A Review on Indian’s Wrath Against COVID-19
In Respect to First Wave

Ishu Garg¹, Dr. Raj Kumari¹, Amisha Goyal², Hitesh Kumar Goswami³, Kartik Kumar⁴
¹ITS College of Pharmacy, Murad Nagar, Ghaziabad, Uttar Pradesh, India
²AIIMS, B.Sc. Nursing, Rishikesh, India
³Kirori Mal College (Delhi University- North Campus), B.Sc. (Hons.) Zoology, Delhi, India

Abstract: Background: Novel COVID-19 virus, first registered in Wuhan, China in month of November-December 2019 was declared as a pandemic in month March 2020. The pandemic went for a huge impact over the world’s economy in terms of health sector, socio-economic sector, and pharmaceutical manufacturing sector resulting in a socio-economic and health crisis. To fight against this the world went for a complete lockdown and a complete dependency over the health and pharmacy sector.

Targets: Highlighting India’s pharmaceutical industry growth during this pandemic and effect of COVID-19 virus over Indian economy, social health, increased demand of pharmaceutical product in India, manufacture of pharmaceutical demand, growth of industry, export of material, and new research in pharmacy.

In India many new licenses were granted to manufacture Hydroxychloroquine, the game changer drug in COVID-19 pandemic. India begins manufacturing many drugs, pharmaceutical aids like PPE kit and face mask, soon became an exporter of the same too. With time India went for clinical trials for all the possible COVID-19 drugs. Even in the race of vaccine India participated, and ran a like a cheetah. The two Indian indigenous vaccine COVAXIN and COVISHIELD got the approval for clinical trials in India and India went for the trials of other international COVID-19 vaccines too.

Conclusion: Awareness about importance of personal hygiene, sanitization, and use of pharmaceutical products among citizens and India as an emerging hope for world’s pharmacy, a future to pharmaceutical industry in meeting the need and demand.

Index Terms - COVID-19, Pharma sector, Active Pharmaceutical Ingredient (API), Hydroxychloroquine, PPE kit, N-95 mask, vaccine.

Introduction: Dates back to Nov. 17, 2019, according to the South China Morning Post first COVID-19 case was reported in Wuhan, China. This was already a month back before the doctors ever noticed the existence of this virus [1]. Later scientists suspected COVID-19 virus, COVID-19, originated in a bat which then passed it on to humans. And by Dec 27, Dr. Zhang Jixian, head of the respiratory department at Hubei Provincial Hospital, reported to health officials in China that a novel COVID-19 virus was causing the disease. As of March 13, 2020 there were nearly 148 thousand cases globally and more than 81 thousand cases in mainland China [1].

Table 1: Role of World Health Organization (WHO) and WHO statement:

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
</tr>
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<tbody>
<tr>
<td>10-12 January</td>
<td>A comprehensive package of guidance documents for countries, covering topics related to the management of an outbreak of a new disease was published.</td>
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<tr>
<td>30 January</td>
<td>Director-General of WHO declared the novel COVID-19 virus outbreak a public health emergency of international concern (PHEIC), WHO's highest level of alarm. Alarm for a rising global pandemic.</td>
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<tr>
<td>8 March 2020</td>
<td>WHO and partners launched the Solidarity trial, an international clinical trial that targets to generate maximum and robust data from around the world to find the treatments effective against COVID-19.</td>
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<tr>
<td>4 April 2020</td>
<td>WHO reported that over 1 million cases of COVID-19 had been confirmed worldwide, the increase is more than tenfold in less than a month. [2]</td>
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<tr>
<td>17 December 2020</td>
<td>Globally there have been 72,556,942 confirmed cases of COVID-19 across the world [3].</td>
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WHO announced that symptoms like dry cough, fever, fatigue, headache, body ache, sore throat, loss of smell and taste, nausea, vomiting, are indicating the COVID-19 infection [3].

India with a population of 1,386,234,317 covering 17.7% of world population, [4] reports a total case of 9979447 covid-19 and a recoveries of 9520827 cases with death of 144789 infected people. The first COVID-19 case in India was reported on January 27, 2020 in a 20 year old female at Emergency Department in General Hospital, Thrissur, Kerala. [8] Since then India started preparing a fight against COVID-19 virus. After the declaration of COVID-19 as pandemic by WHO on March 11, 2020 [2] the Indian Government went as per the plans, initiating with the closure of educational institutes followed by “Janta curfew” on March 22, 2020 and a strict national lockdown to stop the chain of COVID-19 spread. [6], [5].PM Narendra Modi declared a strict lockdown
of three weeks starting from 23rd March 2020 explaining that it’s the only way to break the infection cycle stating “Social distancing is the only way to break the cycle of infection”. Indian government mentioned that all the essentials like groceries, medicinal facilities will be provided with a suspension of all travelling facilities, closure of all public places, working areas, educational institute, and official departments.

