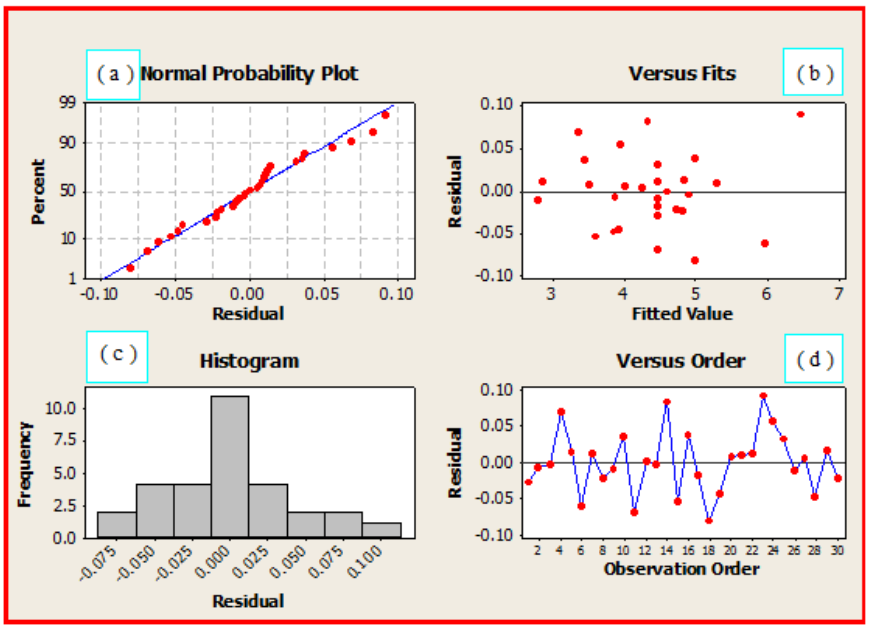


Fig. 2: Residual Plots for HAZ

IV. Result and Discussion

Fig. 3, depicts the main effect plots of the four controllable parameters on HAZ. It is understandable that all variables have more influential impacts on HAZ. The results in the Table 6 support this.

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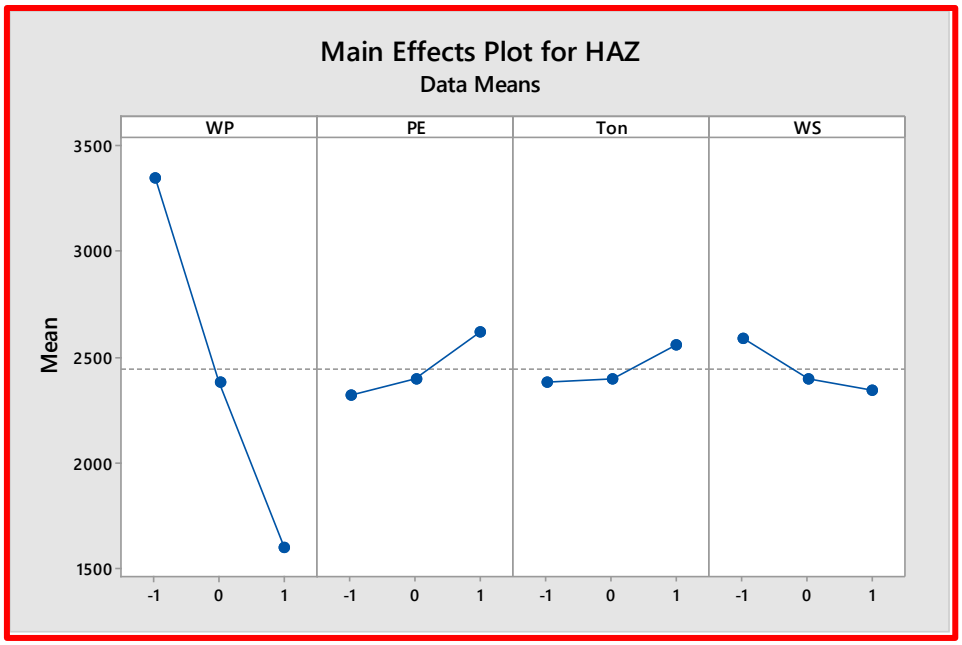


Fig. 3: Main Effect Plots for HAZ

More specifically, transforming the WP alone from C.P. Ti to Ti-6Al- 7Nb, while keeping the other factors constant at their middle levels, can decrease HAZ by110 % (from 3335 µm to 1588µm), which is a higher difference interval than those created by other parameters. This is probably because C.P. Ti has more thermal conductivity than Ti-6Al- 7Nb. The heat input is directly related to the average laser power, the welding speed and welding efficiency. It can be calculated directly from[16]:

$$\text{Heat input} = (\text{ALP}/\text{WS}) \times \eta \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

Where, (ALP) is average laser power, WS welding speed and η is the welding efficiency. According to above, it is evident that the HAZ increase when the PE increases and (WS) decreases, HAZ increases by 11% (from 2268 µm to 2518µm), with PE increases (from 9 J to 15 J) and HAZ decreases by 10% (from 2507 µm to 2257µm), with WS increases (from 3 mm/sec to 7 mm/sec), When the pulse duration increases, the heat input also increases and the HZA increases, HAZ increases by 8 % (from 2290 µm to 2474 µm), with Ton increases (from 4 µsec to 8 µsec).

The HAZ response surface plot with regard to WP and PE are depicted in Fig. 4. As always smaller HAZ is demanded, they can be reached at the higher level of WP and lower level PE. This is due to the weak thermal conductivity of Ti6Al7Nbicompared to CP. Ti and low heat with low energ.

Fig. 5 shows the concurrent effect of WP and Toni. It is obviously visible that higher HAZ can be obtained choosing a higher level of WP (Ti-6Al- 7Nb) with lower Ton. The low HAZ of Ti6Al7N brand decrease in discharge energy on the WP and therefore HAZ decreases.

The effect of WP and WS on the estimated response surface of HAZ is depicted in Fig. 6, PE and Ton remain constant in their middle level of 12 J and 6 µsec, respectively. It can be noted that the HAZ decreases when WP remain at high level and WS at lowr level, for the same reason mentioned above for the WP and the low generated heat accumulation with low WS.

Fig. 7 shows the estimated response surface for HAZ in relation to the process parameters of PE and Ton while WP and WS remain constant at their middle value. It can be seen from the figure, the HAZ tends to increase with the increase in PE and Ton. This can be attributed to the raise the input energy.

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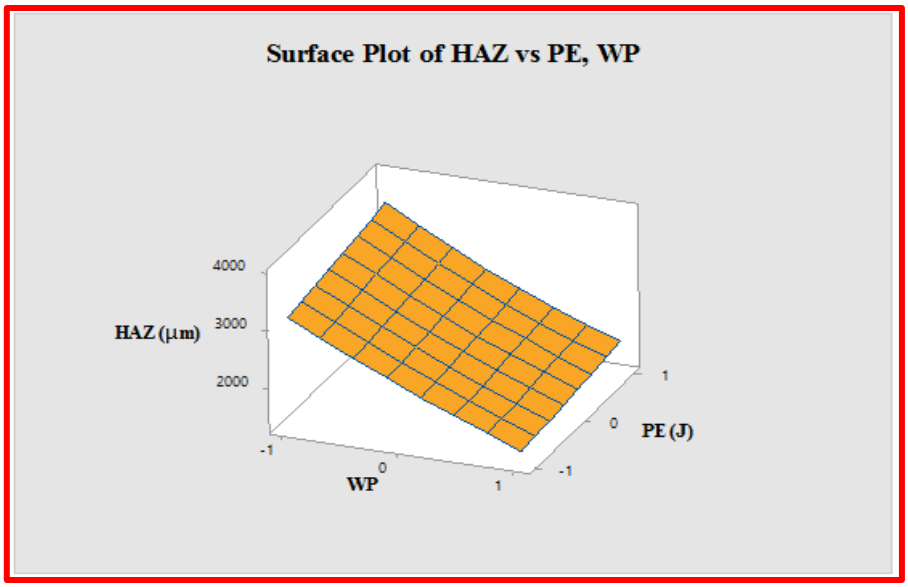


Fig. 4: Response Surface Plot of HAZ versus WP and PE

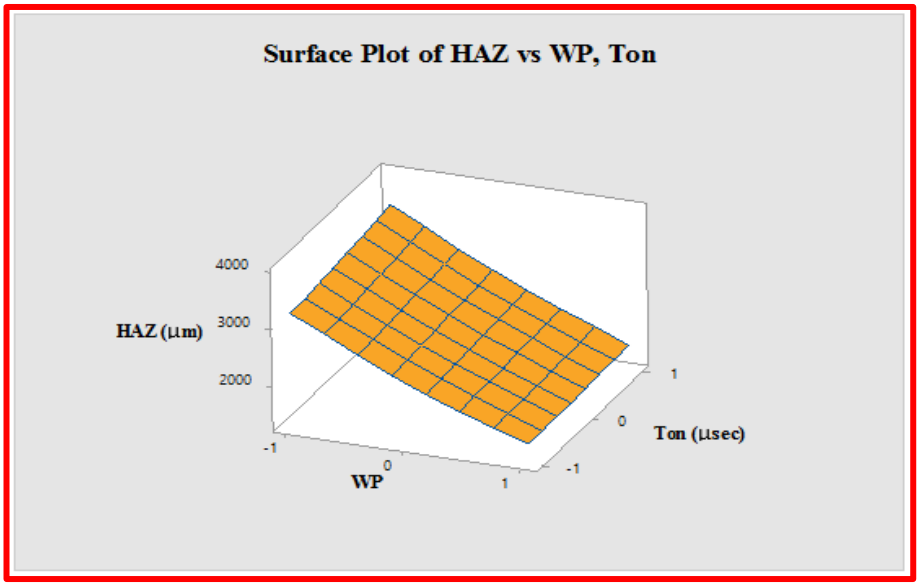


Fig. 5: Response Surface Plot of HAZ versus WP and Ton

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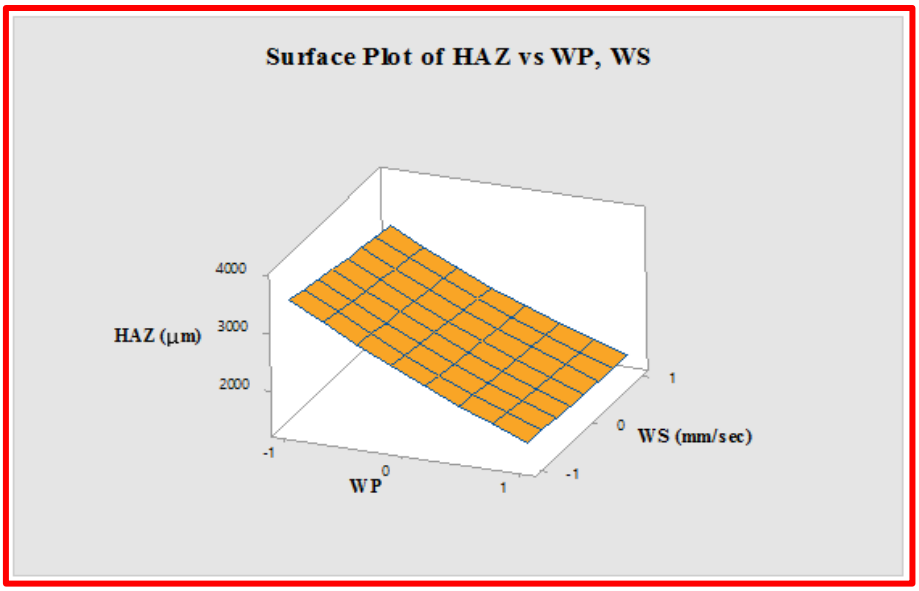


