Deanship of Graduate Studies

Al Quds University

Effectiveness of Cold Chain on Rotavirus Vaccine in Southern West Bank in Palestine

Fahed Tawfiq Abd Al-Salam Tanneinah

M.Sc. Thesis

Jerusalem-Palestine

1444/2023

Effectiveness of Cold Chain on Rotavirus Vaccine in Southern West Bank in Palestine

Written By

Fahed Tawfiq Abd Al-Salam Tanneinah

MD, AL- Quds University, Palestine

Supervisor

Dr. As'ad Ramlawi, MD

A thesis Submitted in Partial Fulfillment of Requirements for the Degree of Master in Infectious Disease Prevention and Control

Faculty of Public Health

Deanship of Graduate Studies

Al- Quds University

1444/2023

Al Quds University

Deanship of Graduate Studies

School of Public Health

Thesis Approval

Effectiveness of Cold Chain on Rotavirus Vaccine in Southern West Bank in Palestine

Prepared by: Fahed Tawfiq Abd Al-Salam Tanneinah

Registration No.: 22012062

Supervisor: Dr. As'ad Ramlawi, MD

Master thesis submitted and accepted, Date 23/5/2023

The names and signatures of the examining committee members are:

1- Head of the committee: Dr. As'ad Ramlawi Signature:

2- Internal examiner: Dr. Nuha El Sharif Signature:

3- External examiner: Dr. Mohamad Rizeq Signature:

Jerusalem – Palestine

1444 / 2023

Declaration

I hereby declare that this thesis submitted for the degree of master is entirely of my own work and research, neither this thesis nor any part of it has been submitted to any degree in higher education universities or institutions.

Fahed Tanneinah

23/05/2023

Acknowledgment

Praise be to Allah for the persistent assistance and insight conferred throughout my studies. It is his guidance that kept me on track even at the point of being extremely stranded.

Plenty of gratitude to my wonderful supervisor Dr. As ‘ad Ramlawi for his feedback and supervision. I am lucky to have a supervisor who is responsive to all aspects of this thesis, not to forget the Program Director Dr. Nuha El Sharif for her support and guidance during the entire program courses with extension to the Faculty of Public Health staff.

Special gratitude and regards to my family. I appreciate their empathy & support, particularly to my parents to whom I dedicate this work, and indeed to my wife for her support.

Exponentially would like to thank my brothers, sisters, and friends, for their encouragement, and for the occasional pleasure escapes that were necessary for refreshments from my research.

Executive summary

Background

The Palestinian Ministry of Health (MoH) has sought measures to contain the severity of the Rotavirus infection. While control techniques are being taken, several global types of research have been conducted to introduce vaccines which is reliable & can potentially prevent the spread of the disease and reduce hospitalization. However, Precautions of general hygiene such as washing hands, and surface disinfection prevailed by the World Health Organization recommendations across the globe for all countries to give children the rotavirus vaccine.

Following a Rotavirus outbreak among vaccinated children in the southern West Bank of Palestine, where the cold chain was suspected. This study aimed to show the relationship between vaccine effectiveness and cold chain. Cold chain is a temperature-controlled based system of a supply chain consisting of storage and distribution, besides the refrigerated production facilities supported by equipment that can continuously maintain the required recommended temperature range for vaccine safety.

Methods

In a cross-sectional study, the study setting is the vaccines cold chain of the Palestinian MoH, since it is the main provider of the vaccine to the community. Particularly focusing on the central vaccine storage in Nablus Governorate at the national level, besides the two sub-national levels in the southern West Bank. Employees from the Primary Health Care Directorates of Bethlehem and Hebron, as well as randomly selected vaccine centers and mobile services were all assessed using the World Health Organization's (WHO) Effective Vaccine Management (EVM) standalone assessment tool.

Results

The results of this study demonstrated high performance and strength among most indicators of the Palestinian MoH cold chain, which have scored above the recommended standard scores of 80, particularly the temperature monitoring indicator and storage capacity indicator, the cold chain equipment and transport indicator scored high as well as the stock management indicator. Nevertheless, the sub-indicator of health worker knowledge and experience besides the frequent training scored high. The sub-indicator of deep freezers temperature as well as cold boxes and carriers scored above 80 as well which is performing well. Other indicators showed variable performance among various service levels, the National, Sub-national, and lower service levels. The building indicator did not perform well at all levels and show variable results, this was attributed to factors with management issues and maintenance craftsmen, the indicator of distribution performed variably among various levels, some scored high and some scored low as well as the maintenance indicator which has scored low across all service levels. The distribution task is performed in participation between Palestinian MoH-owned vehicles and contracted corporate of private sector vehicles. The information system indicator scored variably among various service levels which obviously attributed to the computerization of data and further documentation issues.

Conclusion and recommendations

The conclusion is that the Palestinian vaccine cold chain is generally performing well at all levels. It is in good standing when compared to other countries' chain assessment according to studies in the literature, particularly Tolo District of West Ghana in Africa in a study conducted in 2019 & Gujarat of India in Asia in a study conducted in 2011. Mobile outreach services performance was adequately effective and compliant with global recommendations despite the limited resources and various influencing factors of sun exposure and transportation issues.

It is strongly recommended to implement an action plan to improve the weak indicators and amend the defects, besides conducting a routine evaluation of the cold chain to spot the weaknesses and carry out improvement, conduct timely and efficacious maintenance of cold chain equipment besides management in terms of SOP's and computerization of documents and procedures as well as the transportations.

فعالية سلسلة التبريد على طعم فيروس روتا
في جنوب الضفة الغربية في فلسطين

الطالب: فهد طنينه

المشرف: د. اسعد الرملاوي

الملخص التنفيذي

المقدمة
سعت وزارة الصحة الفلسطينية إلى اتخاذ إجراءات لاحتواء شدة الإصابة بفيروس روتا. أثناء اتخاذ تقنيات المكافحة، تم إجراء العديد من الأبحاث العالمية لإدخال لقاحات موثوقة ويمكن أن تمنع انتشار المرض وتقليل الاستشفاء. ومع ذلك، فإن احتياطات النظافة العامة مثل غسل اليدين، وتطهير الأسطح سادت توصيات منظمة الصحة العالمية في جميع أنحاء العالم لجميع البلدان لإعطاء الأطفال لقاح فيروس روتا.

في أعقاب تفشي فيروس روتا بين الأطفال الملقحين في جنوب الضفة الغربية من فلسطين، حيث تم الاشتباه في سلسلة التبريد. هدفت هذه الدراسة إلى إظهار العلاقة بين فعالية اللقاح وسلسلة التبريد. سلسلة التبريد عبارة عن نظام قائم على التحكم في درجة الحرارة لسلسلة إمداد تتكون من التخزين والتوزيع، إلى جانب مرافق الإنتاج المبردة المدعومة بمعدات يمكنها الحفاظ باستمرار على نطاق درجة الحرارة الموصي به من أجل سلامة اللقاح.

طرق البحث
في دراسة تقييميه، فإن مكان الدراسة هو سلسلة تبريد اللقاحات لوزارة الصحة الفلسطينية، لأنها المزود الرئيسي للقاح للمجتمع الفلسطيني. التركيز بشكل خاص على تخزين اللقاح المركزي في محافظة نابلس على المستوى الوطني المركزي، إلى جانب المستويين الوطنيين الغير مركزيه في جنوب الضفة الغربية. تم تقييم الموظفين من مديريات الرعاية الصحية الأولية في بيت لحم والخليل، بالإضافة إلى مراكز اللقاحات والخدمات المتنقلة التي تم اختيارها عشوائيًا باستخدام أداة التقييم المستقلة لإدارة اللقاحات EVM التابعة لمنظمة الصحة العالمية WHO.

النتائج
أظهرت نتائج هذه الدراسة أداءً عاليًا وقوة بين معظم مؤشرات سلسلة التبريد التابعة لوزارة الصحة الفلسطينية، والتي سجلت درجات أعلى من الدرجات القياسية الموصي بها البالغة 80، ولا سيما مؤشر مراقبة درجة الحرارة ومؤشر سعة التخزين، وسجل معدات سلسلة التبريد ومؤشر النقل عالية وكذلك مؤشر إدارة المخزون. بالإضافة، فإن المؤشر الفرعي لمعرفة وخبرة العاملين الصحيين إلى جانب التدريب المتكرر سجل درجات عالية. المؤشر الفرعي لدرجة حرارة المجمدات العميقة وكذلك الصناديق الباردة والناقلات التي سجلت أعلى من 80 والتي تعمل بشكل جيد. أظهرت مؤشرات أخرى أداء متفاوتًا بين مستويات الخدمة المختلفة، الوطنية والمحلية ومستويات الخدمة الأدنى. لم يكن أداء مؤشر البناء جيدًا في جميع المستويات وأظهر نتائج متغيرة، ويعزى ذلك إلى عوامل مع مشاكل اداريه وماليه وحرفي الصيانة، ومؤشر التوزيع يظهر بشكل متفاوت بين مختلف المستويات، بعضها مرتفع وبعضها منخفض وكذلك مؤشر الصيانة التي سجلت درجات منخفضة عبر جميع مستويات الخدمة. يتم تنفيذ مهمة التوزيع بالمشاركة بين المركبات المملوكة لوزارة الصحة الفلسطينية

والشركات المتعاقدة لمركبات القطاع الخاص. سجل مؤشر نظام المعلومات درجات متفاوتة بين مستويات الخدمة المختلفة والتي تعزى بوضوح إلى حوسبة البيانات والمزيد من قضايا التوثيق.