The Government mentioned that the lockdown will come at an “economic-cost” for the nation, but the top priority was to save lives. [6] Social distancing, wearing face mask, rubber gloves, marinating personal hygiene, regular sanitization and following other safety measure as per WHO is the only way to deal with this pandemic, government said. With the strict follow up of all these measures the national recovery rate hiked to 95.40% and a depletion in spread and death rate was seen by the month of December.

COVID-19 virus versus Indian economy- The outbreak of COVID-19 has an impact of as terror to nation, and nationwide lockdown aided this by a socio-economic dead end. Virus slowed down all the economic activities and took national growth to a negative curve. In 2019 the WHO gave a prediction that the world is unable to cope up with an upcoming pandemic resulting in fall of gross domestic product (GDP).

As per news reports in Economic Times published on 23 March 2020, the economists are pegging the cost of the COVID-19 lockdown at US$120 billion or 4 per cent of the GDP (The Economist, 2020). Showing that India is now going to grind under the burden of this COVID-19 pandemic. According to data released by the statistics ministry, real GDP for India’s economy contracted by a whopping 23.9% in the first quarter (April-June) of the 2021 financial year in comparison to the same quarter a year ago. In the January-March quarter of this year, the Indian economy had grown by 3.1% on a year-on-year – the lowest rate ever in past 17 years, and by 5.2% in the June quarter of 2019-20. The rate of India’s GDP growth had declined from 6.1% in FY19 to 4.2 per cent in FY20, the slowest record in last 11 years. This COVID-19 pandemic affected the manufacturing and service sector [7].

COVID-19 and the Indian pharma sector - With a rise in COVID cases the burden over the health care sector and pharma sector hiked overnight. The work load of doctors and other health warriors was at peak. PPE kit, sanitizing materials, masks, various active pharmaceutical ingredient (API), and other pharmaceutical products were the demands of the time. And now the pharma sector was very well aware that with no imports of APIs and no existing industries to manufacture PPE kits, masks they had to meet the need and demand of the nation.

The Indian pharmaceutical industry is said to be the world’s third largest drug producer. A report for Indian pharmaceutical industry, mentions that the source of APIs is a crucial part of the pharma industries strategic plan to takeover this COVID-19 pandemic. And the majority Of APIs for generic drug manufacturing across the globe are sourced from India, supplying about 30% of the generic

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**Graphs:**

**Graph 1:** Average comparison of confirmed, recovered, dead COVID-19 cases in India, per month [22]

**Graph 2:** Average comparison of active cases, new cases, and new recoveries of COVID-19 cases in India, per month [23]

**Graph 3:** India’s economy

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APIs used in the US. The problem arises when the impact of the COVID-19 virus outbreak, resulted in no import of APIs, procuring around 70 percent from China, for the production of medicine formulations. And to overcome the problem the Indian government undertook applaudable steps against this, initiating with a proposal of incentive package of 13.76 billion Indian currency for the domestic manufacturing of critical key starting materials, APIs, drug intermediates, and other medical equipment’s.[9][10]

The profits to India’s pharmaceutical manufacturing sector and economy by increased demand in US- “India now started receiving a higher share of Abbreviated new drug applications (ANDA) approvals led by significant manufacturing facility clearances, Generic Drug User Fee Amendments (GDUFA), and a strong filing momentum aided by historical investments in research and development (R&d),” India ratings and research (Ind-Ra) added in a report. Ind-Ra has seen an increasing drug demand since the Covid-19 pandemic led by supply chain issues, channel filling, and demand for Covid-19 led preventive products. [10]

As hydroxychloroquine (an anti-malarial drug) was considered as an effective drug against COVID-19, India imported about 50million hydroxychloroquine drug to US for fight against COVID-19 which gave the pharma manufacturing sector new heights. Though the side-effects like abnormal heart reactions and heart beat were known but the US health department and doctor decided to continue with its use for an emergency treatment to control COVID-19 spread as there was a sudden hike in infection spread rate recording an average of 60 thousand COVID cases per day.

“There is high demand for hydroxychloroquine in the international market including US,” Viranchi Shah, senior vice-president, Indian Drug Manufacturers Association (IDMA), told Reuters.