Fig. 6: Response Surface Plot of HAZ versus WP and WS

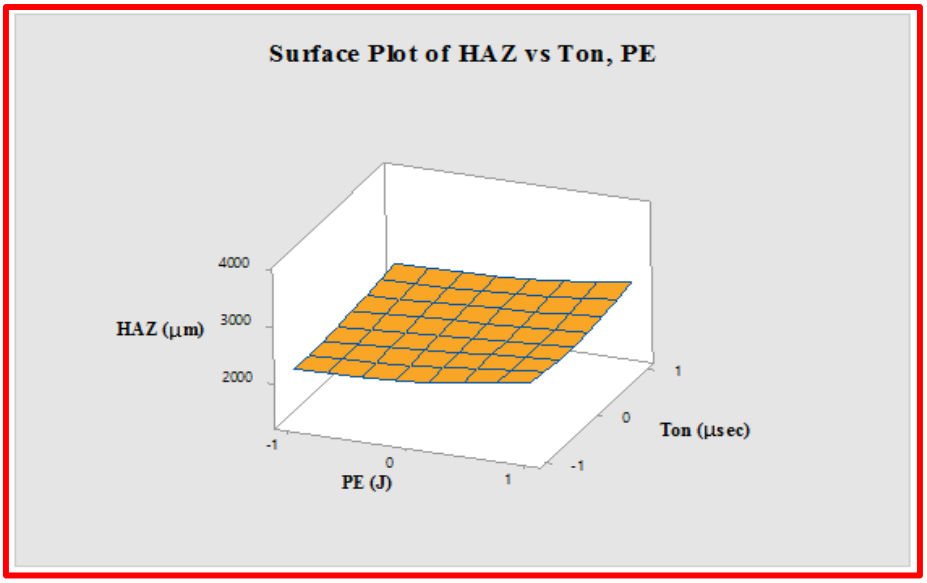


Fig. 7: Response Surface Plot of HAZ versus PE and Ton

V. Conclusion

In this study HAZ of welded (C.P. Ti and Ti-6Al-7Nbralloys) via variable parameters PE, Ton, and WS as well as WP which is an essential point of pulsed Nd: YAG laser were analyzed. The significant items were concluded as following:

1. All the main effects of input parameters, i.e., WP, PE, Ton, and WS were found to be highly significant in affecting the HAZ.
2. In the HAZ response, changing WP from C.P. Ti to Ti-6Al-7NB and increasing WS results in decreasing in the HAZ, whereas an increasing PE and Ton causes there verse effect.
3. The interaction effects of (WP×PE), (WP×Ton), (WP×WS) and (PE×Ton) as well as only pure quadratic (squarer) of (WP2) have been found to significantly control the HAZ.
4. Multi response optimization indicates that the optimal combination of parameter settings are WP with number 9 and 27, PE of 15J, Ton of 0.888 µ sec and WS of 0.756mm/sec for achieving the required lower HAZ.
5. The error between experimental and predicted values at the optimum combination of parameter settings for HAZ lies within 0.1919%. Obviously, this confirms excellent reproducibility of the experimental conclusions.

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An Overview of the Immune Dysregulation in COVID-19 with Immunization Priority in the Indian Context

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University of Calcutta

Abstract- The review was aimed at understanding the immune dysregulation by the novel virus, COVID-19. The review also highlighted the major findings that have been published in the previous studies through secondary research about the mechanism of immune dysregulation, transmission and progression of the virus across the globe. Adults above the age of 60 years and with co-morbidities such as cardiac and renal dysfunction, hypertension and diabetes are predisposed to greater risk of COVID-19 infection. The virus impairs the physiological, psychological and metabolic functioning of the patient. The paper gained an insight into the need for immunization priority for the Indian population and recommendations for the effective policy making in vaccine development and distribution.

Keywords: Covid-19, transmission, immune dysregulation, Covid-19 vaccine, immunization, immune dysregulation.

GJMR-K Classification: NLMC Code: WD 308



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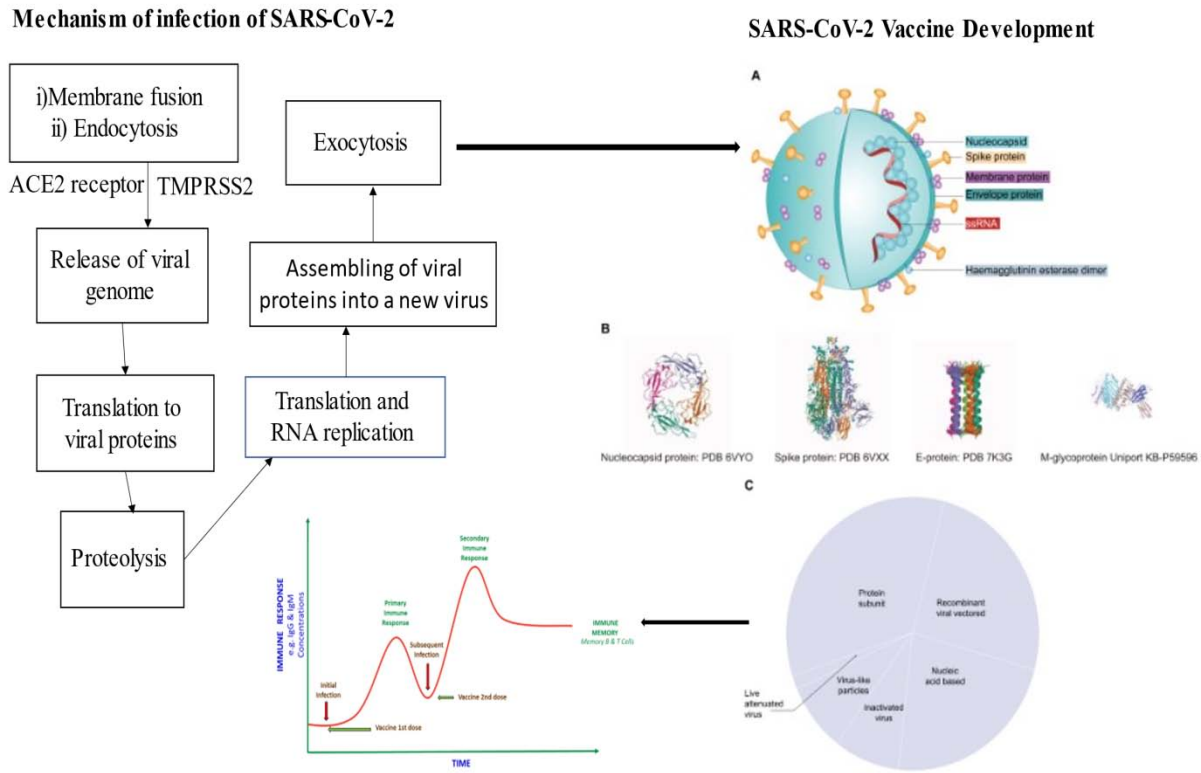
An Overview of the Immune Dysregulation in COVID-19 with Immunization Priority in the Indian Context

Aditi Munmun Sengupta [α], Diptendu Chatterjee [σ], Salil Kumar Bhattacharya [ρ] & Rima Ghosh [ω]

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Keywords: *Covid-19, transmission, immune dysregulation, Covid-19 vaccine, immunization, immune dysregulation.*

Graphical Abstract



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Types of COVID-19 Vaccines

Active Immunity (Vaccination)

- DNA Vaccine(Inovio)
- RNA Vaccine(Moderna , Pfizer)
- Viral Vector(Oxford,Astrazeneca,Janssen,Gamalaya - Sputnik,CanSino Biologics)
- Viral Subunit (Novavax,Adaptvac,Clover Biopharma)
- Live Attenuated(Codagenix,Indian Immunologicals Ltd.)
- Inactivated Virus (Sino Vac, SinoParm)
- VPL(Virus Like Particles)
- Split Virus Vaccines (eg. Flu Vaccines)
- RNP(Ribonucleoprotein) Vaccine.

Passive Immunity (Antibody Administration)

- Antibodies

Monoclonal Antibodies(e.g.Bamlanivimab)
Polyclonal Antibodies(e.g.Regeneron)

- Convalescent Plasma
- mRNA induced Antibody

Vaccine availability and Eligible groups

a)Health care workers and first responders
b)Patients with one or more comorbidities
c)Patients over 65 years with no comorbidities
d)Over 65 years in congregate settings
e)Essential workers not fitting other categories
f)Street residents and homeless

Expected Herd immunity threshold : approximately 70%

I. Introduction

Until the outbreak of Corona virus (CoV), this family of viruses was greatly overlooked. With the outbreak of SARS, these viruses are being studied in elaborate propelling the research for vaccines. After the emergence of mysterious cases of pneumonia detected in the Wuhan city (China), this causative agent transmitted extensively to 210 countries and across territories. According to the World Health Organization (WHO), this disease is referred to as Corona virus Disease-2019 (COVID-19) suspected to have its origin from Huanan seafood market. Ji et al., (2020) made the first claim and identified snakes as COVID-19 host and then many claims were made until experts collectively concluded that bats harbor the virus (Gorbalenya et al., 2020). The main mode of COVID-19 transmission is human-human via droplets generated during sneezing, coughing or talking inhaled by a healthy individual (Keni et al., (2020). Asymptomatic carriers are super infectors with no sign or mild symptoms of the disease posing challenges for the Indian Government on how to identify them as they could account for 80% of the infections (Keni et al., 2020).

Apart from cytopathic effects witnessed in non-survival COVID-19 cases, immune dysregulation substantially contributes to pathogenesis. Immunomodulatory agents like glucocorticoids, interleukin-6 blockers have been observed to be beneficial for the treatment. This virus is associated with reduction in number and function of the CD8+ T-cells and NK-cells (Natural Killer) leading to immune dysregulation and delayed viral clearance (Praveen et al., 2020). The combination of antiviral drugs like remdesivir, IFN therapy and hydroxychloroquine combined with immunomodulatory therapy in hyper-inflammatory phase can be considered a suitable approach in COVID-19 management. The development of a vaccine with use of mRNA-based approach can be a more viable option for producing immunity against COVID-19 including isolated spike virus proteins and live attenuated virus.

As recognized by WHO, immunization through vaccination is the need of the hour and essential health service to be taken up by the countries for the prevention of COVID-19 (World Health Organization, 2020). Scientists around the world are joining hands to develop vaccines to impede the progression of this overwhelming pandemic. Moderna and the Vaccine Research Centre is working on mRNA based vaccine encapsulated in lipid nanoparticles whereas Serum Institute of India in collaboration with Codagenix is currently focused on development of live attenuated vaccine. Biotech ventures in India are working together to develop subunit vaccines, inactivated viral vaccines, attenuated recombinant vaccines and using codon-optimization. Therefore, the following review paper will gain insights into the emergence, transmission, immune dysregulation concerning public health, immune response of the individuals, and overview of vaccine development and understanding of COVID-19 vaccine.

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II. Literature Review

a) Impact of COVID-19 regarding the health concern

For the past 30 years, novel coronavirus is a once-per-decade that has pushed health infrastructure to limits posing a serious health concern. Transmissibility and severity of the disease are the two critical factors that would determine the public health impact of the pandemic. The virus has high transmission rate and quite severe case fatality rates (CFR) is greater being a potential health threat (Binns, Low & Kyung, 2020). The pandemic has affected millions of lives making them sick or being killed due to disease spread. One out of every six individuals gets affected by the virus and develops difficulty in breathing. They can also develop pneumonia and breathing complications requiring urgent medical admission. COVID-19 majorly affects the respiratory system causing shortness of breath and coughing. People above the age of 60 years are at high risk of severe infection. The body's immune response to the infection includes fever, pneumonia, loss of taste and smell, sore throat, muscle pain and cough. It has a major impact on health where tiny sacs in lungs are filled with fluid causing breathing difficulty. People with serious heart conditions, type 2 diabetes, weakened immune system due to transplant or surgery, kidney and respiratory diseases are at higher risk of being infected. The incubation time is 2-14 days during which the suspected patients remain in quarantine. Patients suffer from acute respiratory distress syndrome (ARDS) that requires ventilation and it has been observed that mortality rate becomes high within two days of admission (Zheng et al., 2020).