الخلاصة والتوصيات

الاستنتاج هو أن سلسلة تبريد اللقاح الفلسطيني تعمل بشكل عام بشكل جيد على جميع مستويات الخدمة. إنها في وضع جيد عند مقارنته بتقييم سلسلة التبريد في البلدان الأخرى وفقًا للدراسات في الأدبيات، وخاصة في إفريقيا وآسيا. كان أداء خدمات الوصول للمناطق البعيدة والنائية فعالًا بشكل كافٍ ومتوافقًا مع التوصيات العالمية على الرغم من الموارد المحدودة والعوامل المؤثرة المختلفة للتعرض لأشعة الشمس وقضايا النقل.

يوصى بشدة بتنفيذ خطة عمل لتحسين المؤشرات الضعيفة وتعديل العيوب، بالإضافة إلى إجراء تقييم روتيني لسلسلة التبريد لتحديد نقاط الضعف وإجراء التحسينات، وإجراء صيانة فعالة في الوقت المناسب لمعدات سلسلة التبريد إلى جانب الإدارة من حيث إجراءات التشغيل الموحدة وحوسبة المستندات والإجراءات وكذلك عمليات النقل.

Table of Contents

List of Pictures.

List of Tables.

List of Figures.

List of Abbreviations

1. CHAPTER ONE
BACKGROUND

1.1.Introduction.

The disastrous effect of the Rotavirus disease (RV) have burdened the universe for decades, negatively affecting the global health care system, and many industries as well as economies. Rotaviruses were reported in 2003 globally as 114 million cases in children less than five years of age, from those 24 million cases needed mild medical care & 2.3 million cases required hospital admissions. On the other hand In 2013, rotaviruses caused about 200,000 mortality in children less than five years of age globally(Crawford et al., 2017).

The prevalence of rotavirus infection in children admitted to hospitals complaining of diarrhea worldwide average to 40%. Concurrently low-income countries were more susceptible than high-income countries for Rotavirus infection, for instance the percentage of rotavirus hospitalizations in children less than five years of age that occur in infants is 43% in Africa but only 27% in Europe causing a great stir worldwide(Omatola et al., 2021a).

Given the severity of this disease, World Health Organization (WHO), along with the Palestinian Ministry of Health (MoH)have sought measures to contain the severity of this infectious disease. As the control techniques are being in place, many studies have been conducted to introduce vaccines which is reliable, that can potentially prevent the spread of the disease and reduce hospitalization.

Immunization and vaccination to the RV make it possible for the disease to be contained and classified as a vaccine preventable disease. Interestingly a lot of research efforts have been put into the development of reliable vaccine schedule in several countries. Currently, several RV vaccines like (Rotarix, RotaTeq, Rotavac), have been introduced for use in children immunization programs in most countries. The burden particularly falls on the supply chain where experts worries are with the issue of ensuring that the potential vaccines through the appropriate cold chain distribution lines reach the target population from the pharmaceutical production corporations to the service sites(Velázquez et al., 2017).

The development of RV vaccines was the first step in reducing the disease severity and mortality. Crucial steps in vaccination and immunization programs are the vaccine production thereafter the distribution, which require proper planning then application in accordance with many requirements. However, strict temperature requirements and many influencing factors such as timeliness, pose significant challenges to a country's cold chain logistics and for effective vaccine distribution. Nevertheless, allocation and distribution of large quantities of RV vaccines to targeted countries are ensured by global equity programs, (Henschke et al., 2022).

It’s far more complex than it sounds but the cold chain system is a temperature-controlled supply chain composed of refrigerated phases of production, storage then distribution

facilities, all phases refrigeration is maintained by equipment that can constantly keep the required low-temperature range (Sinha et al., 2017).

The requirement of temperature is so strict, that if the temperature deviates outside the target range, for example, some vaccines require temperature steady range from the time they are produced until they are dispensed for use, even for a short time, the vaccine could lose its potency and become unfit for use(Kumru et al., 2014).

RV vaccine requires a freezing temperature that is low, -20 °C throughout the whole process of transport and storage to keep potent & effective. To vaccinate infants of the entire population was the primary goal of the RV vaccination program introduced 2016 in Palestine, therefore a higher and timely coverage is very important to accomplish the process as early as possible. The end users were having access to them despite the potential presence of poor cold chain logistics and practices where no studies conducted to date(Grimwood & Lambert, 2009).

1.2.Study Justification & Significance.

Previous studies indicated that Rotavirus death rate of the infected children was high before vaccine was introduced(Velázquez et al., 2017). Rotavirus infects millions of children around the world in the winter season, which may need medical care and hospitalization quite further(Cascio et al., 2001). Palestinian MoH has confirmed that the introduction of the rotavirus vaccine has significantly reduced the incidence of various severity RV infections and hence reduced the hospitalization rate in children. However, the burden of the disease throughout the world was disastrous(Guardado et al., 2004). RV vaccine requires a low freezing temperature of -20 °C during transport and storage to remain effective(El-Hamadi et al., 2015). The primary goal of the RV vaccination program introduced 2015 in Palestine was to vaccinate infants of the entire Palestinian infants, therefore a higher and timely vaccine coverage took place. However, the high recurrence rate among vaccinated children globally sounds an alarming bell (Henschke et al., 2022), & most importantly in Palestine.

Despite the abundancy of studies regarding RV globally, to date there is no study in Palestine that would clearly identify the link of Rotavirus seasonal epidemics across the West Bank among vaccinated children below five years of age to show the performance of MoH cold chain logistics & consequent effectiveness of the vaccine due to cold chain equipment & the potential mal-practice of techniques and the Standard Operating Procedures (SOP), in addition to workers qualifications & level of training and knowledge.

The particular significance of this study is to incorporate the authorities and official of the Palestinian MoH to implement an action plan based on the results of this study. Thus improvement of the low performing indicators of the cold chain system would participate in maintaining a highly performing cold chain system and subsequently safe and effective vaccine delivery. Further studies can be launched from this platform to amend the subtle gaps in vaccination services and put further efforts into focusing on a targeted training of health professionals.

1.3.Study Problem.

This study has been launched to assess the cold chain logistics and indicators implemented in MoH for potential link behind the recurrent seasonal outbreaks of rotavirus among vaccinated children in the southern West Bank to imagine the presumed vaccine effectiveness with respect to conferred immunity. Nevertheless, according to personal interviews with medical professional in Pediatric departments of MoH and Private Hospital's professionals, there is an increase in the rate of diarrheal diseases among infants & children less than 5 years of age in the southern West Bank of Palestine. Patient stool samples were tested in the laboratories and majority found to have rotavirus infection.

Recurrent RV infection outbreaks in southern West Bank in the period between Nov 2021-April 2022, acknowledged in personal interviews by professionals in the hospitals of southern West Bank, thereafter, the unclear vaccine related immune status in young children of age groups less than 5 years whom were fully vaccinated against RV and hospitalized, warranted conducting a study to determine the association of RV outbreak to cold chain equipment & performance for effective vaccine distribution and the ultimate effectiveness of the vaccine. Knowledge of employees as per training, as no studies were conducted in the literature before. Thus several locations with different capacities and logistics including the central MoH storage warehouse and south West Bank Primary Health Care Directorates (PHC) were to be evaluated using World Health Organization (WHO) Effective Vaccine Management (EVM) assessment tool. Thus, logistics' managers on the bases of this assessments' results where the proposed key-management insight can help better understand the key indicators cross-interactions of the vaccine cold chain system.

1.4. Aim of The Study.

The study aimed at assessment of the Cold chain equipment & logistics of the MoH in terms of vaccine effectiveness presumably rendered and the subsequent knowledge and training of the health worker, the potential impact and association to the recurrent seasonal Rotavirus infected cases spike among vaccinated children in Palestinian MoH southern West Bank facilities

1.5. Objectives of The Study

Objectives are formulated based on the ground of understanding what is characterizing and may affect the vaccine supply chain of the MoH in the area of West Bank of Palestine with a particular focus on southern west bank, in an attempt to assess the influence of inadvertent simple changes to the cold chain protocols adopted and shortage of logistics in relation to vaccine effectiveness & recurrent RV infections.

1. Assess the techniques and settings under which the vaccine has arrived to the central store of Palestinian MoH in the Governorate of Nablus.

2. Assess the infrastructure of cold chain and transportation logistics of vaccine from central storing unit of MoH in Nablus to governorates directorates.