In month of April India said it would allow some exports of hydroxychloroquine after Trump hyped it as a “game changer” and urged Narendra Modi, PM, India to send supplies. 68 new licences were granted to drug manufacturer’s allowing them to manufacture hydroxychloroquine formulations in Gujarat by, H.G Koshia, commissioner, Food and Drug Control Administration (FDCA), told Reuters. Besides this Teva Pharmaceutical Industries, IPCA Laboratories and Cadila Healthcare are among India’s leading suppliers of this anti-malarial drug.

Cadila Healthcare said “it was ramping up production tenfold to 30 metric tonnes per month”.

“Pharma companies in Gujarat are continuing to produce and export hydroxychloroquine in large quantities,” IDMA’s Shah said.

These was one of the biggest achievements of India’s pharma sector and a gift to Indian economy. By this time the Indian products started supporting the world and itself in terms of both humanity and economy. [11]

Stepping towards an Atmanirbhar India (Self-reliant India) - With the increase number of COVID-19 cases, India now need proper facilities and equipment’s to deal with this. The demand of PPE kit, N-95 mask, drugs, and sanitizers increased over night. As India never required PPE kit and N-95 masks ever before at this demand hence there were no working production units till date, India was completely dependent over the imports. But with the invasion of this fatal virus in India the need to manufacture all this generated for making the nation under the agenda of ‘Operation PPE Coverall’.

Manufacturing all these was the first step to self-reliant India. With the spread of COVID-19 in India the local manufacturers find themselves in a deep crisis due to their inability to manufacture PPE kits like body coveralls, classified as class-3 protection level under ISO 16603 standards required to deal with this pandemic situation. As India was utterly dependent on imports, so another crisis in the form restrictions in flow of essential medical supplies around the globe worsened the health crisis. In March, Niti Aayog estimated that India would need 20 million PPE kits and 40 million N-95 masks, which translated to 20 thousand PPE kits and 400 thousand h-95/FFP-2 class masks per day by July. With zero capacity of manufacturing, India needs a high quantity of PPE kits and masks for all the health warriors. This time the nation knew that with this exponential growth of virus, healthcare centre will soon collapse with a shortage of PPE kits. Hence an immediate decision regarding this is need to be taken.

Indian government began with planning, which involved a joint study by Ministry of Health and Family Welfare (MoHFW) and Ministry of Textile (MoT) undertaken in February-March for understanding the gaps in the existing infrastructure, resources, and for end-to-end production, testing, and packaging of the PPE kits as per the quality standards defined by WHO. Both textile and healthcare industry experts got completely involved along with industry associations and major manufacturing companies in India, with the Government of India (GoI) at the helm. [12]

The new challenge arises with the quality of the manufactured PPE kits, which had to conform to the stringent quality standards. The planning stage revealed that a majority of local manufacturers were not able to produce the right fabric to withstand Synthetic Blood Penetration Test in accordance with ISO 16603:2004 (Class-3 exposure) specifications. The South India Textile Research Association (SITRA), a textile research organization was instrumental in testing samples during the run and by 22 March 2020, test samples of only four manufacturers could pass the test, thus preventing the initiative from scaling up. This led to another bold decision for nation, launch of “Operation PPE Coverall” by MoT on 24 March 2020. During the lockdown, on 8 May 2020, it was reported that seven more NABL-accredited laboratories besides SITRA have been approved for testing PPE Coveralls. For a large scale testing, a well-developed network across the labs was required. Building up a network of labs ensured efficient testing of PPE kits across India and reduction in post-production timeframe involved in testing, clearance and dispatch of the final product. [12] MoT and MoHFW started focusing on development of a PPE supply chain, getting special approvals and clearances for coverall and fabric manufacturers, facilitating inter-state logistics, streamlining international coordination, and enabling round-the-clock support to the manufacturers on operational issues. The GoI constituted an empowered committee to manage all operational challenges and thus facilitating the availability of time-critical medical supplies. [12]

In a matter of 60 days India achieved all its target and went for world recognition. [12] As per the reports of 12 May 2020, India was manufacturing 200 thousand units of PPE kits and 200 thousand units of N95 masks on a daily basis. By the time of July, India’s indigenous supply of PPE kits had exceeded the domestic demand and started an export
of 23 million personal protection equipment to the US, the UK, Senegal, Slovenia, and UAE. India was thus transformed from an importer country to a self-sufficient one and later an exporter country in terms of PPE kits.