The main cause of death is the inflammation of lungs discussed above that serves as an entry point for infections associated with secondary infections, coagulopathy and end-organ failure (Shi et al., 2020). The age-dependent defects like excess type 2 cytokines production in the B-cell and T-cell may lead to delayed pro-inflammatory responses and deficiency in viral replication control leading to poor health outcomes. In addition, bacterial infections could also cause sepsis syndrome reported in 40% of community-acquired pneumonia because of viral infection (Chaubey, 2020). About 58,064,186 are infected cases with a mortality rate of 1,380,548 worldwide. In India, out of 90,54,528 confirmed cases, 1,32,797 are deceased cases with a recovery rate of 84,80,299 (Worldometer, 2020). The deaths are occurring among people aged above 60 years and with underlying comorbidities. COVID-19 is resulting in severe disease posing a public health system including admission to intensive care units, hospitalization and death. The cases are doubling every 5-10 days challenging the health system and disrupting the socio economic condition of India.

80% of COVID-19 cases are asymptomatic or mild with 15% and 5% critical infections requiring oxygen and ventilation ensuring case isolation. The increased severity and mortality of the disease includes individuals above the age of 55 years with multiple co-morbidities, hypertension, obesity, immune-suppression and hypoxia. This predisposes patients to unfavorable treatment with increased risk for in tubing and death (Verity et al., 2020). In a paper published by Gallo Marin et al., (2020) the disease severity includes coagulation defects, cardiac dysfunctions, alterations in WBC blood cell counts, liver injury and renal dysfunction. Large-vessel stroke is one of the major health concerns that have been witnessed in severe COVID-19 cases even in younger patients. 12 out of 67 patients died on admission due to elevated D-dimer levels, developed hypercoagulability, delayed prothrombin time and thrombocytopenia (Zhang et al., 2020). Liu et al., (2020) studied that severe fulminant myocarditis and systolic dysfunction were reported in COVID-19 patients. The patients who received ICU care were more likely to suffer from acute cardiac injury as compared to non-ICU patients with elevated troponin levels being an independent risk factor for mortality.

Another health concern in COVID-19 patients is WBC count alterations along with lower granulocyte counts linked to severity of the disease. Huang et al., (2020) conducted a meta-analysis and identified that significant reductions in lymphocyte counts, B cells, CD8+ T cells and CD4+ cells and NK cells is associated with severe COVID-19 cases as compared to mild or moderate cases. Huang et al., (2020) highlighted that in critical COVID-19 patients, elevations in level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are more likely to occur and end-organ damage. The need for mechanical ventilation increases for patients with hypoalbuminemia, abnormal liver enzyme levels also being an independent predictor of COVID-19 mortality. Kidney dysfunction and failure has been reported in severe COVID-19 cases (Guan et al., 2020). Systemic inflammatory and vascular complications may be indicative of renal failure strongly suggesting that this virus has the capacity to infect the tubular renal epithelium. Therefore, to improve health outcomes in COVID-19 patients, it is vital to identify and validate the predicting factors in COVID-19 progression.

b) Overview of the immune response concerning COVID-19 infection

As COVID-19 virus in severe patients mainly spreads to the respiratory tract with cytokine storms and lymphopenia as accompanying agents, the early recognition of immunological phenotypes can be helpful in prompt identification of patients who would progress to severity. The virus has a crown-like single stranded RNA having a ridge on the concave surface. It has a large binding interface that makes more contact with the N-terminal of Angiotensin-Converting Enzyme 2(ACE2) with greater affinity (Ong et al., 2020). The virus is

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transmitted through droplets from sneezing and coughing entering the nasal system through inhalation. It then gradually starts replicating where ACE2 acts as the main receptor. The spike (S protein) on the surface of the virus enters inside the host cell and binds to the ACE2 receptor. The enzyme, furin present in the host cell acts as the main factor for the virus entry into the host. The virus starts to propagate with the help of the host's innate immune response and as such is detected in nasal swabs. Then, it reaches the respiratory tract when there is clinical manifestation of the disease as cytokine (innate response), may be a predictor of the clinical course (Chowdhury et al., 2020). For 80% Individuals with mild or moderate symptoms has virus infection mainly restricted to conducting and upper airways that can be managed at home. However, rest 20% of them develops severe cases due to pulmonary infiltrates leading to high mortality rates. Once COVID-19 virus reaches the alveolar and bronchiolar spaces, it targets the bronchial epithelium cells and type-II ACE2+ pneumocytes in alveolar epithelium. It induces autophagy, basal membrane detachment and ACE2 expression inhibition. Hence, it allows angiotension II binding to the AT1aR receptor resulting in acute damage of lungs. Here, the infected cells show early defense mechanisms through production of IFN (type-III and I) activating inhibition. Later, virions release reaches the neighboring cells resulting in systemic infection by ACE2+ widely distributed in tissues (Azkur et al., 2020).

When our body detects a novel pathogen or virus like COVID-19, the defensive cells in innate immunity release cytokines that alerts the other cells involved in immunity. After the virus entry into the host cell, the Pattern Recognition Receptors (PRR), TLR7 and TLR8 are expressed by the epithelial and local cells of the innate immunity like alveolar macrophages. PRRs after ligand binding, recruits adaptor proteins for the activation of down-stream transcription factors like NF-κB, interferon regulatory factor (IRF) and AP-1 for the production of chemokines and antiviral Interferons (Type-I and -III) (Mortaz et al., 2020). The innate response cells like monocytes, dendritic cells (DCs) NK cells and polymorphonuclear leukocytes that in turn produce more chemokines like MCP-1, IP-10 and MIG that are capable of lymphocytes recruitment. This, in turn, makes DCs recognize the COVID-19 virus antigens. This is supported by the fact that viruses infect pneumocytes (type-I and type-II), alveolar macrophages depicting better capacity of replication in pulmonary tissues supported by elevated serum levels in positive patients (Prompetchara, Ketloy & Palaga, 2020).

The transition from innate to adaptive responses is quite critical for the infection progression. Although poorly understood, the immune regulatory cells may develop either exacerbated or protected inflammatory response. The protective response is provided by T cell dependent cells with CD4 aided B cells binding geared towards neutralizing antibodies production and elimination of infected cells by cytotoxic CD8 cells. In 80% of cases, CD8 acts as infiltrating cells. The exacerbated response is unable to inhibit and eliminate the viral replication in the infected cells leading to cytokine storm and disseminated intravascular coagulation peak at day 14 up to day 28 (Giamarellos-Bourboulis et al., 2020).

NK cells and Cytotoxic lymphocytes (CTLs) are also important for the viral infection control and exhaustion of functional cytotoxic lymphocytosis that may increase the severity of the disease. The cell numbers and function decrease with up regulation of NK inhibitory receptor CD94/NK group 2 member A (NKG2A) upregulation in COVID-19 comprising immune response. There is an increase in T cell apoptosis with decreased CD4+ and CD8+ T cells in the COVID-19 patient's peripheral blood. In addition, these cells have impaired activation with the appearance of CD25, CD28, and CD69 on the subsets of T cells. This fact supports the prolonged clearance of virus and delayed adaptive immune response in severe patients (Rao et al., 2020).

The Indians could have intrinsic immunity to resist the COVID-19 infection as compared to other countries across the globe. India has lowest test positivity rates with 3.3% critical or severe cases with less mortality rates are remarkable and quite encouraging. Firstly, the immunity of Indian population is broad due to exposure to a wide range of pathogens and microbial load that could specifically make them immunologically strong and mechanisms of cross-reactive memory T cells that need further exploration (Chinnaswamy, 2020). Further, BCG vaccination usage in India may have provided innate and adaptive immunity against the pathogens like COVID-19. Indians had begun to react aggressively to this pandemic where Indians have a lower number of deaths as compared to other countries. Trained innate immunity is a new paradigm like adaptive immunity arm that could have some memory to fight against this sort of encounter. The innate immune cells like NK, DCs and macrophages get trained due to first encounter with similar stimulus and retain the training as memory in epigenetic landscape. The Indian hosts have been exposed to endemic intracellular pathogens like protozoan or M. tuberculosis. This training of innate immunity and Indian host exposure to a myriad of viral infections could be helpful in protecting the majority if Indian population from COVID-19 (Singh, Maurya & Singh, 2020).

c) Immune dysregulation in COVID-19 Infection

COVID-19 affects multisystem and exhibits an array of health issues, therefore, understanding of metabolic, physiological or psychological consequences in the immune system is important for better health outcomes. For a COVID-19 patient, metabolism undergoes changes at all levels of

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organization and adaptive responses by the immune host. Poor metabolic health with abnormalities like cardiovascular abnormalities or hyperlipidaemia can be detected in COVID-19 patients (He et al., 2020). There might be disruptions in lysophosphatidylinositol (LPI) that could in turn hamper glucose homeostasis suggesting abnormal insulin release and metabolism. Physiological changes like damage to metabolic and endocrine organs like liver, pancreas may contribute to further metabolic syndrome in COVID-19 patients. Hyperglycemic condition lowers the immune response in COVID-19 patients that causes abnormality in the metabolism of the host. The immune profiles of patients depicted high levels of LDH, cTnI and pro-BNP indicating severe cardiac dysfunctioning and cardiac failure. Low levels of uric acid indicated potential dysfunctioning of renal or liver metabolism in severe patients. The exhaustion of T cells makes the patient potential towards other pathogens with chances of cross-contamination (Ayres, 2020).

COVID-19 also affects the physiological functioning in patients affected with the virus. Zhao et al., (2020) conducted a study on COVID-19 survivors to study the pulmonary functioning and physiological characteristics after three months of discharge. The results suggested that physiological and radiological abnormalities with impaired pulmonary functioning exist in survivors like abnormal carbon monoxide diffusion capacity (DLCO) because of D-dimer levels at the time of admission. Moreover, diffuse alveolar damage (DAD), pneumocyte activation, lymphocytic inflammation, hyaline membrane formation and proteinaceous edema are a wide range of respiratory abnormalities witnessed in positive patients. Diaphragm weakness due to mechanical ventilation in ICU patients demonstrated muscle thinning and reduced motion in critical patients (Brosnahan et al., 2020).

The psychological impact of COVID-19 is concerning as it has spread widely becoming pandemic. The strict lockdown, social restriction and isolation had a mental impact linked to feelings of uncertainty and frustration and individuals with pre-existing mental problems are at high risk. The pandemic acted as a stressor for the patients that affected their mental health in response to the stressful event called as “coronaphobia” (Dubey et al., 2020). High levels of anxiety, perceived stress and Post Traumatic Stress Disorder (PTSD) presented among the patients in response to the pandemic. COVID-19 recovered patients showed signs of anxiety, confusion and insomnia that make them prone to compulsive disorder and depression symptoms. The virus has serious implications on one's well-being and they are likely to experience long-term mental issues. As discussed above, ACE2 malfunctioning is associated with covid-19 propagation and transmission. As it is widely spread in tissues and present in the brain and blood-brain barrier, the virus may target the ACE2 receptors and cause central nervous system (CNS) infections.

d) Basic principles of immunization in COVID-19 infection

A variety of COVID-19 vaccines are being developed around the world. All of them share one thing in common: they all stimulate a primary immune response so that body can develop memory B and T cells against the SARS-CoV-2 virus. The development of immune memory by vaccines is what will protect the person against subsequent COVID-19 infection.

Depending on how many times the body is exposed to the virus or vaccinated, the body can generate two types of immune responses.

The body generates a primary immune response when exposed to SARS-CoV-2 virus for the first time or gets the 1st dose of the vaccine. The primary immune response is slow and weak as it takes days for the body to generate enough antibodies and T cells to eliminate the virus. However, the body generate enough antibodies and T-cells that ‘remember’ the SARS-CoV-2 virus, generating immune memory.

When the virus enters the body for the second time or the 2nd dose of the vaccine is given, the body develop a secondary immune response. The secondary immune response is stronger and quicker than the primary immune response as memory B and T cells are rapidly inactivated.

This results in higher antibody concentrations and T-cell counts around the body to eliminate the virus more quickly, reducing the symptoms and severity of COVID-19.In addition more memory B and T cells are produced after infection which strengthens the memory of the SARS-CoV-2 virus. The development of immune memory by vaccines is what will protect the individual against subsequent COVID-19 infection.