3. Assess the information system besides vaccine management including alarming system associated with changes to freezing temperatures in all settings.

4. Assess the infrastructure and transportation of vaccines' cold chain within south West Bank PHC directorates to the belonging clinics in the governorates of Hebron & Bethlehem.

5. Assess the vaccinations' teams in the perspective of previous training and level of knowledge.

6. Assess the local governorate Clinics' cold chain logistics and freezers.

7. Assess the service delivery point of outreach settings in terms of cold chain and vaccine management.

8. Assure all children registered to the MoH Primary Health Care Clinics were vaccinated fully particularly in regard of RV Vaccine according to the designated MoH schedule.

1.6. Thesis Structure

This thesis is presented in six chapters as follows:

1. Chapter One: is a background and is including the introduction, study justification and significance, study problem and aim, study objectives and structure.
2. Chapter Two: is the literature review of the studies and research articles and papers conducted globally and regionally.
3. Chapter Three: contains the conceptual framework of the study.
4. Chapter Four: contains the methodology of the study including the study area and settings, population and sample frame, sampling technique and size, ethical consideration, data collection tool and data processing and analysis.
5. Chapter Five: is presenting the results of the study and contains the data as well as tables and graphs representation of the data.
6. Chapter Six: includes the discussion of the data, limitations of this study, conclusion and recommendations.

2. CHAPTER TWO

LITERATURE REVIEW

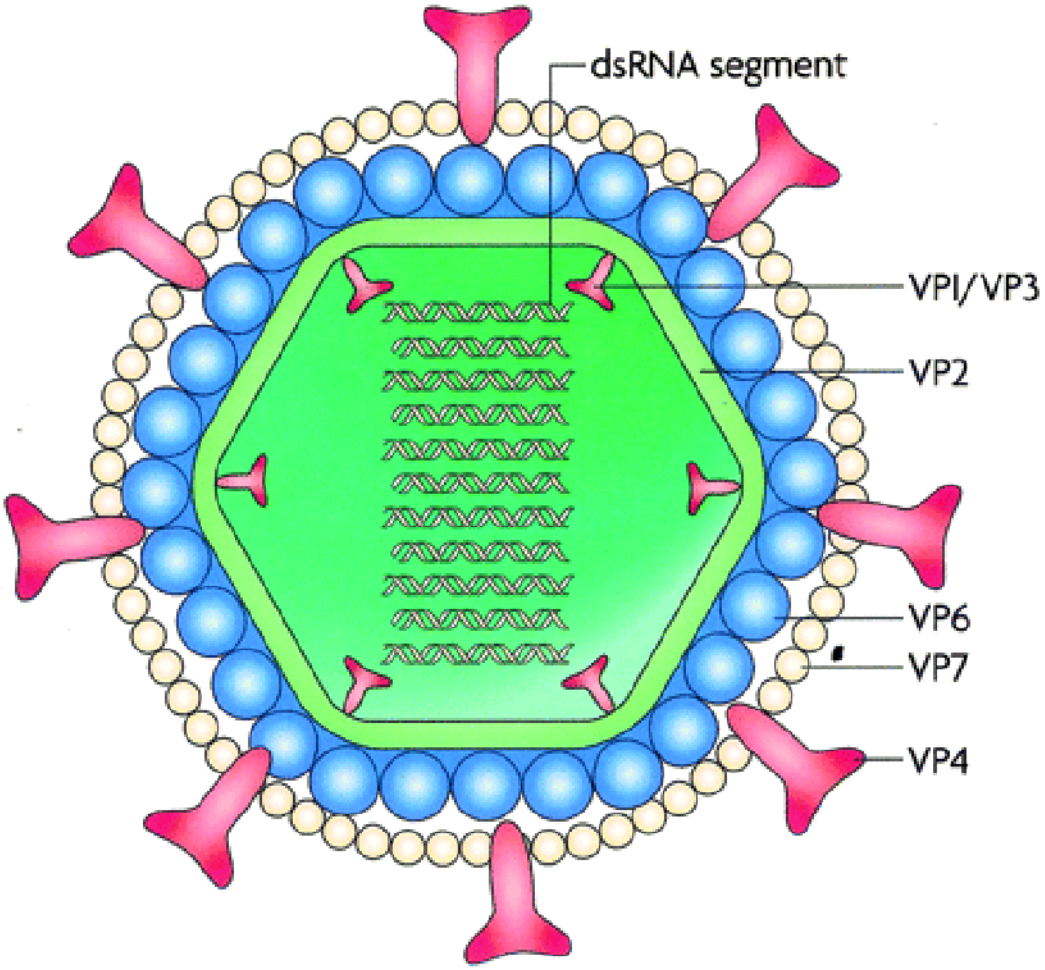
2.1.Introduction

Rotavirus is a highly contagious virus that causes diarrhea among other pathogens (Hopkins et al., 1984) & is the most common diarrheal causative agent in pediatrics (Omatola et al., 2021b). Diarrhea caused by sodium and glucose malabsorption due to replacement of damaged mucosa by immature lining. Before the vaccine was developed, most children were infected with this virus at least once by the time they reached the age five(Velázquez et al., 2017). Low income countries were the most affected specially before the 1970's as the death toll from Diarrhea was overwhelming and reached the limit of 500000 globally till the virus was identified after 1973(Crawford et al., 2017).

Rotaviruses were reported in 2003 globally as 114 million cases in children less than five years, of those 24 million cases required mild medical care & 2.3 million cases required hospital admissions. On the other hand, in 2013, rotaviruses caused about 200,000 deaths in children less than five years of age globally. The prevalence of rotavirus infection in children admitted to hospitals complaining of diarrhea worldwide average to 40%. Concurrently low-income countries were more susceptible than high-income countries for Rotavirus infection , for instance the percentage of rotavirus hospitalizations in children less than five years of age that occur in infants is 43% in Africa but only 27% in Europe(Crawford et al., 2017).

Rotaviruses is non-enveloped double-stranded RNA viruses, classified into ten species range from A-J, Group A rotavirus is the crucial human virus(Crawford et al., 2017). Exposure to infection in children less than five years of age in most studies reflected that 90% of children have antibodies against one or more genotypes (G & P various combinations of the VP7 & VP4 respectively) of rotavirus which indicates the previous exposure status, 39% Prevalence rate in which Rotavirus was Responsible among total Gastroenteritis admissions (Badur et al., 2015).

Rotavirus infection begins within two days of exposure. Early symptoms include fever and vomiting, followed by watery diarrhea for a period of three to seven days. The infection can also cause abdominal pain and the second most common fatal disease in pediatric community.(Badur et al., 2015), Rotavirus infection becomes a concern if the child has diarrhea for more than 24 hours.(Omatola et al., 2021a)



Picture 1:Illustration Of Rota VP & classes

"Source of Photo is online search engine"

Rotavirus is in the stool of an infected person two days before symptoms appear and for up to 10 days after symptoms improve. The virus spreads primarily in water (Hopkins et al., 1984), particularly in the winter time between November and April and additionally can spread easily and directly by touching (fecal oral route) even if the infected person does not show symptoms. Rate of Rotavirus Cases inadvertently reduced due to social distancing and standard safety precautions applied during COVID 19 pandemic.(Chan, 2022) If hands were not washed, the virus is transmitted to anything touched, including food, toys and utensils, and the virus can remain contagious if found on Surfaces that have not been disinfected for weeks or months (Abu Elamreen et al., 2007), besides exposer to rotavirus can cause infection more than once even if children were vaccinated.(Velázquez et al., 2017)

Rotavirus can still circulate and persist in recycled water & for recycled water and sewage sludge in Ghana and for an epidemiological and molecular surveillance description of rotavirus in tap water, a study was conducted for the detection of rotavirus VP7 & VP4 genes using Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). Rotavirus where genotyping analysis of both G and P genotypes, the sequences of human rotavirus

strains showed a close genetic relationship. Rotavirus strains found in this study including the high nucleotide identified to the rotavirus strains indicates that it is derived from a human source.(Dongdem et al., 2010)

Clinical symptoms severity in 401 children in Italy who presented with acute gastroenteritis due to rotavirus was assessed through a scoring system for vomiting, diarrhea frequency and duration, and fever, as well as patient needs for intravenous rehydration. The double-stranded RNA to identify the viral strains, the P type by RT–PCR, the G type and subgroup identified by a panel of monoclonal antibodies. G2P4 type were associated with uniquely severe form of gastroenteritis and older children were identified to have G1P8 or G4P8 types.(Cascio et al., 2001)

The burden of the disease throughout worldwide outbreaks was disastrous. Rotavirus Diarrheal disorder was accounted for overwhelming child hospitalization and increased death rates.(Guardado et al., 2004)

2.2.Preventive Measures

s rotavirus infection is highly prevalent among children between the ages of 3 to 24 months with a high rate of hospitalization in severe cases of acute diarrhea that leads to dehydration, which becomes life threatening, considering the risk of infection that can be prevented by complying to the safety precautions of general hygiene such as washing hands, Surfaces disinfection. In addition to the World Health Organization recommendations across the globe for all countries to give children the rotavirus vaccine(Crawford et al., 2017).

