A Review on COVID-19 Vaccine Storage And Opportunities in Storage Management

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Abstract- *COVID-19 has taken a toll on mankind in terms of economy as well as lives. This has turned into an economic tragedy and devastation. Until this date, no drug has yet been derived that can destroy the virus from the root. This leaves us only one option to intake vaccines that are available in the market such as Covaxin, Covishield, and Sputnik V, etc. These vaccines are requested to store under the controlled environment which is prescribed by the manufacturer, as well as by World Health Organization. If these vaccines are not stored in the prescribed temperature and humidity conditions, their chemical composition changes drastically due to bacterial growth reducing its effectiveness over the disease. Cold Chain plays a prominent role in maintaining these ranges and is better than all other preservation methods available. In this paper, a review has been taken on the importance of cold chain, scope, and opportunities in improving cold chain facilities available in India.*

Keywords- COVID-19, Vaccine, Cold Chain, WHO

Abbreviations:

COVID-19: Corona Virus Disease 2019
WHO:World Health Organization
UNICEF:United Nations Children's Fund

I. INTRODUCTION

As per WHO prescription and guidelines most of the vaccines likes Covishield, Covaxin, Diphtheria, Tetanus, Pertussis, Hepatitis A are required to be preserved at refrigeration temperature 2°C to 8°C. As vaccines are highly thermo-sensitive, any minor change in the surrounding temperature conditions drastically affects their life and potency. The potency losses majorly include the change in chemical compositions, odour, physical appearance, etc. The vaccines are then termed as deteriorated and are no longer useful for disease cure for which it is designed. Unfortunately, 25% of the vaccine deterioration occurs due to improper storage and handling. In India, this value is about 40%, which makes it a serious concern. If these deteriorated vaccines are consumed by the end-user or patient, his/her health might get hazardously affected sometimes cost their lives. As per the WHO data, Vaccine-preventable diseases are responsible for about 25% of the 10 million deaths occurring annually for children under five years of age. Also, the economic losses due to this are very high and irrecoverable. The pharmaceutical industry has seen a rapid growth of products that are typically temperature sensitive, and need to be refrigerated or frozen or maintained at room temperature for the complete duration of shipment or transit before it reaches its valued customer. [1]

The Cold chain plays an important role in preserving vaccines as per the vaccine storage and guidelines prescribed by World Health Organizations and it is better than most other preservation methods. The purpose of the vaccine “cold chain” is to sustain product quality from the time of manufacture until the point of administration by guarantee that vaccines are stored and transported within recommended temperature ranges. The refrigerated trucks are used to transport the vaccines from the manufacturer to the local distributor or pharmacist. It consists of active refrigerating systems which require a large amount of constant power supply and thus often fail to maintain the required temperature which is 2-8 degree Celsius during power cut-off conditions. But the most important problem in this process is exposure to higher temperatures and/or fluctuations of storage temperature beyond the prescribed range produce permanent adverse effects on the potency of a vaccine, which is the primary cause of vaccine deterioration marketed through retail channels. In the conventional cold chain facilities, the compressor works in on-off mode. During the compressor on mode the refrigerant of the evaporator coil takes the cabinet heat from the cabin resulting in providing a cooling effect to the cabinet and its occupant vaccines. Whereas during the off mode of the compressor, the temperature inside the evaporator cabin starts rising due to heat released by the vaccines and also due to ambient conditions. Because of this on and off making a temperature fluctuation inside the evaporator cabinet, ultimately vaccines grade decreases. The physical and chemical changes caused the loss of quality of the product.In

this paper, a review has been taken on the cold chain facilities and challenges in building a full-proof infrastructure that is currently involved in vaccine storage and transportation. Literature has been thoroughly surveyed to determine the future scope to improve its storage management.

II. COVID-19 SITUATIONS

The COVID-19 has turned into a global human tragedy and economic devastation. It has taken a toll in terms of lives as well as the economy of humankind. Governments have implemented lockdown measures, blocked international travel, and enforced other public containment measures to overcome the virus spread ability and further mishappenings. As of today, no drug has the power to fight the infection and bring an utter chaos. This leaves us with only one choice of an effective and safe vaccine intake that is available in the market such as Covishield, Covaxin, Sputnik-V, as early as possible. Researchers over the world have made immense efforts to create the perfect formula for the vaccine and succeed in the same.