Each COVID-19 vaccine has distinct advantages and disadvantages, but the development of different COVID-19 vaccines provide some redundancy and overlap. In case a vaccine is unsafe in humans or fails to protect people against COVID-19, the world has other COVID-19 vaccines that it can trial and produce. It is this pursuit of multiple vaccines that will allow the global population to be immunized sooner, allowing the possibility to allow COVID-19 to be eliminated so that the world can start to recover from the pandemic (Speiser et al., 2020).

e) Overview of vaccine development for COVID-19 infection

In the current pandemic triggered by corona virus, immunization through vaccination of the population is recognized as a major priority in public health. Immunization in corona virus is of utmost priority where pandemic has hit the most. As no clinical data has suggested an effective candidate vaccine for corona virus, development of vaccines and

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immunization humans is the need of the hour and in curtailing the risk of spread of the disease. Extensive research is going on in vaccine development that would be effective for preventing the disease (Schwartz, 2020).

"Candidate" vaccines would be promising and the fastest process that may take weeks. More than 160 vaccine candidates are battling to combat the novel corona virus at different stages of clinical trials where 27 have reached human trial phase. Reports suggested that by the beginning of 2021, Oxford University's candidate vaccine 'ChAdOx1 nCoV-19' is a front runner currently undergoing the last stage of clinical trial, phase III of human trials in Brazil, UK and South Africa among 1600 volunteers dosed with it. Serum Institute of India (SII), Pune is conducting Phase II and III trials with Swedish-British firm AstraZeneca for producing vaccines for middle and low-income countries (Chen et al., 2020). mRNA-based vaccines have been a popular approach over conventional vaccines. SII has also tied up with Codagenix, a US-based biotech firm for the development of a live-attenuated vaccine. It also tied up with Themis Bioscience, Austrian Biotech Company to deploy measles virus as a vector for injecting antigen or corona virus protein.

Biontech and Pfizer is concluding phase III candidate vaccine, BNT162b2 that ensures to meet the entire primary efficacy among adults over the age of 65 years. It showed 95% primary efficacy against the virus beginning 28 days after the first dosage, 170 confirmed cases and 162 in placebo group versus vaccine group having 8. They have achieved FDA milestones of safety data and are well tolerated among the participants with no safety issues. Pfizer is confident to provide 50 million vaccines by the end of year 2020 (Le et al., 2020).

Russia is developing Liposome-encapsulated DNA-protein COVID-19 Spike antigens vaccine and DNA coding sequence based on HSB antigens called Sputnik V. Moderna's mRNA-1273 is the first vaccine going for human trials having promising prospects like mRNA sequence encoding for S protein (Burki, 2020). After phase I, the vaccine produced a mean antibody tier that is neutralizing in elderly subjects with a safety profile. Therefore, immunization through vaccination can be helpful in putting an end to the current pandemic situation.

f) Herd immunity and COVID-19 vaccine in India

The guidelines for vaccination in India is under development by Ministry of Health, Government of India. It is expected that the vaccine for the novel virus SARS-CoV-2 will cost 1000 INR per dose. In 2020, the estimated total population of India amounted to approximately 1.38 billion people. Achieving a target of 70% in herd immunity is expected to stop the transmission of the virus. Currently, there is insufficient confirmed information on reinfection to determine how that will influence the course of the pandemic. Vaccine allocation can be specifically targeted to highly exposed populations, such as health care workers and first responders, second priority can be given to the task force like the police and individuals who are susceptible and have possibilities of frequent contacts. They may have a significantly greater impact on reducing viral circulation than naturally acquired immunity specifically if the acquired protective immunity requires boost through reinfection.(Dhot PM et al.,2020)

A measure of the infection levels in the population has been provided through the sero-surveys conducted by the Indian Council of Medical Research (ICMR). The study done between August 17 and September 22, 2020 found the prevalence at 15.6% of the population in urban slums and 8.2% in non slum areas. In Delhi, a seroprevalence of 29.1% was found in the second round estimates. The study revealed that for every reported COVID-19 case, there were 26-32 infections, down from 81-130 infections per reported case in May. In Mumbai, an independent study estimated around 45% prevalence in slums and 18% seroprevalence in non slums in the second round (ICMR Serosurvey.,2020; Serology Survey.,2020)).

It can be predicted that the susceptibility of a considerable section of people, who are still unexposed to SARS-CoV-2 does exist and the risk of urban slums is twice that in non slum areas; and almost 4 times higher than the risk in rural settings. Therefore, in the absence of a reliable vaccine, the vast majority of people everywhere irrespective of waxing and waning in daily caseloads continue to be vulnerable.

III. Research Gap

The overview discussed the serious implications of COVID-19 on the metabolic, physiological and psychological well-being of the patients affected with the disease. Corona disrupts the functioning of the immune system that indicates immunization of the population and development of vaccines. The previous sections illustrated that there is a need for immunization priority among the individuals especially Indian population. Hence, this review provides an update on the immune dysregulation that can act as a basis for the vaccine development. In this present review paper, immunization priority has been highlighted in context to Indian population where the existing literature has helped in explaining the predisposing factors and reasons for immunization priority that further helps in filling the knowledge gap.

IV. Findings and Discussions

This section summarizes the findings that are based on the analysis that has been made reviewing the existing literature. Since the outbreak of corona virus, the virus has affected 210 countries across the globe. It disrupts the immune system of an individual and makes

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them susceptible to other infections. People above the age of 60 years and with co-morbidities are prone to virus infection. The patient develops symptoms like fever, coughing, shortness of breath and loss of taste and smell. Individuals with co-morbidities like renal dysfunction, hyperglycemia, hypertension, cardiac issues make them predispose to the infection. The innate and adaptive immune cells and responses are involved in the viral infection. The pandemic has seriously challenged the health system of a country. Countries are working at breakneck speed to develop vaccines to curb the risk of infection. The paper highlighted the updates on vaccine development that are happening across the globe. However, the review paper helped to bridge the potential knowledge gap and tried to raise awareness about prioritizing the laboratory studies and scientific analysis of viral transmission and pathogenesis for immunization and vaccine development.

V. Conclusion

The review paper gave an insight into the trends of emergence, transmission and progression of the disease across populations. The immune dysregulation in COVID-19 makes the patient susceptible to other infections and co-morbidities acts as a risk factor for the progression of the disease. The pandemic has challenged the healthcare system in the context of vaccine development and its approval. India's journey to recovery from this pandemic could be possible by developing strategies for quickly producing, gaining access and effective delivery of vaccines for the population. There is a need to establish a task force for determining production, accessibility and distribution of covid-19 vaccine. A nationwide plan is required for the development and distribution of vaccines that balances efficiency, effectiveness and equity. Lastly, strong resourcing in resource and time intensive efforts would help the scientific community to respond to the virus quickly.

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Contribution of authors:
AMS- Conceptualized and designed the study, literature search, prepared first draft of the manuscript, critical revision of the manuscript; DC- Conceptualized the study, Interpretation, critical revision of the manuscript; SKB- Concept of the study, revision of the manuscript; RG- Literature search, review of the study

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Covid-19 Infection: Prerequisites for New Areas of Research

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Abstract- The pandemic of COVID-19 infection caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) has posed a significant threat to global health. Now, we have witnessed an unsurpassed increase in the number of clinical trials worldwide. In clinical trials old and new drugs are tested as potential treatments either for their direct anti-viral activity, or for their ability to provide management of respiratory and cardiovascular symptoms and complications, characteristic of COVID-19. Despite the worsening trends of COVID-19, no drugs are validated to have significant efficacy in clinical treatment of COVID-19 patients in large-scale studies. Such a strategy is likely to give rise to a range of safety and efficacy challenges that could be addressed through preliminary pharmaco-genetic research on identification of risk groups for personification of therapy approach. Addressing the personification of drug treatment COVID-19 becomes an urgent need to interpret the conflicting results of clinical trials and establish the apparent efficacy of any particular drug.

Keywords: *coronavirus, COVID-19, drugs, toxic and side effects, gene polymorphism, pharmacogenetics, therapy personification.*

GJMR-K Classification: *NLMC Code: WC 505*



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Covid-19 Infection: Prerequisites for New Areas of Research

Iskandar R. Mavlanov [α], AbdurashidKh. Ashirmetov [σ], ZiyodullaI. Mavlanov [ρ] & GavkharJ. Jarylkasimova [ω]

Abstract- **The pandemic of COVID-19 infection caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) has posed a significant threat to global health. Now, we have witnessed an unsurpassed increase in the number of clinical trials worldwide. In clinical trials old and new drugs are tested as potential treatments either for their direct anti-viral activity, or for their ability to provide management of respiratory and cardiovascular symptoms and complications, characteristic of COVID-19. Despite the worsening trends of COVID-19, no drugs are validated to have significant efficacy in clinical treatment of COVID-19 patients in large-scale studies. Such a strategy is likely to give rise to a range of safety and efficacy challenges that could be addressed through preliminary pharmaco-genetic research on identification of risk groups for personification of therapy approach. Addressing the personification of drug treatment COVID-19 becomes an urgent need to interpret the conflicting results of clinical trials and establish the apparent efficacy of any particular drug.**

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I. Introduction

The recent outbreak of COVID-19 in Wuhan has become a worldwide health emergency. An analysis of the global situation with COVID-19 today convincingly indicates that humanity has faced a serious threat associated with the high prevalence of coronavirus infection [1]. The global importance of the COVID-19 pandemic problem for the world community also proves the exponential increase in the number of publications devoted to this problem. Since the beginning of 2020, the number of publications on the problem of COVID-19 has grown from several tens to several thousand and today it continues to increase [2]. Nevertheless, despite the sharp increase in relevant information and the replenishment of our knowledge with new data about this infection, so far there are much more questions than answers. A comprehensive analysis of the recent contradictory, and sometimes even opposing opinions of scientists on this issue makes a deep understanding of not only the epidemiological process of coronavirus infection, but also the pathophysiological processes associated with the expansion of the virus into the body and, above all, with the response of the organism in the form of an immuno-inflammatory response to viral aggression [3]. And this should be the basis of ongoing developments in the field of drug treatment of COVID-19 infection.

Currently known mechanisms for the development of pathological processes in coronavirus infection include: 1) multi-tissue expression of ACE2 receptors [4]; 2) a pronounced systemic increase in inflammatory cytokines and mediators; 3) diffuse endotheliitis and 4) impaired iron metabolism homeostasis, leading to oxidative stress and inflammatory response.

The SARS-CoV-2 virus was found to enter the host cells through the ACE2 receptor on the surface of cell membranes, where it encounters an innate immune response that inhibits viral replication through expression of interferon (IFN) -stimulated genes (ISGs) and the release of pro-inflammatory cytokines such as IL1b, IL-2, IL-7, TNF-a, GSCF, MCP1, etc. [5]. How coronavirus manages to evade the inhibitory function of ISG has not yet been fully resolved (it is only known that this virus has 8 proteins that can block interferon), but in the future the clinic of seriously ill with COVID-19 indicates an excessive immune response with such a huge amount of cytokines in the tissues that such a condition was described as a "cytokine storm". Moreover, an increase in the concentration of anti-inflammatory cytokines such as IL10 and IL4was completely unexpected, which is considered unusual for the acute phase of a viral infection.

Since ACE2 is detected in the greatest amount on the surface of the cell membranes of the pulmonary alveoli and blood vessels, apparently, therefore, the main place of aggressive exposure to the SARS-CoV-2 virus is the lungs. However, since this protein is also spread in other organs and systems, in particular, in the blood vessels of the kidneys, intestines, liver, heart, the developing pathological process leads in severe cases

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to rather rapid development of disorders in many organs, which turns into multiple organ failure.

In addition, it was shown that the protein sequences of the SARS-CoV-2 virus can form a complex with porphyrin and also affect heme in the 1-β chain of hemoglobin, leading to iron dissociation [6]. In turn, an increase in iron levels can contribute to the development of viral infections [7] associated with a number of respiratory diseases, including acute respiratory distress syndrome and pulmonary fibrosis.

Therefore, the COVID-19 virus for the most part only triggers the pathological process, and the further development of events will depend on the nature of the reaction of the body's defense systems, i.e. the body in response to viral aggression will fiercely fight against its own substrates of the body's compensatory systems, similar to the "cytokine storm" and the development of oxidative and other stress syndromes, much like sepsis or autoimmune diseases.