This is what India’s self-efficiency is about. Even in the hardest time and stressful condition of COVID-19, the pharma sector is enough strong to pillar the Indian economy. [12]

COVID-19 and new edges of Indian Pharmacy- Invasion of COVID-19 virus created a health emergency across the world. Due to this the world started expecting a lot from health and pharma sector to end this pandemic, expectations in terms of vaccine development, spread control, drug, diagnosis and proper treatment. For this the world went for a race to develop a highly efficient COVID vaccine and to find out a proper diagnosis and treatment plan against COVID-19.

In India Molecular (RT-PCR) tests, COVID-19 Antigen Tests and COVID-19 Antibody Tests were performed for the diagnosis of COVID-19 infection. [13] Initially the diagnosis kits were not indigenous but later the tests were developed indigenously in coordination with R&D department of pharmacy.

Talking about the treatment of COVID-19, India went for a complete national lockdown to maintain social distancing, proper sanitization caught up with self-isolation in case the individual doubted to be an infected one. This was the basic and effective step taken up by the whole world and Indian government to break the spread. In the early period of COVID-19 outbreak there was no vaccine and any antiviral drug against COVID-19. All the drugs which were found to be effective were under the evaluation and clinical trials. The vaccines were under process and clinical trials too. An anti-malarial drug Hydroxychloroquine was the first recommended drug for prophylactic use by the asymptomatic healthcare personnel handling COVID-19 cases. With time a combination of HCQ and azithromycin antibiotic drug was recommended for patients with serious sickness under the appropriate medical supervision. However, no evidence was provided to prove the benefit of this drug (alone or in combination with azithromycin), instead an increased risk of ventricular arrhythmias has been proposed. India has commenced controlled trials of convalescent plasma therapy on severely ill patients with donors having no symptoms after 28 days of recovery and with no past record of any blood trans-fusible disease or any CVS disorder. The clinical trials of Favipiravir drug was also commenced in India. [14] Remdesivir, patented anti-viral drug, earlier tried on Ebola was under clinical trials and shorter recovery time was observed. Tocilizumba drug used for rheumatoid arthritis was also under clinical trials and a reduced immune inflammation was seen due to inflammatory effect of COVID-19. Other drugs like Iotolizumab, steroids, Methympredmisolone, and antibiotics Azithromycin, Ivermectin were also under clinical trials for treating COVID-19. [15]

With-time the COVID-19 cases were increasing at a rate of forest fire, and to counter this India needs a relief rain of COVID-19 vaccine. With high research and dedicated work Indian scientist developed two effective vaccines against COVID-19, although these vaccines were under clinical trials, dated 23 December 2020. The vaccine includes viral-vectored, protein subunit, nucleic acid (DNA, RNA), live attenuated and inactivated type vaccines.

COVAXINTM, India’s indigenous COVID-19 vaccine, developed in collaboration with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV). This indigenous, inactivated vaccine is developed and manufactured in Bharat Biotech's Bio-Safety Level 3 (BSL-3) high containment facility. The vaccine received approval from Drug Controller General of India (DCGI) for Phase I & II Human Clinical Trials, by Phase II Randomized, Double blind, Multicentre Study to Evaluate the Safety, Reactogenicity, Tolerability and Immunogenicity of the Whole-Virion Inactivated COVID-19 Vaccine (BBV152) is done. After the success of phase I and phase II trial the DCGI approved phase III trial in 26,000 participants in over 25 centres across India. [16] [17]

The Serum Institute of India (SII) and Indian Council of Medical Research are jointly conducting a Phase II/III, Observer-Blind, Randomized, Controlled Study to Determine the Safety and Immunogenicity of Covishield, another indigenous COVID-19 Vaccine. [16]

As per the reports by SII, 7 December 2020; The Pune-based Company has collaborated with Oxford University and pharmaceutical company AstraZeneca for making the vaccine and trials in India are now under progress. In starting of December, Pfizer India said it has applied to India’s drug regulator DCGI for emergency-use authorisation for its COVID-19 vaccine. [18]

Dr Reddys Laboratories Limited and Sputnik LLC are jointly conducting Multi-centre, phase II/III adaptive clinical trial to assess safety and immunogenicity of Gam-COVID-Vac (Sputnik) combined vector vaccine in India. [16] The vaccine is discovered by Russia and received a registration certificate from the Russian Ministry of Health and under emergency rules adopted during the COVID-19 pandemic. Sputnik is the first ever registered COVID-19 vaccine. [19]

The Indian pharma sector found a growth in field of defining new mutant forms of COVID-19 virus. As Bani Jolly, PhD scholar at New Delhi’s Council of Scientific and Industrial Research institute of Genomics and Integrative Biology (CSIR-IGIB), said “The clade A2a, which is also the predominant clade in rest of the countries, is the most prevalent clade in India, comprising over 70 per cent of the genomes sequenced till date,” October, 31, 2020.