As per the data provided by Bharat Biotech, all the vaccines that are made in India are designed in such a way that they are required to be stored at the temperature range of 2-8 degrees Celsius. This is since the temperature range can be easily achievable in the Indian climatic conditions. Also during COVID-19, it will be a real challenge to build new infrastructures just to store the COVID-19 vaccines. So the temperature mentioned above with optimum humidity condition will be best suitable for the safe storage of these vaccines.Due to infrastructure unavailability, over 3 billion vaccines got wasted due to improper handling. The economic losses that have to be faced by India will not be recoverable in a stipulated timeframe. So saving vaccine life using available technology will be the key factor to avoid losses.

III. POSSIBLE REASONS AND STAGES FOR VACCINE WASTAGE

The vaccine wastage is broadly divided into two categories:

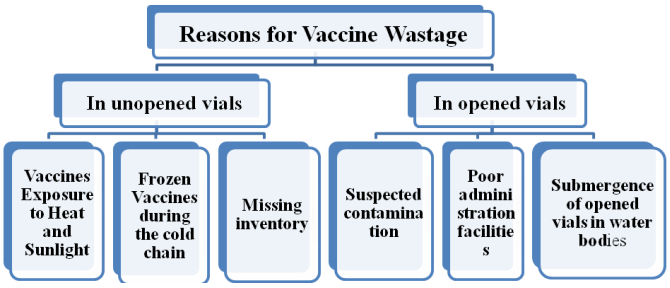

Figure 1: Various Reasons of Vaccine Wastage during supply chain

(a) Wastage in unopened vials:

The vaccine wastage in unopened vials includes wastage of vaccines when the vaccines are not opened even for a single after the manufacturers' point. This wastage often occurs due to broad reasons including;

i. Vaccines Exposure to Heat and Sunlight
ii. Frozen Vaccines during the cold chain mishandling
iii. Missing inventory

(b) Wastage in Opened Vials:

The vaccine wastage in opened vials includes its wastage during its actual dosage to the recipient. The possible reasons may include;

i. Suspected contamination
ii. Lack of administration facilities
iii. Emergence of opened vials in water bodies

As per the reports, 60% of vaccine deterioration occurs in the opened vials which account for a huge number of economic losses. This clearly states that India is still not providing potential cold chain infrastructure.

Stages of Vaccine Wastage:

The vaccine wastage often is observed in the three stages particularly:

1. During Cold Chain Point
2. At Vaccination sites
3. Both at Delivery and Service Sites

At every point of the stage, to avoid vaccine wastage World Health Organization and UNICEF have provided the operational guidelines. These guidelines should be thoroughly followed by the healthcare systems at various points.

IV. WHO GUIDELINES FOR VACCINE COLD CHAIN MANAGEMENT

WHO consultants have prepared some guidelines and plans of action to avoid vaccine losses during its distribution. These are summarized as follows:

- The majority of the commonly prescribed vaccines are required to be constantly maintained under the storage temperature of 2°C to -8°C. The most optimal

temperature is 5°C at which vaccines remain stable and safe for the highest duration.

- All vaccines get deteriorated after their expiry date, but if are stored above or below the required temperature, this deterioration rate increases rapidly and may turn hazardous if consumed by the recipient.
- Certain freeze-sensitive vaccines majorly contain aluminium adjuvant which if are exposed to freezing temperature gets precipitated in turn loses vaccines' designed chemical structure. So the containers in which the vaccines are stored should not allow vaccines to get freeze.
- On the other hand, some exceptions like varicella vaccine and LAIV are requested to be stored continuously in the frozen state and if exposed to sunlight loses their effectiveness. So if the manufacturer has provided some special guidelines regarding storage conditions that must be followed without fail.
- The temperature inside the storage system must be monitored frequently and documented at a particular time interval. Different sensors, temperature indicators, thermometers should be effectively implemented to detect even a single deflection in temperature.

V. NEED OF VACCINE COLD STORAGE SYSTEM

Here a discussion has been done about cold chain and Current Cold Chain systems in India and States along with Vaccine and Immunization Logistics Chain.