Apparently, the more severe course of this infection in people with concomitant chronic diseases, especially autoimmune genesis or using ACE2 in their pathogenesis, also indicates that the initially impaired immune balance in the body serves as an engine for the development of an inferior and perverse response in case of viral aggression and will determine the nature and severity of the course of the pathology [8]. In addition, recently revealed positive results from the use of basic anti-inflammatory drugs and the modified biological gene used to treat rheumatoid arthritis can also confirm this assumption.

Therefore, current evidence suggests that the pathogenesis of COVID-19-induced pneumonia closely resembles autoimmune / autoinflammatory syndromes, thereby supporting attempts to use antirheumatic drugs of a chemical or biological nature. However, a number of questions appear here. For example, as indicated by Caso et al.[9],emphasizing the similarities between COVID-19 and autoimmune / autoinflammatory syndromes, it remains to be determined whether a genetic predisposition can contribute to the variability of clinical phenotypes. Another important issue is the identification of triggers responsible for the development of lung damage and hyperinflammation in the late phases of COVID-19. Of course, a large amount of evidence indicates ACE2, used by SARS-CoV-2 for entry into the cell, however, whether there is direct relationship between the viral damage of ACE2 and the development of hyperinflammation with lung disorders is still not very clear. And the answer obtained can be quite significant, because if it is mediated, the number of viral load will play a smaller role compared with the body's genetic predisposition to a hyperinflammatory response. Based on the preliminary results available today that it is not possible to confirm the relationship between the progression of lung damage and activation of viral replication [10], apparently the last assumption will gather all the chances to reflect the real situation.

Since the reactions of the body's protective and adaptive systems to any aggression have individual characteristics and are genetically determined, belonging to a particular variant of the polymorphism of genes that control these body functions can be of limited value in predicting the likely response of the body to infection [11]. These markers include gene polymorphisms of the angiotensin-converting enzyme, tumor necrosis factor, interleukins, HLA systems and others. Such an approach to solving the problem would make it possible to determine in advance a predisposition to the severe course of coronavirus infection, form risk groups and their stratification, and also develop a new, scientifically based strategy and tactics for administering patients with this infection. Moreover, this would be a good help for the development in our country of such a direction as the development of gene modified biological preparations based on genomic, epigenomic and transcriptome approaches. Such circumstances open up new horizons for the prevention and control of coronavirus infection in general.

There is currently no specific effective antiviral treatment for COVID-19. Based on in-vitro data and available information on safety and biological efficacy, the World Health Organization (WHO) prioritized several drugs for further research at COVID-19 and recommended them for evaluation in the context of the "Solidarity" clinical trials (www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus/en). For this study, WHO selected an experimental antiviral agent, remdesivir; used for the treatment of malaria-chloroquine (or its chemical counterpart, hydroxychloroquine); a combination of HIV drugs-lopinavir-ritonavir; and the same combination plus beta interferon - the messenger of the immune system.

Although clinical trials are still ongoing, negative actions are already being identified. So, in relation to chloroquine, its well-known toxic and side effects began to appear, and its cardiotoxic effect in the form of a change in heart rhythm has already led to deaths in Brazil, due to which a number of tests were stopped (https://www.nytimes.com/2020/04/12/health/chloroquine-coronavirus-trump.html).

The very first test of a combination of lopinavir-ritonavir drugs in Wuhan (China) for 199 patients with COVID-19 did not lead to statistically significant differences between the groups with and without these drugs, which was explained by the possible too late treatment of severe patients [12]. Recently, developed by Gilead Sciences specifically to combat the Ebola virus, the drug remdesivir showed excellent performance in vitro against the SARS and MERS viruses. However, in practical terms, this drug was not able to effectively help patients with Ebola virus during the 2019 outbreak in the

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Democratic Republic of the Congo, but some of its negative manifestations (for example, nausea, vomiting, rectal hemorrhage and liver toxicity) were already known.

Of course, research is ongoing and final conclusions will be drawn later. Now the WHO International Clinical Trials Registration Platform has already registered over 700 clinical trials of various drugs and treatments of COVID-19 (https://apps.who.int/trialsearch).

As a result of the accumulation of knowledge on the pathophysiology of COVID-19, in addition to the use of certain antiviral drugs, many medicinal substances that are commonly used to treat other autoimmune and metabolic diseases have been proposed as possible treatment methods [13].

Currently, the number of ways to combat SARS-CoV-2 that are undergoing clinical trials has reached 62. Moreover, fifteen procedures are based on the use of both known and new antiviral drugs: lopinavir and ritonavir[14], arbidol, hydroxychloroquine, chloroquine, DAS181, remdesivir, azvudine, baloxavir, azithromycin, amiodarone, verapamil, ivermectin, APN01, alvesco, CYNK001, virazole, as well as convalescence plasma therapy and Yeliva. Whereas, the second line of treatment is based on the use of anti-inflammatory drugs and immunomodulators, including glucocorticoids, tocilizumab, jacotinib hydrochloride, leukin, lenzylumab, CD24Fc, colchicine, tradipitant, siltuximab, anakinra, sarilumab, vazepal 1, IFX-1,leronlimab, aviptadil, fingolimod, piklidenozon, selinexor, akalabrutinib, clazacizumab, zanubrutinib, gimsilumab, TJ003234, halidesivir, etc.

In addition, a test was undertaken of the following drugs used to treat pneumonia after a viral infection: danoprevir + ritonavir, darunavir, ruxolitinib, bevacizumab, AiRuiKa ™, tofacitinib, deferoxamine and meplazumab; as well as some drugs used to prevent organ failure, such as: valsartan, dapagliflozin, losartan [15].

If we consider drugs that are only offered for clinical trials, their number already exceeds one hundred, they affect many other, including recently identified, pathogenetic links, they have a diverse mechanism of action, they are well known and are already effectively used to treat many, including non-infectious diseases (premarin, pioglitazone, melatonin, thalidomide, pirfenidone, chlorpromazine, sildenafil, cyclosporine, ouabain, bufalin, dapagliflosin, dapsone, doxycycline, amantadine, vitamin D, etc.) [16].

On this background, as one of the important aspects of the problem of COVID 19 infection, in terms of interpreting the conflicting results of clinical trials and quickly establishing the apparent effectiveness of a particular drug, the issue of personifying its medical treatment becomes a question. This problem is associated with the individual characteristics of the patient's body in the manifestation of the reaction to the drug, because now there are enough examples when similar drugs in similar doses seemed to give different results in almost identical clinical situations both in terms of effectiveness and safety.

This is indeed a difficult question, because it is associated with the functioning of a number of body systems that are involved in the processes of absorption, adsorption, bioavailability, distribution, transportation, metabolism and elimination of drugs. Moreover, the initial state of these systems and their full functioning regulates the formation of an adequate pharmacological response to a specific drug.

Perhaps this is the basis of the preliminary conflicting results of research conducted under the "Solidarity" program. After all, it is known that remdesivir is a prodrug [17], which means that its action will be fully manifested only after its metabolism inside the cell, and the extent of readiness of the enzymes metabolizing it before taking the drug is not established. The lopinavir / ritonavir complex is a protease inhibitor used in the combination therapy of immunodeficiency in a person infected with HIV. Since lopinavir inhibits the cleavage of the gag-pol protein, while ritonavir inhibits the cleavage of the precursor of this protein and at the same time the metabolism of lopinavir through the P-450 cytochrome system (CYP3A4), to increase the concentration of lopinavir, these drugs are always prescribed together as a complex. However, depending on the initial state of the metabolizing enzymes, both toxic properties and insufficient effectiveness of these drugs may occur. The same can be noted for chloroquine, which has been used worldwide for more than 70 years as an antimalarial drug.

It is known that the above systems that regulate the fate of drugs in the body, like other components, are genetically controlled. Enzymes carrying out transmembrane transport of drugs, their efflux from the cell, as well as biotransformation and elimination from the body are carried out by expression of the corresponding genes, in particular glycoproteins of the MDR1 type, a family of cytochrome isoforms. The candidate genes responsible for the pharmacokinetics of drugs have numerous mutant variants that contribute to the formation of an appropriate response of the body to drugs.

Based on the experience of prescribing antiretroviral drugs for the treatment of HIV infection, some of which are effective against COVID-19, the question of preliminary pharmacogenetic studies has long been raised. So, the effectiveness of a number of drugs widely used in HIV infection is very dependent on the single nucleotide polymorphism of the HLA system genes, cytochrome P-450 and glycoprotein carriers, for example: for abacavir - HLA B * 5701, HLA-DR7 and HLA-DQ3 genotypes [18], for nevirapine - HLA-DRB1 * 01: 01, HLA-cw8 / HLA-B14, ABCB1 (MDR1) 3435C> T,

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cytochrome P-450: CYP3A4 \ 5, CYP2D6 and CYP2B6; for the efavirenz, CYP2B6 516G> T, 983T> C, 785A> G and 21563C> T, CYP2A6 -48T> G. A similar CYP3A5 gene polymorphism is closely associated with faster clearance of indinavir, an antiretroviral drug from the class of protease inhibitors that is currently undergoing clinical trials against COVID-19, like other drugs of this class: lopinavir, ritonavir and darunavir.

Extensive information on the pharmacogenetics of almost all currently used drugs, the activity of pharmaco-metabolizing enzymes and individual body parameters that determine the effectiveness of the used drugs is well reflected in many publications [19]. Therefore, we believe that the study of the variants of carriage of the polymorphic diversity of these genes from the standpoint of the efficacy and safety of the pharmacotherapy of COVID-19 infection would significantly increase the effectiveness of therapeutic measures for this pathology. And the accumulation of data on preliminary pharmacogenotyping of people from the perspective of the possible choice of certain drug groups for the treatment of this pathology would contribute to personification and significantly reduce the risk of side effects.

The above mentioned points, in our opinion, is a definite prerequisite for planning a vector of scientific research in the future. Of course, it is premature to talk about conducting such scientific research now, at the height of the epidemic, but we believe that there is a need to conduct such research in the future, the results of which will serve as a theoretical foundation for the development of effective platforms for the prevention and control of not only coronavirus, but also with any other infections.

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A Critical Review on *Shvitra* (Vitiligo) & their Management

By O.P. Vyas, Abhilasha Sahu & Muraree Girare

Abstract- Vitiligo is an acquired depigmentation of the skin. It affects 1% of the world population. It is a pigmentary disorder characterized by circumscribed loss of melanin pigment secondary to melanocyte attrition. It is an acquired, sometimes familial condition, an autoimmune disease in the majority. Vitiligo is associated with other autoimmune diseases such as thyroid disease, diabetes mellitus, Addison's disease, and pernicious anemia. In *Ayurveda*, *Shvitra* is correlated by vitiligo.*Shvitra* is caused by the vitiation of all three *Doshas* but sometimes it manifest by either single or three or two *Doshas*. In modern medicine, steroids and corticosteroids are used in the treatment of vitiligo, which has so many side effects. In *Shvitra, Samshodhana* (purificatory therapies) for the entire body should be administered at the beginning of treatment of *Shvitra* after that applied *Samshamana* therapy.

Keywords: *vitiligo, skin, shvitra.*

GJMR-K Classification: *NLMC Code: WR 265*



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Keywords: vitiligo, skin, shvitra.