Since faeco-oral route is the main mode of transmission of Rotavirus, hand hygiene & proper disposal of feces as well as the use of safe drinking water, promotion of exclusive breast feeding and immunization against Rotavirus are the most important measures to prevent diarrheal disorders (Bresee et al., 1999). Hand washing after defecation is considered an effective hand hygiene besides the hand washing before preparing food or feeding their children , soap and water hand washing can prevent the risk of diarrheal disorder by 42-47% (Lopez-Quintero et al., 2009).

In Palestine, hand washing is being encouraged among school children through the school hygiene program with soap before handling or consumption of food. Hand washing is encouraged after using of toilets and education in addition to various media campaign on the hand washing(Al-Khatib et al., 2015).

In addition, reduction in the incidence of diarrhea and associated deaths is enhanced by vitamin A supplementation, it is promoted in children aged six months to five years(Bhutta et al., 2008). Furthermore, worldwide burden of Rotavirus disease can still be reduced by safe and effective vaccine which remains the promising way(Kocabaş & Dayar, 2015).

2.3.Rotavirus Vaccines

It is important to introduce safe and effective immunization, since improvements in hygienic life style have a limited effect on RV infection occurrence, thereafter vaccine is the safest to decrease the consequences of rotavirus infection in the community(Glass et al., 2006). The very first approved vaccine by US-FDA (Food and drug administration),

the rotavirus vaccine Rota-shield and was introduced in United States on 1998, in addition to ACIP (advisory committee on immunity practices) approval.

The RV vaccine success in better transforming human child health is well established. Resulted in the reduction of disease severity and case hospitalization in Palestine and other parts of the world. The last two decades involved the development of world-wide approval and administration of important RV vaccines offering protection for the entire childhood against severe RV infections. Furthermore, to manipulate the complexity of the vaccination schedule a new formulations of advanced and well-established vaccines were promoted commercially, indeed to improve efficacy as well(Henschke et al., 2022). Important challenges in terms of distributing vaccines worldwide were raised by the availability of numerous new vaccines and improved formulations according to the cold chain regulations. Besides that there have been a major leaps in our scientific comprehension that led to victories in introducing new vaccines over the past decades, a comprehension of the basic biological mechanisms of the human innate and adaptive immune systems as well as the mechanism of the molecular basis by which RV can cause human disorder(Jiang et al., 2002).

In terms of controlling severe gastroenteritis caused by group A Rotavirus, clinical trials in the United States, Finland and Venezuela had proved the vaccine to be 80-100% effective (Grimwood & Lambert, 2009) . Later on since the vaccine was associated with high risk of intussusception the vaccine was withdrawn from the market by the manufacturer in 1999 which is demonstrated to be 1 in 12000 among vaccinated children (Grimwood & Lambert, 2009).

Vaccine manufacturing is the process of transforming vaccine antigens to medicines, commercial dosage form not only maintains the potency and stability throughout production process and storage thereafter, but is also meant to be conveniently administered to target population(Josefsberg & Buckland, 2012). The vaccine formulation current development process starting at discovering of an immunogenic particles to reach a usable vaccine includes crucial steps, firstly the antigenic component physical and chemical characterization, secondly stability-indicating assays development including potency and thirdly the administration route and adjuvants in clinical trials evaluation and optimization, the last is to maximize the candidate vaccine's stability, shelf life, and immunogenic potential efficacy required the formulation of a design(Grimwood & Lambert, 2009).

In many cases a major topic of vaccine formulation development, since many candidate vaccine’s immunogenic fail to transfer from the laboratory to the target population due to suboptimal efficacy in humans, is the enhancement of potency through the use of vaccine adjuvants(Skansberg et al., 2021). To ensure the appropriate formulation in the presence of commonly associated adjuvants, is one important approach to increase the success rate for new candidate vaccine. Adjuvants not only move the immune response in the desired direction also can enhance the rate and extent of an immune response, e.g., humoral vs. cellular immune responses(Josefsberg & Buckland, 2012).

During both clinical development and commercial distribution, more efforts were employed in the context of maintenance of vaccine potency across the vaccine cold chain. Hence, the analysis used to measure and monitor the physical, chemical and biological integrity is used to virtually identify vaccine stability and potency.

Two new vaccines “Rotarix and Rota-teq” for Rotavirus Group A infection were firstly introduced in 2006 (Grimwood & Lambert, 2009). Fortunately, Mexico Rotavirus vaccine was the first to be introduced in the world and the results showed that diarrheal deaths decreased by more than 65% in children less than 2 years(Bresee et al., 1999).

Rota-Teq is a multivalent modified Jenner vaccine while Rota-rix is an oral live attenuated monovalent vaccine, thereafter the issue of coverage depends on cross protection between serotypes. Bovine G serotypes combined with human P serotypes against severe rotavirus gastroenteritis caused by G1or G2 serotypes of Rotavirus was found to be highly efficacious (Velázquez et al., 2017)

The disease severity and frequency of Rotavirus infection has decreased remarkably in communities that have fostered vaccination. Based on the data from the Global Surveillance Network of 2009 an average of 36% of children less than five years of age with acute diarrhea showed positivity for Rotavirus. In 2009, the WHO recommended that Rotavirus vaccine shall be enrolled in all national immunization programs(Mangin, 2020) . The two Rotavirus vaccines (Rotarix and Rota-teq) have been approved in more than hundred countries(Mangin, 2020).

Previous trials concluded that Rotarix and Rota-Teq were an effective vaccines, besides demonstrated that they were not associated with risk of intussusception in immunized children(Kocabaş & Dayar, 2015).

In India, Studies show that 90,000 - 1,53,000 children die due to Rotavirus infection each year in India, around 4% of overall mortality in children, early on was a huge debate in introduction of Rotavirus vaccine due to lack of assessments regarding death rate by diarrhea and also economic burden of the vaccines. (Chow et al., 2007).

Another international study conducted as meta-analysis for efficacy of firstly developed vaccines of RotaTeq RV5 & Rotarix RV1 showed that the risk of various severity rotavirus linked gastroenteritis rate reduced by 65% and the severe gastroenteritis by 82% against non-vaccinated.(Velázquez et al., 2017). However, both vaccines efficacy against hospitalization remarkably reduced the hospitalization and emergency visits by 85% for RV1 and to 90% for RV5 in industrial countries while it is far less in developing countries which has be thought to be linked to vaccine cold chain. Both vaccines were most effective in preventing more severe gastroenteritis and did not increase risk of intussusception.(Velázquez et al., 2017)

India recently has developed a new vaccine against Rotavirus in 2013 ‘Rotavac’. Clinical trials have showed high efficacy and a wide margin safety profile. Rotavac obviously with protection extending into the second year, it has reduced severe diarrhea at the percentage of more than 56% during first year of life also. Further, the vaccine also demonstrated a great impacts against severe diarrhea of all causes(Skansberg et al., 2021).

As the mortality and morbidity of diarrhea in children are significantly high in developing countries, International non-governmental organization are involved to bring Rotavirus vaccine to them. Integration of Rotavirus vaccination within National Immunization Schedule is strongly recommended in countries in which diarrhea related death rate is more than 10% in children below five years(Naghipour et al., 2008).

2.4.Molecular characteristics of vaccine antigens.

Purpose of most vaccines is to use pathogenic organisms to simulate natural infections. Hence, the use of the live as well as attenuated viruses provide natural agents and have usually comprised the majority of the most successfully efficacious vaccines. However, attenuated viral vaccines are scientifically created under different temperatures by prolonged passage of the wild-type virus in cell culture to weaken the virus, where the resultant attenuated viruses are immunologically highly similar to the wild type agent and retain the ability to replicate, but demonstrates drastically a reduced pathogenicity(Grimwood & Lambert, 2009).

Scientifically the enveloped and non-enveloped viruses have been developed as vaccines, the enveloped requires both complex formulations and subsequent lyophilization to acquire the requested storage stability because it is containing a lipid bilayer and typically less stable and rapidly lose potency. On the contrary rotavirus, have been formulated as liquid preparations which possess higher stability for oral administration(Josefsberg & Buckland, 2012).

Most viruses including RV have layers of one or a few proteins attached in an organized shape on their surface in which the innate immune system possesses receptors that have evolved to recognize the patterns of such particles, hence, vaccines particles better in similarity to the natural pathogen accounting and simulate it for their increased effectiveness as immunogenicity (Badur et al., 2015).

Most viruses are of the size as small as tens to hundreds of nanometers. Thus in terms of stabilization and manufacturing of vaccines, the diversity of size and consequently internal structure present a significant challenge. Still a few comments can be portrayed despite the fact that there is no direct relationship between size and stability. Small, non-enveloped viruses such as RV are quite more stable due to the known nature of the interaction between their protein subunits(Hu et al., 2012).