5.1 Cold Chain:

The "cold chain" includes all of the materials, equipment, and procedures used to maintain vaccines in the required temperature range of +2-degree Celsius to +8 degrees Celsius from the time of manufacturing until the vaccines are administered to individuals.

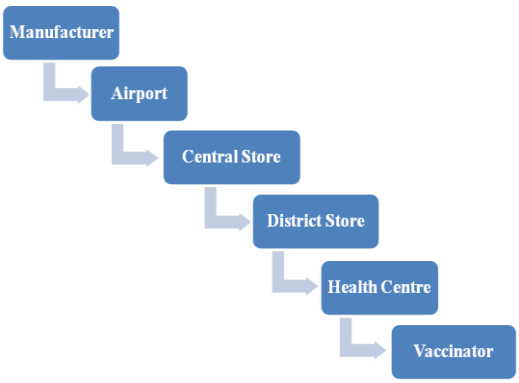

Figure 2: General Cold Chain for Vaccines

5.2 Importance of the Cold Chain for Vaccines:

- Vaccines are highly thermo-sensitive chemical substances that can lose their potency and effectiveness when they are preserved in temperatures (heat as well as cold) outside the prescribed temperature range of +2 °C to +8 °C or when presented to light.
- Freezing of vaccines occurs when they are stored below the freezing temperatures or under 0°C. Vaccines may not seem to freeze but are damaged at these temperatures. Ultra-freezing of the vaccines refers to a condition where vaccines appear to be frozen and also get disturbed in their chemical structure.
- Also if they are not stored at the required temperature and not consumed before the expiry date they may again get wasted.
- Inability in providing the required infrastructure for vaccine storage may vanish vaccine potency which diminishes its possibility of reacting against preventable disease.
- The loss of vaccines due to cold chain inactivity is cumulative, permanent, and irreplaceable.
- Vaccines wastage results in huge economic losses as the vaccine costs are high. The wasted vaccines must be replaced with better ones. If the vaccines are consumed by the recipient, it may cost their lives as well.
- Due to irregular supply deficiency, it is not possible to get extra vaccines to replace the damaged ones to mitigate the huge vaccine demand.

5.3 Challenges in Cold Chain system and scope of work:

As vaccination is one of the most effective disease prevention strategies its implementation should properly do across all sections at-risk population. The system used for storage and distribution vaccines in good condition is called the "cold chain." Cold Chain is a system of storing and transporting vaccines at the recommended temperature range (2-8°C) from the point of manufacture to point of use.

Three major challenges in vaccine storage management are; Inadequate energy to power cooling equipment, Performance of refrigerators inadequate for vaccine storage and freezing icepacks, Short cold-life of passive-cooled containers [2]. This cold chain involves an active refrigeration system that requires a power supply for its working. Rural Indian areas are still facing electricity cut-off problems which are a big reason for the failure of full-time active systems. There we need to have a passive cold storage

facility that can maintain the required temperature for a longer duration even in the absence of a power supply. When the vaccines are preserved above or below the required temperature, the potency of vaccines is lost. So that excess heat and cold can damage the potency of vaccines. Also, they are sensitive to sunlight, UV and infrared rays, fluorescent rays. The damaged vaccine is very harmful to the health of children and adults alike. The main reason for the damage of vaccines is improper storage and transportation. The vaccine can be transported far last time for a long duration. The "last mile" transportation of vaccines is necessary. Also, a technology that can transport a larger volume of vaccines is needed as existing cool boxes can transport a limited number of vaccines at a time. The temperature, humidity, and other parameters should be continuously monitored during its transportation as it may affect the vaccine life drastically. An alternative system should be designed and implemented if the core system loses its capacity during transportation. As the COVID 19 vaccine is launched in India, it is necessary to provide a better medium for its storage and transportation. Leakage detection and alerting system also should be designed for better control. The need for appropriate equipment to store and transport vaccines in tropical developing countries led to innovations in refrigeration equipment as well as the introduction and widespread adoption of novel high-performance vaccine cold-boxes and carriers. [2]From the above discussion, it can be concluded that a transport and storage system which is portable, economical should be designed and that will be a better option over the existing solutions.