I. Introduction

Skin is one of the most important body organs because it protects the internal organ from the deleterious environmental influences[1]. The major pigment of the skin is called melanin. It is produced inside special cells called melanocytes, which are located along with the basal cells in the epidermis and contain small granules called melanosomes[2]. Vitiligo is an acquired condition affecting 1% of the population worldwide[3]. Vitiligo is skin depigmentationin which the melanocytes in localized areas of the body stop producing melanin. Clinically it manifests as macular areas of depigmentation. Occasionally, the skin in certain areas may only be hypopigmented. There is no other change in the skin. In some lesions the hairs may also become depigmented. This is called leucotrichia. The lesions very in shape and size and may appear on any part of the skin and mucous membranes[2].The border is often convex, a feature that differentiates it from many other conditions of depigmentation. Sometimes at the margin of an active patch, three colors are seen from inside outwards, a depigmented zone, a hypopigmented zone, a normal-looking skin. This is known as 'trichrome vitiligo'. A treated patch often shows an additional perifollicular hyperpigmented zone, and this is known as 'quadrichrome vitiligo'[4]. Vitiligo is correlated with *Shvitra* in *Ayurveda*. *Shvitra,* also known as *Kilasa* and *Daruna*, is pointed to similar to *Kustha*, is nonexudative and arising from the three *Doshas* and three *Dhatus* (*Rakta. Mamsa and Medas*)[5]. At the beginning of treatment of the *Shvitra, Samshodhana* therapy should be administered. After that, *Samshmana* therapy should be applied[6].

a) *Epidemiology*[4]

The onset is most common in young adults, onset of disease is before the age of 20 years in approximately 50% of the patients, with a quarter of the patients having onset by 15 years of age. Rarely disease is present at birth and is then known as congenital vitiligo.

b) *Etiology*[7]

In vitiligo, there are focal areas of melanocyte loss, which is considered to be due to cell-mediated autoimmune attack. Some patients have antibodies to melanin. It may be associated with other autoimmune disease such as diabetes, Addison's disease, and pernicious anamia.

Genetic factors may play a role; 20 to 30% of patients may have family history of vitiligo.

Extrinsic factors also may play a role. Trauma, certain chemicals, and sunburn may precipitate the appearance of vitiligo.

c) *Classification*[8]

Localized vitiligo- (a) A single macule or a few macules may be localized to skin or mucosa. (b) Segmental distribution of macules.

Generalized- (a) Vitiligo Vulgaris – a common form of vitiligo with symmetrical distribution over trunk and limbs. (b) Lip-tip vitiligo – only tips of fingers or with mucosal surfaces like lips, nipples or palms, or penis. (c) Acrafacial vitiligo – involvement of periorifacial and distal digits. (d) Universal vitiligo – Involvement of most of the body with only afew areas spread.

d) *Clinical features*[7]

Lesions may start at any age, but generally in early adolescence or adult life.

Segmental vitiligo is restricted to one part of the body.

Generalized vitiligo is characterized by many widespread macules, often symmetrical, and frequently

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involves the hands, wrist, knees, and neck as well as the area around the body orifices.

The patches of depigmentation are sharply demarcated.

Sensation in the depigmented patches is normal, unlike leprosy.

The Course is static or slowly progressive. Some patients may experience spontaneous repigmentation.

e) Differential Diagnosis[7]

Postinflammatory hypopigmentation.

Piebaldism (a rare autosomal dominant disorder; depigmented patches surrounded by hyperpigmented areas)

Morphea (localized scleroderma)

Leprosy (lesion are usually hypoesthetic)

Lichen sclerosus

Pityriasis alba

Chemical leucoderma

Leukoderma due to melanoma

In Ayurveda

*Shvitra*is also known as *Kilasa* and *Aruna,* is said to be produced by the same causes which produce *Kustha*, is nonexudative and arising from the three *Doshas* and three *Dhatus*[9].

Nidana

Untruthfulness, ungratefulness, disrespect for the gods, insult of the preceptors, sinful acts, misdeeds of past lives, and intake of mutually contradictory foods are causative factors of Shvitra[10].

Rupa

It is classified into three subtypes, namely *Daruna, Charuna,* and *Kilasa*.

All of them are generally caused by the simultaneous vitiation of all the three *Doshas*. If located in *Rakta dhatu,*it is red color, if located in *Mamsa dhatu*(muscle tissue) it is coppery in color, and if located in *Meda dhatu,* it is white in color the subsequent ones are more serious than the previous ones[11].

Shvitra produced by *Vata*, the skin is dry and*Aruna* (light red), in that produced by *Pitta*, it is coppery has burning sensation and destroys the hairs, in that produced by *Kapha*, the skin is white (*Shveta*), thick, heavy and itching[12].

Sadhya- asadhyata

*Shvitra*in which the hairs have not become white, the skin not become thick, the patches have not fused with one other and which is of recent origin, and that not due to burning by fire is curable, where as those of opposite varieties are incurable that which has arisen on the genital organs palm of the hands and lips, even though of recent origin are to be rejected by the physician[12].

f) Management

In modern medicine[7]

Corticosteroids: Topical corticosteroids are the first choice for patients with limited disease. A topical preparation of fluticasone propionate or mometasone, once a day for four to six months has to be applied.

Calcineurin inhibitors

Ultraviolet light: Topicalor oral psoralens plus ultraviolet A radiation (PUVA), or ultraviolet B (UVB) radiation (phototherapy) is used in patients with extensive vitiligo.

Surgery: Split- skin grafts and blister roof grafts can be used to cover vitiligo patches.

Depigmentation therapy: If there is extensive vitiligo with only small areas of normal skin, these normal skin areas can be depigmented to make the ski look uniform.

In Ayurveda

Nidana Parivarjana is the first step of treatment.

Chikitsa: 1) *Shodhana Chikitsa* 2) *Shamana Chikitsa,*

The patient of *Shvitra* should be purified by the administering of elimination therapies followed by the administration of pacification therapies.

The patient should, first of all, take oleation therapy as per once strength followed by intake of the juice of along with jaggery is an excellent tregimen cause *Shamsana* (a type of purgation). After the administration of this recipe, the patient should expose himself to the heat of the sun. This will induce purgation. After this purgation therapy, the patient will feel thirsty, for which the patient should be given *Peya* for three days[13].

Shamana chikitsa:

Rasa Aushadhi: Dose: 125 mg – 250 mg

Gandhka Rasayana

Talkeshvara Rasa

Rasamanikya Rasa

Vati: Dose: 250mg- 500mg

Kaishore Guggulu

Arogyavardhani Vati

Panchatiktagrita Guggulu

Churna: Dose: 3-6 gm

Bakuchi churna

Panchnimba Churna

Ghrita: Dose: 5-10 ml

Mahatiktaka Ghrita

Khadiradi Ghrita

Pachatikta Ghrita

Somaraji Ghrita

Taila: For local application

Somaraji taila

Bakuchi taila

Tuvarak taila

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Kashaya: Dose: 15ml-20 ml

Aragvadhadi Kashaya

Khadiradi Kashaya

Manjishthadi Kashaya

*Ashva-Arishta:*Dose: 15ml-30 ml; *Anupana*-: *Sama Bhaga Jala*

Manjistharishta

Sarivadyaashva

Khadirarishta

Treatment of Pustular Eruption[14]

Pustular eruption over the patches of *Shvitra* should be punctured with the help of a thorn for removal of serous fluid from these pustules. After the exudation of the fluid, the patient should take every morning continuously for fifteen days, the decoction of *Malapyu, Asana, Priyangu,* and *Satapushpa* prepared by boiling with water. Alternatively, the *Kshara* of *Palasa,* along with *Phanita,* should be given an appropriate dose as per strength.

External application[15]*:*

Nilotpala, Kustha, and *Saindhava* made to a paste by adding urine of elephant.

Seeds of *Mulaka* and *Avalguja* made to a paste by adding cow-urine.

Kakodumbara, Avalguja, and *Chitraka* made to a paste by adding cow-urine.

Manhashila made to a paste by adding pea-cock bile.

In rare cases, patients of *Shvitra*, who are free from the effect of their sinful acts, get cured by the administration of elimination therapies, blood-letting, and intake of ununctuous food like *Saktu*.

II. Conclusion

Vitiligo is skin depigmentation due to the selective destruction of melenocytes. It is a common acquired idiopathic discoloration of the skin characterized by well-circumscribed, chalky white colored macules. Vitiligo is correlated with *Shvitra* in *Ayurveda. Shvitra* is caused by the vitiation of all three *Doshas* and three *Dhatus* (*Rakta, Mamsa,* and *Medas*). Generally, *Shvitra* has no harmful effect on the body, but the patient suffers a socially inferiority complex. *Ayurvedic* medicine & purification therapy give better results than modern medicine, which has so many side effects. In *Shvitra roga, Samshodhana* (purificatory therapies) is the first line of treatment described by *Acharya Charaka*. After that, administered *Samshamana* therapy does dhatusamya.

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Role of Plants in a Pandemic: Learning from the COVID-19 Situation

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Abstract- Plants have been curing the humans from a very long time. The secondary metabolites present in the plants play a crucial role in healing of the people. The current review article deals with the roles of plants in tackling a pandemic. Several works on herbal medicine efficacy againstCOVID-19 proves that plants are one of the cheapest prophylactic treatment for an unknown disease. Plants-people relationship have been helping many people to overcome anxiety and depression during the social isolation period. Here we explore how traditional medicines from different parts of world is showing the path of effective prophylactic treatments along with it we also explore the role of plants in developing natural antiviral surface protective agents. We also explored all the herbal medication recommendations given by different countries to tackle the disease. Pandemics can occur anytime and plants will help us in from all the corners of life. We all need to come together to fight it out, and also, we need to chalk out the ways to prevent future pandemics too.

Keywords: *traditional medicine, COVID-19, psychological health, antiviral agent.*

GJMR-K Classification: *NLMC Code: QV 766*



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Role of Plants in a Pandemic: Learning from the COVID-19 Situation

Snehangshu Das [α] & Minakshi Mahajan [σ]

Abstract- Plants have been curing the humans from a very long time. The secondary metabolites present in the plants play a crucial role in healing of the people. The current review article deals with the roles of plants in tackling a pandemic. Several works on herbal medicine efficacy againstCOVID-19 proves that plants are one of the cheapest prophylactic treatment for an unknown disease. Plants-people relationship have been helping many people to overcome anxiety and depression during the social isolation period. Here we explore how traditional medicines from different parts of world is showing the path of effective prophylactic treatments along with it we also explore the role of plants in developing natural antiviral surface protective agents. We also explored all the herbal medication recommendations given by different countries to tackle the disease. Pandemics can occur anytime and plants will help us in from all the corners of life. We all need to come together to fight it out, and also, we need to chalk out the ways to prevent future pandemics too.

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I. Introduction

Pandemics have existed since time immemorial. The humanity has seen horrific pandemics in the past and presently, it is experiencing one too. The outbreak of coronavirus illness 2019 (COVID-19) reportedly happened in a wet market at Wuhan, China, which can be accounted for a zoonotic transmission[1]. During the early days, the unexpected outbreak of the virus took more than 1800 lives and over 70,000 individuals got disease-ridden. The main warning symptoms comprises of excessively high body temperature, dry cough, and body weakness, whereas several patients have symptoms of myalgia and bowel disorders too[2]. In many cases, respiratory system failure, septic shock, and also deaths have been recorded. The World Health Organisation has declared the coronavirus disease (COVID-19) as a pandemic in March 2020, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2)[3]. As of December 14, 2020, 72.6 million confirmed cases, 50.8 million cured cases (64.74 %) and 1.6 million (2.23 %) deaths have been reported worldwide[4]. Regrettably, the total number of confirmed cases continues to upsurge due to common man's negligence. The healthcare infrastructure of world is trying its level best to cope up with the upsurge in cases. Right now, the world is hearing about vaccines for SARS-CoV-2 which are being developed through extraordinary hard work[5]. But, the concern over its long-term efficacy and post vaccine effects on the body makes it a sensitive issue of discussion. Several therapeutic methods have been proposed which includes the use of Lopinavir/Ritonavir, Hydroxychloroquine, Remdesivirto cure COVID-19. However, the medical utility of these synthetic drugs to counter COVID-19 infection is still unclear[6]. In the absence of an appropriate treatment, herbal medications are becoming an adjuvant treatment to heal the symptoms of the disease.

The early evidence related to the use of herbal preparations in tackling a disease nearly dates back to 1500 BC by Egyptians. Later, Romans and Greeks improved the combinations and were recognized in the earliest known drug books named as Pharmacopoeias[7]. From Black Death to Spanish Flu, plant-based medicines have been used extensively in the absence of drugs[7]. Even in this century, phytomedicines are the lone healing option for a large chunk of global population who are residing in the developing countries. But then, similarly in the developed nations, the practice of traditional phytodrugs is undergoing a revitalization, as it is considered as a safer and healthier option than artificially synthesised chemical drugs. Undeniably, traditional medications have existed since the inception of humanity. With a trend in increasing publication on the subject, a transformed shift of scientific interest can be seen on to plant-derived medications in the current decade[8]. The therapeutic potential of plants is solely due to the presence of secondary metabolism. Only the availability of resources to perform clinical trials of traditional medicines has limited its applications in modern world of drugs.