Intensive stability testing is essential despite the nature of an antigen to conduct, both under experimental conditions e.g., freeze or thaw ,pH, temperature, as part of vaccine development, as well as to establish shelf-life and expiry dating testing under realistic storage conditions within the recommended storage temperature shall be conducted(Josefsberg & Buckland, 2012).

2.5.Vaccine adjuvants

Materials that are added to vaccines which is inactivated and subunit to boost the protective immune responses. However, vaccines have been shown generally to confer protection, the precise induced protective immunity remains under research of the immunological mechanism of vaccine, it is mainly induced by the presence of neutralizing antibodies in some cases, others associated with the presence of certain T-cells types linked to cellular immunity besides the complement activation(Josefsberg & Buckland, 2012).

In comparison to live, attenuated RV vaccines which had no adjuvant combined, the subunit vaccines are basically well tolerated in vaccines with no risk of alteration and consequent infection, hence, they simply aren't highly immunogenic in terms of generating deep immune responses needed for perfect protection(Bresee et al., 1999).

In terms of vaccine formulation, adjuvants may not work effectively causing destabilization of vaccine antigens during the process of storage in subunit vaccine as well as live vaccines when combined into, therefor causing insufficient levels of the correct immune response or excess reaction. One will have to notice that the route of administration might have an impact on immune response resulting from different adjuvants. Different vaccine preparations can be variously administered by intradermal, subcutaneous, parenteral injection, intra-muscularly or without injection particularly either oral or sometimes nasal administration(Skansberg et al., 2021). As an instance by IM injection the Hepatitis B vaccines are administered. This vaccine usually contains in a lipid bilayer a recombinant, purified viral surface protein in addition an aluminum adjuvant(Josefsberg & Buckland, 2012).

Interestingly oral live RV vaccine, however, remains an advanced achievement in the field of vaccine due to the elimination of needles goal was previously set so far, and the improved compliance in addition to the enhanced immune responses. However, Monitoring the stability of vaccine in the cold chain During manufacturing and distribution is of great focus and importance. Instability of vaccine and possible potency loss can occur from the manufacturer throughout the entire vaccine supply chain to child administration(Hanson et al., 2017).

The supply chain necessitate maintenance because of the particular temperature sensitive nature of vaccines, applied to either refrigerated or frozen temperatures referred to as vaccine cold chain. During long-term vaccine storage potency loss can occur, shipping and manipulation to various distribution centers across the world, and the period immediately prior to administration(El-Hamadi et al., 2015).

Ensuring that the vaccine cold-chain is maintained has led to an increasing awareness and knowledge of critical challenges in securing and monitoring the vaccine cold chain from the manufacturer to the end-user, both in the industrial and developing countries, to ensure efficacious vaccines delivery to end-users worldwide(Hanson et al., 2017).

There have been During the past decades, a tremendous efforts to confirm that vaccine potency is maintained through implementing the vaccine cold chain policies worldwide, during transportation and receiving to storage at distribution warehouses, storage at health vaccination centers, and ultimately at the point of use(Maglasang et al., 2018). The loss of potency of the immunogenic material can happen from other environmental stressors such as inappropriate reconstitution and light exposure besides the temperature sensitive degradation cases during storage, which may cause vaccine inactivation(Sinha et al., 2017).

One effective tool, Vaccine Vial Monitors (VVMs), in which vaccines could have been exposed to potentially damaging heat conditions is used to reduce this risk and was implemented to various vaccines(Kartoglu & Milstien, 2014). Numerous VVMs are available depending on the target storage temperature requirements as well the type of vaccine. The same vaccine type could have a different VVM class based on the factory

and the final presentation, as the VVM class used for a given vaccine is based on the stability data available for a specific vaccine(Kartoglu & Milstien, 2014).

Various approaches to better control temperature change events are being studied in the vaccine cold chain. It include improved training techniques and infrastructure frame to reduce the frequency of their occurrence, in addition to implementations of new temperature monitoring technology that will identify thermal change events, , in addition to vaccine stability programs regulatory oversight to mitigate temperature changing events, and finally, implementing of a testing procedures of exposed vials to high temperatures by directly examine vaccine vials accidently exposed (El-Hamadi et al., 2015).

Recently the Widespread vaccination would significantly lower the global financial burden and mortality due to Rotavirus infection as estimates demonstrated. In 2015, Palestinian ministry of health adopted the introduction of the vaccine into the national child vaccination program, which throughout the past few years demonstrated a significant decrease in the hospitalized cases of severe RV gastroenteritis. Rotavirus Vaccine Was Introduced in Palestine in three successive doses, 2,4,6 months.

2.6.Immunity

Rotavirus infection immune response is multi factorial & includes the three immune components, Innate, cellular and humoral immunity(Fischer et al., n.d.), all contributes to eliminate the infection(Angel et al., 2012). To prevent severe disease on successive infection, humoral immunity has a dominant role among them or on primary infection after immunization(Jiang et al., 2002).

After successive infection Cross protection between different serotypes occurs. Additionally, duration of immunity against Rotavirus infection is limited. Generally reinfections are common in Rotavirus disease, in children and adults reinfection occurs but generally with less severity(Anderson & Weber, 2004). Frequently found the Asymptomatic infections in infants below the age of six months, which is exactly the time during which the maternal antibody confers protection. These infection protects against severe disease but does not protect against reinfection.

The role of breast feeding protection against Rotavirus gastroenteritis in infantile is obscure. In Bangladesh, A study conducted in one of the hospitals postulated that breast feeding prevents Rotavirus less effectively than gastroenteritis caused by other agents, it has performed among children admitted with Rotavirus gastroenteritis (Bresee et al., 1999). However, in some clinical studies of Rotavirus infection, , it is noted that breast feeding is associated with lower risk of hospitalization & less frequency of vomiting and less severe dehydration as well(Kurugöl et al., 2003).

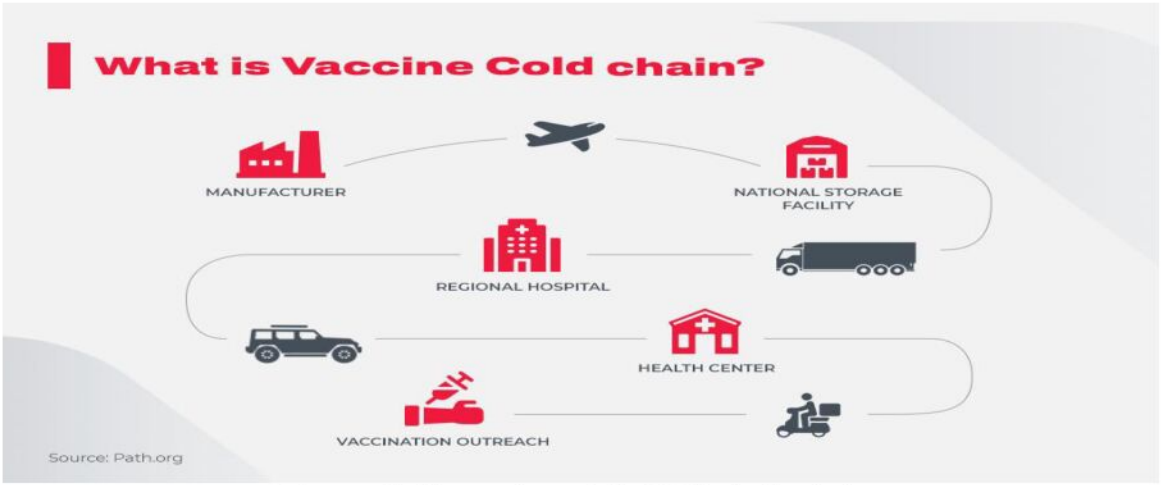
Secretory IgA or Interferon in young children who can acquire up to five re-infections by the age of two years, plays an important role in protection against Rotavirus infection and 90% of the children show antibodies against Rotavirus by the age of three years(Fischer et al., n.d.). Local immune factors in the gastrointestinal tract are the main defense line(Angel et al., 2012).

Neutralizing monoclonal antibodies blocks the attachment of sialic acid dependent Rotavirus to host cells, particularly that recognize the VP8 fragment of VP4. Antibodies

against the VP7 protein blocks Virion un-coating, post binding entry events is blocked by antibodies that recognize VP5 fragment of VP4 (Narváez et al., 2012).

2.7.Cold Chain

WHO formally define the system of vaccine cold chain as a system for storing as well as transporting vaccines in the recommended temperature from production to the administration. Adherence to specific temperature requirements is necessary to delivering vaccines to the end-user. Thus it can be achieved with effective cold chain logistics and systems. (Kartoglu & Milstien, 2014).