Jolly explained that this is defined by two mutations. First one is D614G, which is a mutation in the spike protein of the virus. The second mutation is P314L, in what is known as the ‘Orf1b’ gene.

“This is the second most prevalent clade in India and what we have named in our study as clade I/A3i. This clade comprised about 20 per cent of the genomes sequenced from India,” Jolly explained.

This clade is defined by four mutations - A88V in the Orf1b gene, P13L in the nucleocapsid protein, T2016K in the Orf1a and C23929T in the Orf1a. Most genomes in this clade also share the mutation L3606F in the Orf1a, which is a characteristic mutation for another clade, A3. Interestingly, the I/A3i clade was found to be present in distinctly large numbers in India, Delhi, Maharashtra and Telangana- are the major areas from where this clade is extracted.

The Indian Ayurveda relates the COVID-19 pandemic with making immunity stronger than before. The Ayurveda suggest to take some defined kahada’s and herbal teas to boost the immunity, followed by a regular meditations and respiratory system related yoga like pranayama (Bhastrika, Kapala Bhati, Anuloma Viloma, Brahmari, Ujjayi, Uteet, and finally Sheetali and Sheetkari). Taking some natural herbs and spices with antibacterial and antiviral properties like turmeric (haldi), mulaithi, ashwagandha, ajjwain, cinnamon (dal-chini), giloy, tulsi and some others. [21] Swasari Coronil kit 200 GM was introduced by Patanjali as an immunity booster against COVID-19. [21] This is one of the biggest achievement by Indian Ayurvedic pharmacy during this COVID-19 pandemic.

Conclusion
Though the COVID pandemic and lockdown pushed socio-economic life of nation in a deep well of grief bringing it to a dead-end, affecting the physical health, mental health, social health and emotional health. As the social movements ended the people suffered with anxiety, loneliness and with rising COVID-19 cases a fear for life took place in hearts. All this leads to depression and many suicides, a negative effect over mental, social and emotional health. The COVID effect over physical health is known very well by everyone but the mental and emotional health got a hit at different height. What comes in favour due to COVID-lockdown is something worthy. Starting with the concept of hygiene and cleanliness, all citizens are now well aware about how to maintain and why to maintain personal, community and national hygiene. The sustained use of sanitizers, soaps, hand gloves, masks and other cleaning equipment’s are in knowledge of natives along with the information on how and when to use them. The next comes to the changes in vision towards pharmacy education and pharmacy as a carrier. After the successful researches in pharmacy during COVID-19 pandemic and watching pharmacy as an emerging pillar to India’s economy the natives realized true value of pharmacy education and carrier. The natives realized the value of health warriors other than doctors and medical staff, which include army officers, police team, cleaning and sanitizing staff, pharmacists, biotech staff and many more. Pharmacy also lead to development of self-sufficient India as India started manufacturing its own PPE kit and N-95 masks, their export too leading to stronger and new international bonds. The lockdown healed the nature, improved air quality and water bodies, as report says. [25]

As India is performing clinical trials of various international vaccines and soon it will start the production of Russian vaccine Sputnik [24]. The manufacture of various drugs and their export raised exponentially too during this lockdown. India’s biotech institute developed one of the most effective COVID-19 vaccine. Also the manufacture of PPE kit and N-95 masks and their exports were done under such a stressful condition. Proving India a self-efficient country and a hope to world’s pharmacy which can meet all its demands in terms of research, clinical trials and manufacture.

Abbreviations:

1. WHO: World Health Organization
2. PHEIC: Public Health Emergency of International Concern
3. GDP: Gross Domestic Product
4. API: Active Pharmaceutical Ingredient
5. ANDA: Abbreviated New Drug Applications
6. GDUFA: Generic Drug User Fee Amendments
7. R&d: Research and Development
8. Ind-Ra: India Ratings and Research
9. IDMA: Indian Drug Manufacturers Association
10. FDCA: Food and Drug Control Administration
11. MoHFW: Ministry of Health and Family Welfare
12. MoT: Ministry of Textile
13. GoI: Government of India
14. SITRA: South India Textile Research Association
15. ICMR: Indian Council of Medical Research
16. NIV: National Institute of Virology
17. BSL-3: Biotech's Bio-Safety Level 3
18. DCGI: Drug Controller General of India
19. SII: Serum Institute of India
20. CSIR-IGIB: Council of Scientific and Industrial Research institute of Genomics and Integrative Biology

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