One role of the plants in the pandemic is in the form of medicinal values and the other role explores the importance of people-plant relationships in reference with the psychological well-being of humans. The primary measures taken to control the pandemic was completely through non-pharmacological interventions (NPIs)[9]. NPIs for preventing the disease included social distancing, isolation, quarantining the infected

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people and treating the cases[10]. From educational institutes, and work places to leisure venues, every possible place were locked up to avoid public gatherings. These recommendations were, and are still very much in place in some countries right now, which created job losses, scarcities of food and societal unrest with anxiety of the unknown at the global level[11]. Drastic changes in the daily routines led to affect the mental health among the people of all ages. They showed symptoms of trouble in concentrating, tetchiness and anxiety[12]. To a certain extent, despair, wretchedness, stress and nervousness have affected people during this period. Stress is principally associated with the existing information that does not provides a clear picture with respect to perils, extent of the pandemic, effect on the economy, and many other factors[11].Gardening and other horticultural practices as a therapy creeped in to rescue the mental health of the human beings during this time. The innate relationship between plants and people has been helping in bringing a positive change in mindset of the people. Through this review, we will explore both the roles of plants on humans during this pandemic tenure.

II. Plants as Medicines and Surface Protective Agents

The unique property of plants to produce secondary metabolites has enabled the world to make them a source of medicinal compounds. From the preliminary outbreak phase of the COVID-19, plant-based therapeutics have been implemented in China. The use of qingfeipaidumixture, gancaoganjiangmixture, sheganmahuangmixture and qingfeitouxie-fuzhengmixtureseems to be helpful in the treatment of SARS-CoV-2[13]. A total of 701 patients were healed by qingfeipaidumixture, among them 130 patients healed in just 12 days. 319 patients lost clinical symptoms and got cured in 20 days, while 252 cases showed stability in their symptoms[14]. These results show that qingfeipaidumixture has an efficacy of 90% and above in treating the COVID-19[14]. The molecular interaction analysis has shown that patchouli alcoholic mixture, ergosterol and shionone extract could be a new high-quality drug choice against SARS-CoV-2. An oral liquid known as shuanghuanglian, which comprises of three plants including *Lonicera japonica*, *Scutellariabaicalensis* and *Forsythia*[15]. Since, it's low price and no grave side-effect, it is used for healing sore throat, fever, upper throat infection and cough[15]. A recently published article showed Shuang huanglianin combination with conventional treatments (immunoglobulin injections, doses of dexamethasone, antiviral and antibiotic medications) were used against COVID-19. The outcome exhibited that this cocktail of drugs can help the body improve without any known side-effects and resolve the symptoms[16].With the help of Out of the 214 patients, traditional herbal medicines have helped 193 patients to recover completely[17]. A latest publication showed that 60107 cases were healed by Chinese herbal medicines[14]. Besides, some herbal drugs prohibited the virus from infecting healthy individuals and enhanced the health of the affected infected individuals with mild or severe symptoms in many parts of the country[17,18].The Chinese herbal drugs locally called Shu Feng Jie Du and Lianhuaqingwen have been suggested, thanks to their good efficacy against earlier known viruses such as influenza A (H1N1) or Severe Acute Respiratory Syndrome (SARS-CoV-1)[19]. Such positive results led the inclusion of Chinese herbal medicines in the plans for the treatment and stoppage of COVID-19 in the Zhongnan Hospital of Wuhan University. Additionally, to cure the virus, the authorities recommended the usage of diverse herbal combinations in accordance with the disease-stage[20].

In South Korea, Korean herbal medications are being administered to patients for free of cost, and the plant based remedies are surely helping the diseased individuals to be healthy[21]. The clinical experts from the Korean Association of Traditional Pulmonary Medicine and the Association of Korean Medicine both drafted their individual guidelines of traditional medicine on the inhibiting and curing of COVID-19[22]. The guidelines included the use of Youngyopaedoc-san along with Bojungikgi-tang, and Youngyopaedoc-san with the application of Saengmaek-san[22,23]. And, two more Korean plant-based preparations were recommended for patients who recovered from the SARS-CoV-2[23]. It included the combinations of Youngyopaedoc-san with the use of Bulhwangeumjeonggi-san and Bojungikgi-tang with Youngyopaedoc-san for eliminating post COVID-19 complications[22,23]. For patients with mild symptoms, three more herbal medications were suggested, which includes Youngyopaedoc-san along with the use of Galgunhaegui-tang for those without pneumonia but with excessive warm breath; Bulhwangeumjeonggi-san along with Sosiho-tang was suggested for people with mugginess-heat in the infected lungs[23]. The herbal recommendations for recovery stageinclude Saeng-maek-san with the use of Samchulkunbi-tang or Chungseuiki-tang with the application of Samchulkunbi-tang[23].

In India, Ayurveda, Unani, Siddha and Homeopathy system of medications has been the most sought-after prophylactic treatment for COVID-19. A set of guidelines has been released by the Indian government for each of the traditional medicine system[24]. Additionally, the Prime Minister of India in his address to country also stated that the use of such medicines can help in improving body resistance against COVID-19. Following which the demand of traditional herbal medicines increased in the country. An

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interim report on two traditional drugs combinations, Immunofree and Reginmune, has shown exceptional results when compared with conventional drug treatment[25]. On fifth day, more than 85% recovery rate has been seen only in the use of both the medicines against 60% during the use of only conventional drugs[26]. In 10 days, all the patients recovered completely[26]. Such results are very encouraging as the trials included aged patients of 70 years old with comorbidities[25]. These medicines are a combination of 15 plants which has been also recommended by the Indian government in its herbal medicine guidelines[25]. A southern Indian state, Kerala, has used traditional medicines along with synthetic drugs to treat and mitigate the spread of SARS-COV-2 in its region. And, has been successful in flattening the curve of the disease[27]. The state government has divided the population in seven groups based on the probable spread of the virus, and been recommended to use Ayurveda consequently[28].Some other Indian states have been utilising traditional medicine treatments as an anticipatory measure against the disease, which includes Gujarat is treating all asymptomatic patients with traditional medicines and is also distributing herbal immunity boosters to a large chunk of its population for free[29]. The huge community of traditional medicine practitioners makes it easy to reach the masses with low cost prophylactic treatments for the disease, and that is helping to increase the recovery rate of the nation[30].The African nations are also exploring their rich resource of traditional medicines against COVID-19. In Madagascar, a highly debatable organic drink consisting the herb *Artemisia afra* is making rounds as a viable treatment for COVID-19. It is commonly used all over Africa to improve and treat the symptoms of respiratory ailments, some of which shares similarities with COVID-19 symptoms[31,32]. Following which, the World Health Organisation has set up panel of experts totest African traditional medicine as a probable treatment for the COVID-19 infection[33]. The trials of the herbal remedy have progressed into the third phase[34]. In these similar contexts of African phytomedicines that omics machineries offer scenarios to recognizemode of action for phytodrugs and, thus, Africans are positive towards contributing to the pool of novel molecular markers for therapeutic innovation to fight against SARS-COV-2[35]. All the recommended medicinal plants have been presented in the Table 1.

There are many other secondary metabolites which are needed to be explored. Such as galactans which are antiviral in nature can be extracted from marine algae like *Ruppia maritime* and terrestrial plants such as *Stevia rebaudiana* and *Bassia rubra*[36–38]. The secondary metabolite could easily fight against herpes simplex type virus 1 & 2. A recent study also showed the efficacy of glycosides and flavonoids derived from *Allium sativum*, *Senna,* and *Salvia officinal is* yields different phytochemicals which have the capability tomutilate the gyrase produced by SARS-COV-2[39]. Even, the Persian traditional medicine recommendations include the use of both *Allium sativum* and *Allium cepa* against COVID-19[40]. Such recommendations are tedious to find if they are not available on one platform. A recent Github project has emerged which is helping the common people to store different government recommendations for herbal medicines on one platform[41]. The use of technology is helping the database to reach the masses. The probable list of plants which can be explored for their medicinal purposes has been listed in Table 2.

The current situation has taught us that a formidable vision towards developing future antiviral materials must be developed to tackle future pandemics. Marine algae are the store house of sulphated polysaccharides. Species of *Porphyridium*, a red alga, has high content of sulphated polysaccharides known as carrageenan which are antiviral in nature[42]. A study shows that a layer of sulphated polysaccharides on sanitary items destroys SARS-COV-2 on the surface[43]. Apart from algal derived compounds, tea tree oil and eucalyptus oils with biologically active compounds has natural virucidal properties which can be possibly used to coat surfaces for gaining antiviral properties[44].These essential oils showed significant antiviral action against wide-rangingorganisms such as bacterial, fungal, and virus-related species, and mainly were found to be active in inactivation of airborne influenza virus as soon as it was applied on the mesh surfaces as the pre-coating of the mesh fibers[44]. Recently, a study showed that by modifying cyclodextrins, a naturally occurring glucose derivatives from starch rich natural sources, non-toxic antiviral materials can be developed which have a competence to destroy viruses on coming in contact with the materials[45]. Thus, it exhibits virucidal properties. The oleuropein, a polyphenolic compound derived from olive leaves, have been acknowledged as a good inhibitor to an extensive range of viruses by hindering the manufacturing process of enzymes required for viral replication[46]. Purple Tabebuia (*Tabebuia impetiginosa*) is a very common tree found in South and Central American nations. The inner bark of the species has been advertised as an enhancement to decrease inflammation and encourage loss in weight. The quinoids derived from the purple tabebuia can be instrumental in inhibiting virus reproduction by chemically impairing the DNA and RNA present in the viral proteins[47]. These interesting natural extractions tend to be very capable for becoming antiviral coating contenders. In future, these compounds will play an essential role in developing both natural antiviral materials and drugs.

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Table 1: Recommended medicinal plant extracts for treating and preventing COVID-19 worldwide. (*ATM- African Traditional Medicine; CTM- Chinese Traditional Medicine; KTM- Korean Traditional Medicine)