Picture 2 Illustration of Cold Chain Logistics

"Source of Picture is Online Search Engine"

Most research on cold chain logistics focus on technologies to improve, location of cold storage temperature monitoring, transportation decisions. The biggest challenge which is consistent in all the stages of vaccine distribution is temperature monitoring and control. Phase change materials have been assessed in many studies by many scientists for use in cold chain storage equipment, an essential contributor in maintaining the viability of vaccines is packaging used in vaccine cold chain logistics. Making vaccines thermostable obviously constitute an outlook that is another possible element into eliminating the need for vaccine cold chain(Shea & Prausnitz, 2021).

The Research in the area of cold-chain challenges can be classified into four topic areas:

I. procedural operations in the cold chain e.g., manufacturing, distribution, storage.

II. Policy and bylaws e.g., some related international and local standards.

III. Management e.g., quality maintenance, supply chain coordination, and performance evaluation.

IV. Technology e.g., tracking technology and temperature control.

Virtually, the cold-chain system has an established supply chain structure with a strict relation to the requirement of temperature, this system is a type of supply chain system in which the core requirement is a low-temperature environment that maintains the potency of vaccine products(Sinha et al., 2017).. In comparison to a general supply chain system, cold-chain system consists of three "T" requirements, "time," "temperature," and "tolerance".(Matthias et al., 2007), need to be applied to all Biopharmaceuticals products includes medical drugs, blood products, vaccines, and interferons.

Biological substances are subject to loss of potency with time, Since Biopharmaceutical products are very sensitive to temperature changes and shall need strictest temperature requirements, more or less than −10°C according to product requirements(Gazmararian et al., 2002). Thereafter, vaccines storage must be properly performed from the time of their production until the time that they are used to in vaccination process.

It is important to make sure that there is enough capacity for vaccines to be kept viable at the end of the chain, so it is important to store the vaccines and to maintain during transportation a constant temperature monitoring. Therefore, Cold logistics and systems, include storage, vehicles, human resource and decisions that affect the maintenance of vaccines at the required temperature, equipment and facilities(Sinha et al., 2017).

WHO guidelines "*Good Distribution Practices (GDP) for Pharmaceutical Products*" in 2010 demonstrated that it has not been properly emphasized in regard of the distribution process including the "establishment, control over the activities deployed, development, maintenance. Transportation in a multi-batch is a further complication of the cargo of biopharmaceutical products, as well as they are often, small-lot pattern, but require fast delivery(WHO, 2005).

2.8.Problems and Challenges

The feature of vulnerability of refrigerated products usually require quick delivery and uninterrupted control of temperature. Quality of service and the quality of transport are the two most frequently encountered problems in the cold-chain supply(Kumru et al., 2014). Hence, important areas where improvement to cold-chain service, providers could apply as recognized by most producers, are that of service processes and cost-effectiveness. Besides, were also considered to be as well important aspects are the management and equipment quality, lead-time. When facilities select a manufacturers' cold-chain service provider, the price, range of services, and service levels were identified as being the most important criteria (Sinha et al., 2017).

At the beginning of the 20th century, scientists investigated on closing the loop, hence giving rise to the term Closed-loop Supply Chain. In 2009, suggested updating the framework to a different partnership structures, considering not only production, but also storage and distribution(Saha et al., 2017).

The focus of the members of the pharmaceutical supply chain is to provide cold chain management for temperature sensitive pharmaceuticals, they have standards and global regulatory requirements to fulfil while handling, storing, and distributing environmentally heat sensitive products. Virtually to ensure that the quality and efficacy of the product will be maintained(Kartoglu & Milstien, 2014).

Guidance in regard to cold chain management was comprehensively covered by World Health Organization working guide QAS/04.068 on Good Distribution Practices (GDP) which is a must for those involved in the distribution of pharmaceutical products of all persons and parties including the manufacturers of intermediate and/or finished products, processors, suppliers, transport contractors, distributors, the distribution process has been virtually neglected as indicated regarding control over the activities involved including the establishment, development, maintenance. Furthermore, the distribution section of the pharmaceutical supply chain includes multiple parties, that raise the question to the presence of risks involved will become complex(WHO, 2005).

WHO working guide QAS/04.068 states that "In order to maintain the original quality, every activity in the distribution of pharmaceutical products should be carried out according to the principals of Good management practice (GMP), Good Storage Practice (GSP) and Good Distribution Practice (GDP)." The (WHO) working document QAS/04.068 states "where special storage conditions e.g. temperature and relative humidity are required during transit, these should be provided, checked, monitored and recorded." Another statement: "Temperature mapping of vehicles should support uniformity of the temperature across the vehicle. Documented temperature monitoring datasheet should be available for review(WHO, 2005). The main objective of these protocols is to emphasize the quality and integrity of pharmaceutical products during all steps of the distribution process.

Common Risks associated with distribution paths include the exposure to temperature alteration, humidity and light, related sections for monitoring to contain the apparent risk include Storage in Shipping Docks, Trucks, Warehouses, Pharmacies, and Other Locations, Personnel Training Controlled Room Temperature, Qualification of Cold chain Equipment or Stores, Distribution and Shipment of Pharmaceutical products ,Temperature Challenges, Receipt of Pharmaceutical products, Vehicle Qualification, Distribution Vehicles, Pharmaceutical Delivery personnel, Shipment from producer to distributer, distribution from distributor to Patient service point. These guidelines in conjunction with regulatory guidance to industry, outlines number of common impacting cold chain management(WHO, 2005).

The policies are firstly that are expected to critically understand the stability profile of the products in which, the Responsibility for cold chain management ultimately resides with the manufacturer to maintain necessary control measures during the distribution process which focus on identifying, maintaining as well as ensure that temperature and humidity controls are monitored during transportation, ensuring temperature specifications during shipment, in addition to Shipping and maintaining temperature limits and requirements, transportation map study, Acceptance provisions for storage and movement of material between sites, practice for performance testing to the shipping containers, Validation of shipping carrier, Time out of refrigeration, Standard operating procedures, records and documentation to ensure the above conditions(Kartoglu & Milstien, 2014).

Secondly the increased observation, control of environmental conditions throughout the entire supply chain and management, from manufacturer to user, for pharmaceutical products that are temperature sensitive, It details procedures to maintain proper storage environments and conditions and to ensure a preparation's integrity for products, until it reaches the user, besides, the manufacturers and distributors should work together to establish proper product handling and distribution requirements to achieve the goal of ensuring appropriate product maintenance in transit(WHO, 2005).

Thirdly the escalated importance of temperature control and tracking to identify and mitigate risks during cold chain transport pathways, 36% of all main issues recorded by the Medicines and Good Distribution Practice (GDP) inspectors, Medicine & Healthcare Products Regulatory Agency's(MHRA), during 2003/2004 related to the control and monitoring of transportation temperatures & storage(WHO, 2005). Nevertheless, Compliance issues relating to transportation included, temperature monitoring record sheets, monitoring instruments and devices and their location, shipping containers, controlled use of cooling items, trailer's temperature mapping procedure. Other worth-mentioning challenges included the training of storage facility crews, drivers, returns of cold chain items, calibration of temperature monitoring devices and maintenance of the cold chain from imports to the patient level. Obviously once the product enters complicated distribution systems after leaving the producer's chain of control that includes many handoffs, supply chain mediators, outsourced service providers, prior to reaching the patient. Thus experts believed that during this tangled stage of distribution, the most temperature change occur(WHO, 2005).

Fourthly the heightened priority of individual safety. Manufacturer are expected to be aware of the two regulations, transportation and storage, of the current GMP's, ensuring that guidelines and procedures were implemented for storage and transportation conditions including humidity temperature, light control, besides other regulations necessary to maintain the quality and safe distribution of the pharmaceutical product. Also, transportation and Storage Conditions which prevent any changes to the physical characteristics of the product and potency (WHO, 2005).

Temperature control and monitoring is crucial during the transportation and storage of vaccines. Stable and energy-saving system for monitoring in vaccine cold chains with an accurate and rapid data collection module for transportation is crucially required(El-Hamadi et al., 2015). Radio Frequency Identification which have become increasingly valuable for monitoring individual vaccine packs is in the process of being used, an innovative temperature monitoring model in cold chain in healthcare industries utilizing the internet systems. Radio Frequency Identification technology is integrated with Wireless Sensor Networks, ensuring the quality of the products throughout the supply chain that will automatically record temperature changes in products("Sustain. Radio Freq. Identif. Solut.," 2012).

2.9.Standard operating procedures

Records for shipping of the products and receiving, besides the Standard Operating Procedures (SOP's) are available in all facilities and includes, the product Labeling demands, shipping configuration and the type of protective packaging to be employed for shipping, including storage conditions and the special precautions, Mode of transportation instituted, shipment sealing procedure, Verifications that no damaged container found, In order to cope with the global regulatory requirements, as well as evidence that shipping

requirements e.g. temperature control fulfilled the Quality Management System (WHO, 2005).

Temperature Monitoring System recent consensus on Cold Chain Management for pharmaceuticals portrayed that shipments between countries and within countries of wide geographical extensions should be manipulated as unique in the perspective of the range of temperatures the products may experience(Kartoglu & Milstien, 2014). However, documentation of temperature and humidity by Electronic temperature monitors provide valuable information in a convenient template which includes time and date as well as specific information. Equipment employed for maintaining temperature and humidity conditions, recording, monitoring should regularly be validated and thereafter calibrated on a regular basis(WHO, 2005).