Despite tremendous efforts over the past few decades to provide access to vaccines to as many people as possible, many technical, social, and programmatic obstacles remain [3]. Refrigeration is very important in maintaining the safety and preservation of vaccines and the use of refrigeration is a major contributor to global energy consumption. Due to frequent power cut-offs and lack of infrastructure in rural areas, a pure refrigeration system stays on the back foot in maintaining optimum temperature range. Vaccine exposure to temperatures below recommended ranges in the cold chain may decrease vaccine potency of freeze-sensitive vaccines leading to a loss of vaccine investments and potentially places children at risk of contracting vaccine-preventable illnesses [4]. Using water as a system has suffered from important performance limitations such as 1) Temperature swings above and/or below the upper & lower critical temperature limit of the product; 2) Restricted shipment duration due to incapability of water to maintain the desired/preferable temperature of the product. For example, maintaining a constant 5°C in 2 to 8°C or -15°C in -10 to -15°C shipment for short (4 to 12 hour transit) or long duration (72 or 96 hour transit) [1]. So a phase change material is a substance that can store or release a significant amount of heat energy by changing the phase liquid to vapour or vice versa. Thus it may improve the coefficient of performance of vaccine storage and transportation cycle. The PCMs will maintain the temperature inside the cool box within the prescribed range which is 2-8 degrees Celsius. Meanwhile, implementation of IoT technology is the best way as sensors will continuously monitor the temperature, humidity, and location of the storage box which can be accessed with the help of mobile phones cloud storage. Each country possesses a unique set of challenges to overcome and useful user feedback that can be incorporated into product design and training.

VI. LITERATURE SURVEY

Dr Punit Fulzele1, Amit Kumbhareet. al[2020][5]

In this paper,a modified version of vaccine cold box is developed by using concepts of IoT and Peltier effect. For the safe vaccines, we need the proper environment for maintaining the temperature in between 2 degree Celsius to 8 degree Celsius. For this by using Peltier based thermocouples and some of phase change material the temperature inside the box will be maintained. Also by using different IOT devices such as DHT11- temperature sensor, GPS module, Node MCU- esp8266, and Blynk application. The details of vaccine cold box like location, temperature inside the box will be easily accessible on the smartphone with the help of Blynk application.

Zhao, Y., Zhang et.al [2020][6]

In this experimental study, authors have developed innovative cold storage equipment as per the temperature requirements of pharmaceutical cold chain logistics, based on phase change materials with a phase transition temperature of 2 ℃ ~ 8 ℃. They also have implemented a system that can monitor the temperature of the vaccine in real-time on the user's mobile phone. The cold storage equipment is equipped with a special cold storage box for the vaccine. The vaccine reagent tube can be placed in the storage hole of the cold storage box. In this paper, the theoretical minimum eutectic temperature and latent heat value are determined through theoretical calculations, and then four different ratio mixtures are prepared around the eutectic point to determine the actual optimal ratio.

Zhang Yu, Ma Tianshan [2018] [7]

In this review, temperature-sensitive and efficient cold chain logistics are explained. The technology used in the

cold chain supply for tracking the trucks and their temperature is to use sensors and radio frequency identification devices. They have combined, LTE-A, which is the future of GPS and 3G technologies, and the concepts of extranet and intranet to make the system as transparent as possible. By using this technology it can improve the cold chain supply and storage. The technology is exceptionally helpful and has a minimal expense. By using this type of cold chain technology it is very useful for suppliers, vendors, and customers due to the transparency in the system.

Lloyd, J. and Cheyne, J et. al[2017][2]

In this study, the authors have mainly focused on how the cold chain infrastructure has evolved concerning time, right from its origin. In this paper, the authors point out all the challenges that are being faced by the cold chain facilities and also what possible solutions can be applied to overcome them. According to the paper, cold chain facilities have to face issues due to three main reasons; absence of systems to monitor the temperature of thermo-sensitive vaccines, absence of appropriate equipment to store and transport vaccines, insufficient number of adequately trained staff to handle vaccines. The challenges and solutions are briefly explained with future directions. The paper also concludes that the vaccine cold chain has contributed to one of the world's public health success stories and provides three priority lessons for the future: the vaccine supply chain needs to be integrated with other public health supplies, re-designed for efficiency and effectiveness and work is needed in the longer term to eliminate the need for refrigeration in the supply chain.