Medicine name	Type of Medicine	Commercial label	Traditional medicine name
For Preventive Measures and Mild Symptoms			
Tinosporacordifolia	Liquid mixture	SamshamaniVati	Ayurveda
Andrographis paniculata	Liquid mixture	Nilavembukudineer	Siddha
Cydonia oblonga Zizyphusjujube Cordia myxa	Liquid mixture	Behidana Unnab Sapistan	Unani
Arsenicum Album 30	Tab/Liquid	Arsenicum album 30	Homeopathy
Coronil	Tab	Coronil	Ayurveda
Anu Taila	Nasal Inhaling Liquid	Anu Taila	Ayurveda
Artemisia afra Artemisia annua	Organic drink	CVO Tambavy	ATM
AraliaeContinentalis Radix	Powder/Liquid	AraliaeContinentalis Radix	KTM
Bupleuri Radix	Powder/Liquid	Bupleuri Radix	KTM
AngelicaeDecursivae Radix	Powder/Liquid	AngelicaeDecursivae Radix	KTM
Poria Sclerotium	Powder/Liquid	Poria Sclerotium	KTM, CTM
Ginseng Radix	Powder/Liquid	Ginseng Radix	KTM, CTM
Aurantii	Powder/Liquid	Aurantii Fructus Immaturus	KTM, CTM
Platycodi	Powder/Liquid	Platycodi Radix	KTM, CTM
Cnidii	Powder/Liquid	CnidiiRhizoma	KTM, CTM
Schizonepetae	Powder/Liquid	Schizonepetae Spica	KTM, CTM
Saposhnikoviae	Powder/Liquid	Saposhnikoviae Radix	KTM, CTM
Glycyrrhizaeglabra	Powder/Liquid	Glycyrrhizae Radix	KTM, CTM
Cnidii	Powder/Liquid	CnidiiRhizoma	KTM, CTM
Bupleuri	Powder/Liquid	Bupleuri Radix	KTM, CTM
Mori Folium	Powder/Liquid	Mori Folium	KTM, CTM
Mentha	Powder/Liquid	MenthaeHerba	KTM, CTM
Scutellariae	Powder/Liquid	Scutellariae Radix	CTM
Trichosanthis	Powder/Liquid	Trichosanthis Semen	CTM
Gypsum Fibrosum	Powder/Liquid	Gypsum Fibrosum	CTM
Benincasaepericarpium	Powder/Liquid	Benincasae	CTM
Rehmanniae	Powder/Liquid	Rehmanniae Radix Crudus	CTM
LoniceraeFlos	Powder/Liquid	LoniceraeFlos	CTM
Saposhnikoviae Radix	Powder/Liquid	Saposhnikoviae Radix	CTM
Chuanxiong Rhizoma	Powder/Liquid	Chuanxiong Rhizoma	CTM
Persicae Semen	Powder/Liquid	Persicae Semen	CTM
Mori Radicis Cortex	Powder/Liquid	Mori Radicis Cortex	CTM
Rhei	Powder/Liquid	Rhei Radix et Rhizoma	KTM, CTM
LepidiiseuDescurainiae Semen	Powder/Liquid	LepidiiseuDescurainiae Semen	KTM, CTM
For Moderate Symptoms			
Ayush -64	Tab	Ayush -64	Ayurveda
Agastya Haritaki	Powdery extract	AgasthyaRasayanam	Ayurveda
Anuthaila	Extraction made in oil	Sesame Oily extract	Ayurveda
AdathodaiManapagu	Liquid mixture	AdathodaiManapagu	Siddha
VishasuraKudineer	Tab	Poly-herbal preparation	Siddha
Bryonia Alba	Tab	Bryonia	Homeopathy
Rhus Toxico Dendron	Tab	Rhus tox	Homeopathy
Atropa belladonna	Tab	Belladonna	Homeopathy
Bignonia sempervirens	Tab	Gelsemium	Homeopathy
Eupatorium perfoliatum	Tab	Eupatorium	Homeopathy
Amomi Tsao-ko Fructus	Powder/Liquid	Amomi Tsao-ko Fructus	KTM
Alumen	Powder/Liquid	Alumen	CTM
Cicadae Periostracum	Powder/Liquid	Cicadae Periostracum	CTM
Tetrapanacis Medulla	Powder/Liquid	Tetrapanacis Medulla	CTM
Paeoniae Radix Rubra	Powder/Liquid	Paeoniae Radix Rubra	CTM
PinelliaeRhizomaPraeparatum cum alumine	Powder/Liquid	PinelliaeRhizomaPraeparatum cum alumine	CTM

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For Severe Symptoms			
Astragali	Powder/Liquid	Astragali Radix praeparata cum melle	CTM
Citrireticulatae	Powder/Liquid	CitriReticulataePericarpium	CTM
Atractylodismacrocephalae	Powder/Liquid	AtractylodisMacrocephalaeRhizoma	CTM
Codonopsis	Powder/Liquid	Codonopsis Radix	CTM
Fritillariaethunbergii	Powder/Liquid	FritillariaeThunbergii Bulbus	CTM
Anemarrhenae	Powder/Liquid	AnemarrhenaeRhizoma	CTM
Magnoliaeofficinalis	Powder/Liquid	Magnoliae Officinalis Cortex	KTM, CTM
For Post Recovery Symptoms			
Samchulkunbi-tang	Powder/Liquid	Samchulkunbi-tang	KTM
Ophiopogon japonicas	Extract used as intravenous injection	Saeng-maek-san	KTM
Schisandra chinensis			
Panax ginseng			
Massa MedicataFermentata	Powder/Liquid	Massa MedicataFermentata	CTM, KTM
Phellodendri	Powder/Liquid	Phellodendri Cortex	CTM, KTM
Schisandrae	Powder/Liquid	Schisandrae Fructus	CTM, KTM
Hordei	Powder/Liquid	Hordei Fructus Germinatus	CTM, KTM
Liriopis	Powder/Liquid	Liriopis Tuber	CTM, KTM
Alismatis	Powder/Liquid	AlismatisRhizoma	CTM, KTM

Table 2: A table of herbs which may have the capability to prevent the SARS-CoV-2 and other viruses

S. no.	Plant names	Invitro applications	Aim	Virus
1.	*Acacia nilotica*	Reducing Caginess	–	HIV-PR
2.	*Allium sativum*	Proteo-lytic and haem-agglutinating action and viral duplication	–	SARS
3.	*Andrographis paniculata*	Clampdown	NLRP3, capase-1, and IL-1β	SARS-COV and likely SARS-CoV-2
4.	*Boerhaaviadiffusa*	ReducingCaginess	ACE	–
5.	*ClerodendruminermeGaertn*	Inactivation	Ribosome	SARS-CoV-2
6.	*Clitoriaternatea*	Metalloproteinase inhibitor	ADAM17	–
7.	*Coriandrum sativum*	ReducingCaginess	ACE	–
8.	*Cynara scolymus Cassia occidentalis Cosciniumfenestratum*	ReducingCaginess	ACE	–
9.	*EmbeliaRibes*	ReducingCaginess	ACE	–
10.	*Eugenia jambolana*	ReducingCaginess	Protease	–
11.	*Euphorbia granulata*	ReducingCaginess	–	HIV-1 PR
12.	*Glycyrrhiza glabra*	Hindering of viral duplication; Intonation of membranechangeability		SARS; HIV-1
13.	*Gymnemasylvestre*	The reticence of virus-related DNA production	–	–
14.	*Hyoscyamus niger*	Reticence and Nebulizer	Ca2+	–
15.	*Ocimumkilimandscharicum*	ReducingCaginess	–	HIV-1
16.	*Ocimum sanctum*	ReducingCaginess	–	HIV-1
17.	*Punica granatum*	ReducingCaginess	ACE	–
18.	*Salacia oblonga*	ReducingCaginess	angiotensin II, AT1 signal	–
19.	*Sambucus ebulus*	ReducingCaginess	–	Enveloped virus
20.	*Solanum nigrum*	-	–	HIV-1
21.	*Sphaeranthus indicus*	ReducingCaginess	–	Mouse corona virus and Herpesvirus
22.	*Strobilanthescallosa*	Hindering	–	HCoV-NL63
23.	*Strobilanthescusia*	Hindering	–	HCoV-NL63
24.	*Vitex negundo*	ReducingCaginess	–	HIV-1
25.	*Vitex trifolia*	Reduction in cough	–	SARS-COV
26.	*Terminalia chebula*	Reducing cough and respiratory infection		Influenza A

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III. Plants as a Companion of Human Beings

The period of social isolation and lockdown brought new challenges to human beings from a psychological point of view. Several changes in the behaviours and habits of the families were noted, which can mainly develop changes in the psychological health of the people from all age groups. Difficulty in concentrating, cantankerousness and anxiety can be detected in them[12]. The people-plant interaction offers steadiness through interaction with the nature, facilitating contacts with other people and constructing the aesthetics of surroundings. With this understanding, gardening as an activity can be developed as an occupational therapy. Gardening as a healing remedy was first recognized and recommended by Dr. Benjamin Rush, for dealing with mental health. This effective practice was used for helping the war veterans cope up with their distress and, from that moment onwards, it was implemented to support the treatment of diverse types of mental illness diagnosis[48]. A substantial percentage of the population in large urban metropolises stays in small properties where the space for gardens is absolutely nil. Large apartment cooperatives may have designed places but, with the constraint on societalliving, they are very little in size or are completely not used. This gardening of indoor plants develops another alternative to come nearer to the nature. Some indoor plants like *Sansevieria trifasciata* and *Chlorophytum comosum*canbe grown easily and acts as efficient phytofilters for remediation of numerous pollutants from cigarette smoke[49]. *Zamioculcaszamiifolia* filters formaldehyde (used in various materials, paints, cosmetics, etc.)and toluene (found in paints, adhesives, oil, tanned materials, disinfectants, etc.)[50].These potted vegetations growing indoors help people devote most of their time, as well as develop plentiful of possibilities for experimenting with growing combinations of different plants. It is a simple answer to develop good air quality, while improving to the aesthetics of the location and contributing towards a huge range of benefits in the psychological, physiological and cognitive regions[51]. Many lonely millennials across the world turned to gardening as a resort for comforting their mind and mental well-being during the lockdown[52]. In US, the search term “gardening” reached a peak of daily searches during the prime lockdown phase which was from April 26th to May 2nd[53]. Throughout this time period of social isolation, numerous experts from the arenas of gardening, landscaping and ornamentation have made their living on social medias and have engrossed millions of individuals in pursuit of learning and development. Simple topics such as *how to maintain your plants*, *make your plantlets at home* and *use of cut flowers in diverse activities* were brought to the general public. There are reports that as many as 20 million people participated in many such activities from around the globe simultaneously[11]. Such practices have helped many people cope with the distress and depression faced during the lockdown.

IV. Conclusion

The COVID-19 pandemic has led several scientific and clinical researchers to try to recommend operative drugs to eradicate the disease. The traditional medicines from India, China, Korea, Africa and Iran have centuries of practice in stoppage of pandemic and epidemic transmittable viruses are worth exploring to develop them as alternate contender for regulating SARS-COV-2 infection in patients. Currently, due to the lack of a vaccine or drug, the world has a good capability to explore the traditional medicine decoction and tablets. Confidently, positive outcomes from clinical trials are slowing explaining that phytodrugs alone or in blend with conventional synthetic medicine can help patients to recover from COVID-19. An editorial emphasized on the necessity of funding and exploring traditional medicine data in the background of the present, and probably upcoming, pandemics[54]. It is crucial to develop advance healing medicinal technologies to guard humans from the infection in tandem with phytoremedies can be easier to safeguard against the disease. There is an urgent need study more and conduct clinical trials of the different herbal medicines so as to tackle the infection of novel SARS-CoV-2. Apart from the medicinal uses of plants, we also need to explore natural antiviral surface protective agents so as to develop a sustainable and eco-friendly system to kill viruses on any surface. Increase in mental pressure and depression can also be solved through developing companionship with plants. We all know that how hard times were during the lockdown period and with many people living away from their homes, gardening and floricultural activities helped people maintain a good psychological health. Thus, plants play an integrated role during a pandemic from providing medicinal solutions to improving mental health.

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Certificate, LoR and Momento **2** discounted publishing/year **Gradation** of Research **10** research contacts/day **1 GB** Cloud Storage **GJ** Community Access	**Certificate,** LoR and Momento **Unlimited** discounted publishing/year **Gradation** of Research **Unlimited** research contacts/day **5 GB** Cloud Storage **Online Presense** Assistance **GJ** Community Access	**Certificates,** LoRs and Momentos **Unlimited** free publishing/year **Gradation** of Research **Unlimited** research contacts/day **Unlimited** Cloud Storage **Online Presense** Assistance **GJ** Community Access	**GJ** Community Access

Preferred Author Guidelines

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

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

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

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

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2. Authors must accept the privacy policy, terms, and conditions of Global Journals.
3. Ensure corresponding author's email address and postal address are accurate and reachable.
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5. Authors should submit paper in a ZIP archive if any supplementary files are required along with the paper.
6. Proper permissions must be acquired for the use of any copyrighted material.
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- Writings
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2. Drafting the paper and revising it critically regarding important academic content.
3. Final approval of the version of the paper to be published.

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

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

Acknowledgments

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

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Preparing your Manuscript

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

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

Manuscript Style Instruction (Optional)

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

Structure and Format of Manuscript

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

A research paper must include:

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

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

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

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

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



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Format Structure

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

All manuscripts submitted to Global Journals should include:

Title

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

Author details

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

Abstract

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

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

Keywords

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

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

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

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

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

Numerical Methods

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

Abbreviations

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

Formulas and equations

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

Tables, Figures, and Figure Legends

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

Figures

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

Preparation of Eletronic Figures for Publication

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

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

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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.



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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.

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



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- 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.



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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
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References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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