WHO issued a recent Catalogue of Prequalified Immunization Devices, This Catalogue replaces the former WHO/UNICEF Product Information Sheets (PIS) last edition in 2000. It includes information of all immunization-related products and devices currently prequalified by WHO for employment by the United Nations agencies.

Prequalified products are detail-listed in the Catalogue and combined by information sheets to help manufacturers and distributors select the most appropriate products for their specific requirements. (WHO & UNICEF, 2017).

The Catalogue provides a brief overview of products that have been independently assessed in accordance with WHO verification procedures for use in immunization programs, including only those assessed products and found to meet the requirements of the relevant performance requirements.

Catalogue equipment is listed as follows:

- Cold rooms, freezer rooms, and related equipment
- Refrigerated vehicles
- Refrigerators and freezers
- Cold boxes and vaccine carriers
- Coolant-packs and vaccine carriers
- Cold chain accessories
- Injection devices for immunization
- Waste management equipment
- Injection devices for therapeutic purposes.

Picture 3 Illustration of Cold Chain Equipment

"Source of Pictures is Online Search Engine"

2.10. International foundations for vaccine supply

GAVI (Global Alliance for Vaccines & Immunization), officially known recently, Gavi, the Vaccine Alliance foundation(WHO & UNICEF, 2017), in June 2015 established the Cold Chain Equipment Optimization Platform (CCEOP) as a strategic and targeted approach to mitigate the challenges of transforming the vaccine cold chain with higher-performing Cold Chain Equipment (CCE)(WHO & UNICEF, 2017).Functional CCE is a critical tool to strengthening immunization supply chains and immunization programs, and participate to supporting the equity goal, thereafter reaching more children with lifesaving vaccines and protecting them against deadly preventable diseases. The success and achievements of the CCEOP in improving countries' cold chains led to the continuation of the CCEOP platform into the 2021 – 2025(WHO & UNICEF, 2017).

The CCEOP continues to be a shared investment model for countries to benefit from GAVI CCEOP financial support, they are requested to jointly invest in equipment as well as make clear investment commitments to cold chain management and maintenance(Storeng, 2014).

UNICEF Supply Division is the implementing agency for the CCEOP, thus as a key to improving Sustainable, equitable immunization coverage, promoted Investing in new cold

chain equipment, obviously by extending equipment availability into remote locations and well-enabling mobile outreach activities(Storeng, 2014).

GAVI's goal of reaching zero-dose through reducing the number of zero-dose children by 25% by 2025. The CCEOP is aiming to strengthen immunization supply chains that will reach the largest population of zero-dose children, particularly the urban poor, remote rural communities, and children affected by conflict. Hence, ensuring vaccine availability and potency, and maximizing efficiency where possible(Hogan & Gupta, 2023).

Within the context of GAVI's development, the COVID-19 pandemic led to finding of the COVID-19 Vaccines Global Access (COVAX) Facility which was directed at ensuring equitable access to COVID-19vaccines. Through COVAX, GAVI aims to ensure countries have adequate cold chain capacity at the upper border of the cold chain, where impact on storage capacities for COVID-19 vaccines is the priority(McAdams et al., 2020).

CCEOP aims at that all CCE fulfil World Health Organization WHO Performance, Quality and Safety (PQS) standards and also requires CCE to be "platform-eligible", which includes a higher-level of technology and performance standards than current PQS standards. The CCEOP also requires product employment for Ice-Lined Refrigerators (ILR), Solar Direct Drive (SDD) refrigerators and standalone Remote Temperature Monitoring Devices (RTMD) to be combined with installation and training. Country ownership of any data generated by CCE products employed with GAVI funding was added to the CCEOP platform eligibility requirements in 2020(UNICEF Supply Department, 2018).

Available and implemented new and improved CCE in countries through the CCEOP have important aspect of capacities to improve performance and safety, nevertheless, it keeps vaccines cool and safe even if the power is interrupted or out for few days, e.g. Grade A freeze protection plus freeze preventive technology where accidental freezing of vaccines in storage and transport is unlikely, SDD fridges and freezers should not have batteries while keeping vaccines cool and safe, , contributing to reductions in closed vial wastage(UNICEF Supply Department, 2018).

Temperature and CCE performance monitoring devices, when fridges and freezers are not working properly, which is built in and standalone, send automatic alerts to health facility staff and higher monitoring centers, thus helping ensure that equipment will receive rapid maintenance so that vaccines stay protected(Kartoglu & Milstien, 2014).

In the latest generation of CCE, each one of these devices comes with a solar panel that is technically mounted on a pole or on top of the roof of the health facility, and by a power cable is connected to the device, these vaccine storage devices are designed to keep vaccines cold for long time without any source of power(WHO & UNICEF, 2017).

Cold boxes and vaccine carriers used to transport vaccines between facilities or during field immunization sessions that prevent freezing are insulated containers. These devices prevent freeze damage to particular vaccines which saves time when preparing vaccines for transport(Gazmararian et al., 2002).

Temperature monitoring devices (TMD) which are used to continuously measure and record temperature readings from cold chain equipment are another tools. They display current temperature readings and cases of temperature changes beyond the acceptable limit. 30-day temperature recorders (30-DTRs) virtually on the device log temperatures and alarms locally. RTMDs are the best standalone or integrated. The CCEOP now supports employment of RTMDs for both refrigerators and walk-in cold rooms (WICRs). However, next generation Equipment Monitoring Systems (EMS), which monitor more aspects of CCE performance than temperature, will also be platform eligible as these products become available(UNICEF, 2018).

Voltage stabilizers prevent damage caused by fluctuations in the electricity supply, are devices used to protect refrigerators and freezers powered by main electricity. They protect the refrigerators and freezers for reliable functioning from voltage and frequency levels that are either too low or too high.

Internet of Things, is another tool adopted across several industries as part of the global revolution. Internet of Things that can facilitate the link between goods and services is a worldwide internet architecture. the use of internet of Things ensure that stakeholders of the cold chain adhere to regulations as a supervisory system in maintaining the quality of products like vaccines(Lee et al., 2022).

With the introduction of sustainability, preoccupation with social and environmental design and planning rose as an essential feature of supply chain structures, along with economic concerns, as a crucial features of a supply network. The triple-bottom-line is the integration of environmental and social aspects with economic considerations(Lee et al., 2022).

3. CHAPTER THREE

CONCEPTUAL FRAMEWORK

3.1. Country Back Ground:

Palestine National Immunization Program provides RV vaccine to about 130 thousand infants, annually saving many lives each year. It has contributed significantly into preserving health and saved lives of thousands of children and better thrive.

Functional Immunization Supply Chain system plays a focal role in the effectiveness of the vaccination program by ensuring the abundancy of quality vaccines from the level of the manufacturer to that of the infant in an uninterrupted accessibility. Largest amendments in strengthening of immunization centers and intensive training, of cold chain equipment and distribution was adopted since the plan of RV vaccine introduction in 2015 took place, which all are planned to keep the recommended temperature of the vaccine from the point of production till it reaches the targeted infants.

3.2. Immunization History and Present Schedule

In Palestine the country was recognized for the national immunization campaigns against poliovirus which led to the elimination of the disease by the end of the eighties of 19th century, in addition to the implementation of plans to vaccinate against highly incident hepatitis B at the early nineties of the 19th century, in 2015 the country decided to launch National Immunization program against RV based on studies conducted across many countries and in adherence to the WHO recommendations to contain the impact and burden of the disease among children younger than 5 years of age. During this period, globally a RV new vaccines became licensed and available in the market. The first was Rotarix adopting two dose regimen, thereafter rolled in the Rotateq adopting three doses regimen.

Vaccine schedule adopted in Palestine against RV is three doses schedule at 2,4,6 months respectively and Planned New Vaccine Introductions to replace The current vaccine with the Indian Rotavac, a three doses vaccine that demonstrated a higher efficacy among children based on mass studies in India.

3.3. Vaccine Cold Chain Assessment Tools

Vaccines included in a country's vaccination program is evaluated in sets by WHO vaccine volume calculator, which is a tool that determines the total supply chain storage volume needed. WHO Cold Chain Equipment Inventory(CCI) and Gap Analysis Tool are the WHO's planning tools for conducting and analyzing the cold chain equipment inventory. Its capacities include recording and analysis of cold chain equipment inventory, data generating for appropriate cold chain equipment to match facility profile.

Planning for equipment replacement and renewal is based on type, working status and age of the device, thereafter estimating maintenance and running cost of the existing cold chain equipment.

WHO Effective Vaccine Management(EVM) Tool, help countries to improve supply chain performance, this will provides materials to assess, manage and monitor the vaccine supply chains, hence, It consists of EVM standard operating procedures, background and training resources, EVM assessment tools and user guides.