Hanson, C.M., George et.al [2017][4]

This review explains about the issues of vaccines, when stored below the recommended ranges during multiple stages of cold chain. Vaccine investment losses occur when freeze sensitive vaccines are stored below the prescribed temperature values due to their deterioration. This review also states that most of the vaccine losses are due to its exposure to low freezing temperatures than its exposure to higher temperature. It also suggests that many reviewedstudies emphasize the lack of knowledge of health workers regarding freeze damage of vaccines and how this has an effect on temperature monitoring. It is important to address this issue by educating vaccinators and cold chain staff to improve temperaturemaintenance and supply chain management, which will facilitate the distribution of potent vaccines to children.

Ozan S. Kumru, Sangeeta B. Joshi et. al [2014][8]

This literature glimpses on the challenges faced regarding vaccine instability during its clinical as well as commercial development. The prominent reasons including the composite and intricate structures of antigens, use of adjuvants for enhancing its response to immunity, assessing vaccine integrity and potency, and vaccine stabilization methods for avoiding integration of adjuvants and antigens. As per the authors' suggestion, a combination of formulation approaches with the maintenance of effective cold chain infrastructure can stabilize the vaccines to a higher extent. So maintaining cold chain temperature for the vaccine is an important criterion for vaccine stability and its further lifecycle.

E. Oró, A. de Gracia et.al[2012] [9]

In this paper, a review of TES for cold storage applications using solid–liquid phase change materials has been carried out. The scope of the work was focussed on different aspects: phase change materials (PCMs), encapsulation, heat transfer enhancement, and the effect of storage on food quality. Materials used by researchers as potential PCM at low temperatures (less than 20 ^{0}C) are summarized and some of their thermophysical properties are reported. Over 88 materials that can be used as PCM, and about 40 commercially available PCM have been listed. Problems in long term stability of the materials, such as corrosion, phase segregation, stability under extended cycling or subcooling are discussed. Heat transfer is considered both from theoretical and experimental point of view and the different methods of PCM encapsulation are reviewed.

Samant, Y, Lanjewar et.al [2007] [10]

This paper help remind us that even the best vaccine programs are limited by our ability to distribute the vaccine and maintain its potency. Vaccines are sensitive biological substances that lose their potency, particularly when exposed to higher temperatures. Of course, the places where the vaccination programs are operating are rural areas in developing countries with limited resources and limited staff. Things as simple as coolers or refrigerators may not be available. The article describes the vulnerable areas where potency loss is most likely to occur: out in the rural districts. The vulnerability increases as the vaccine moves from the larger medical centres to the smaller centres.

Rob Liddiard et al. [11]

The tool is demonstrated on a sample of three foods (milk, chicken and fish) in India, which historically has suffered significant interruptions. The effect of interruptions is quantified in terms of tonnage and monetary value of potential

losses, in a number of simple scenarios. The duration of power supply interruptions increases potential losses in domestic refrigerators, and that these losses are considerable when compared to losses expected in previous stages of the food supply chain.

Avesahemad S N Husainy, Gajanan V. Parishwad et al. [12]

In this experimental work, an attempt has been made to reduce the temperature fluctuation occurred by a power cut OFF as well as because of frequently opening and closing the door of system. The main objective of this research is to improve the cooling performance by prolonging the cut OFF period of the compressor, and also maintain a constant temperature inside the system by using Nano-PCM, viz. (CuO + KCl and CuO + NaCl) by considering water as a base fluid.

VII. CONCLUSION

COVID-19 has not only devastated healthcare industry but also the overall human life at a greater extent. Only prevention over this deadly disease is to intake the vaccine as early as possible as no drug has yet arrived which will remove its root cause. But the cold chain infrastructure unavailability always becomes a prominent reason in vaccine losses and in turns it into huge economic losses as they are very sensitive to the surrounding environmental conditions. Though there have been significant improvements made in cold chain over the period, still there is a large scope for its betterment. Maintaining proper temperature range in the rural areas where power cut-off frequency is high is the biggest issue in vaccine storage and transportation management. Technologies like thermal energy storage implementation, IoT system, monitoring devices should be effectively used in storage systems to make the infrastructure smart and reliable.

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