WHO EVM initiative includes in addition a vaccine management handbook which provides practical advice on immunization logistics in the matter of use of vaccine carriers and coolant packs for transport and outreach, including the use of cold boxes and how to monitor temperatures in the supply chain.

A programmatic intervention directed at the most underserved populations, the remote rural, the urban poor, and the conflict-affected child. Energy Sector Management Assistance Program (ESMAP)/World Bank Tool for Climate Friendly Cold Chains (CFCC) for COVID-19 & beyond which is intended for use early in the decision-making process, where countries begin to establish cold chain design strategies, budget requests, and find out their financing options. The CFCC tool includes the strengths of established resources and tools for informing vaccine-related and storage requirements, health facility electrification, and energy efficiency measures, thus to allow users to explore and compare different options for cold chain employment and associated energy solutions.

WHO-UNICEF Joint Statement on temperature-sensitive health products encourages the implementation of a safe and efficient integrated cold chain system and to expanded the scope of existing trainings. These additional trainings will help build capacity for maintenance and use of cold chain data for decision making. The RTMD training requirement is new under the CCEOP, thereafter, Countries have the obligation to plan for refresher and continuous trainings.

EVM indicators by which countries' supply chain performance can be evaluated through a global standard. The 9 indicator areas cover: vaccine arrival, storage temperature, storage capacity, buildings, equipment, and transport, maintenance, stock management, distribution, vaccine management; and information systems and supportive functions. It is measured at three levels of health system: national stores, Governorate stores (sub-national), and vaccination centers (point of service). The recommended Score is 80 % minimum.

3.4.Assessment Levels

EVM assessment structured questionnaire will allow the evaluation of three distinctly different levels in the supply chain.

- The national level main (central storage) where vaccine is received directly from the vaccine manufacturer or from an international supplier. Typically, vaccine is stored in large cold rooms and freezer rooms.
- The sub-national and Governorate level storage where vaccine is received from the primary national store, usually stored for an already arranged period, and then distributed to lower levels stores or vaccination clinics. These clinics may have vaccine refrigerators and freezers.

- Vaccination centers where vaccine is stored for a definite period of time then dispensed to the intended population. Each service delivery point may distribute vaccine to other service delivery points such as outreach vaccination settings. Single refrigerator on a very short-term basis could be used or the vaccine can be delivered in vaccine cold boxes or vaccine carriers.

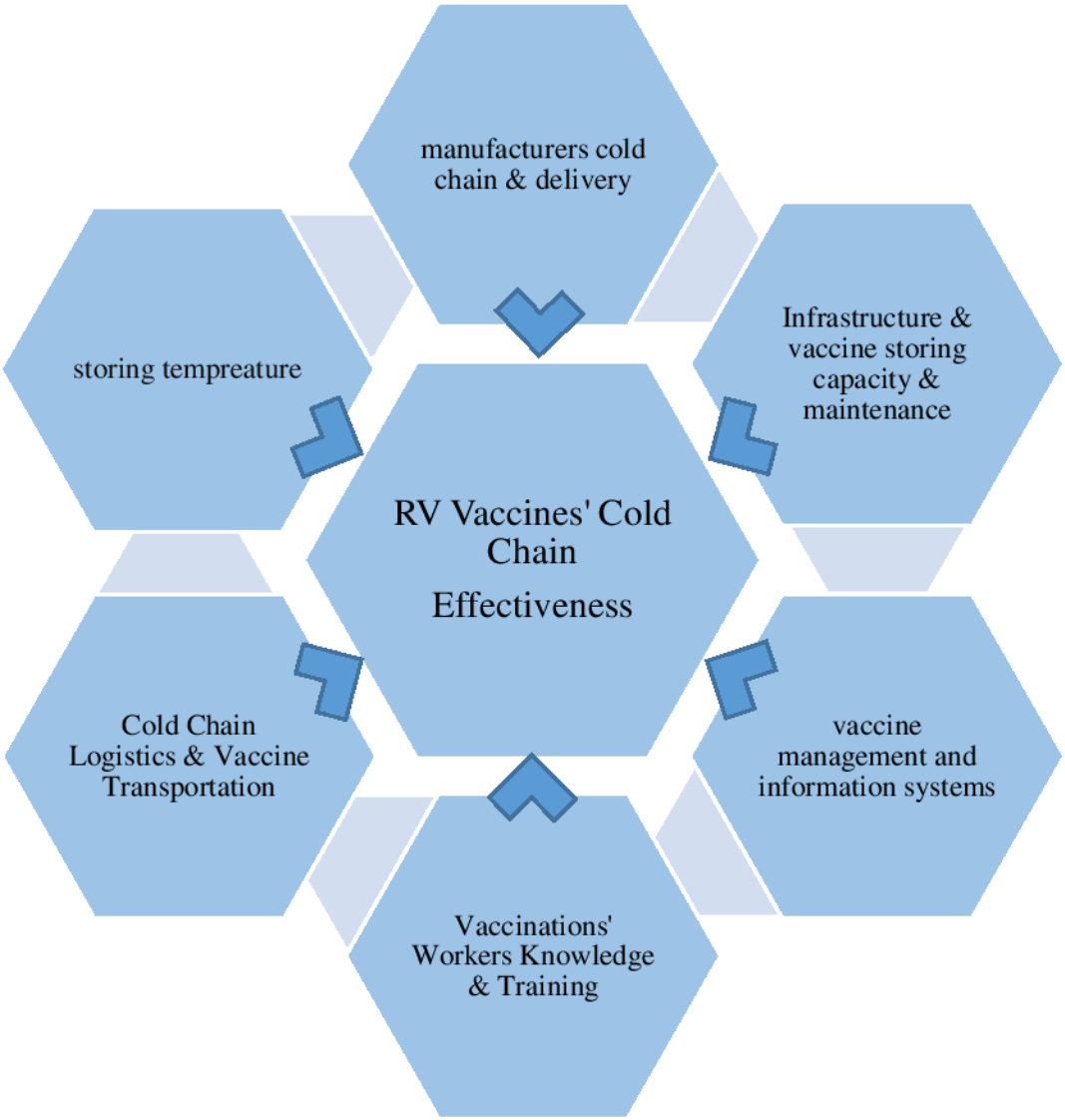


Figure 3.1: Conceptual Framework

4. CHAPTER FOUR
METHODOLOGY

4.1.Study Setting & Sample Frame.

RV vaccines' cold chain of Palestinian MoH, since it is the main provider of the vaccine to the community, the central vaccine storage in the governorate of Nablus (national level) which is located to the north of West Bank and handles the vaccine arrivals where vaccine is stored & distributed to various MoH governorate's at the sub-national levels. The governorate of Bethlehem which is located to the south of West Bank 100 Km from Nablus and serves the population of Bethlehem through an extended service delivery points and vaccine centers consisted of 18 clinics and two mobile outreach clinics that serves the remote underserviced area. The governorate of Hebron that is located in the south of West Bank, 140 Km from Nablus and surrounded by huge complexes of Israeli settlements. Hebron is divided into four health governorate according to Palestinian MoH, north, central, south, and Yatta Primary Health Care directorates and serves about 40% of the population of West Bank, consisted of about 70 clinics including mobile outreach clinics.

4.2.Study Design.

Cross Sectional Study.

4.3.Study Sample & Sampling Technique.

The considered vaccine stores as a source of information are:

1. National level: central vaccines' storing unit "main MoH distribution location in Nablus.
2. The Sub-National level: primary health directorate of the southern West Bank in Bethlehem and Hebron governorates, which is fully equipped with a cold chain logistics and receives vaccine shipments from the central store of Nablus.
3. Lower level: All fellow clinics and service delivery points at the lowest level were also considered, heads of health departments were also considered as a source of information.

4.4.Inclusion criteria.

The inclusion criteria were identified as the facilities that provide vaccine storage & child vaccination services including the outreach vaccination services.

4.5.Exclusion Criteria.

The exclusion criteria were identified as the facilities that did not provided vaccine storage & vaccination services.

4.6.Sample Size.

The sample size included the national vaccine storing facility, since it is the only vaccine depot of the Palestinian MoH, the headquarter of Bethlehem PMC directorate as it is the main Bethlehem sub-national vaccine storage, out of 20 clinics one large population clinic of Obadiah was randomly allocated & the only mobile outreach clinic team. In the governorate of Hebron, the Central Hebron PHC Directorate, the only sub-national vaccine storing facility was chosen, one large population clinic of al-Salam was randomly allocated in addition to the only mobile outreach clinic team from a total of 16 service delivery point clinics. The informants including management posts who were 39 employees at all MoH vaccine storing levels, of which 7 in Nablus governorate, 19 in Central Hebron governorate, and 13 in Bethlehem governorate.

4.7.Study Tool & Data Collection.

The study tool that was used is the WHO & UNICEF standalone designed EVM analysis tool, cold chain logistics' questionnaire in English(*WHO / UNICEF Effective Vaccine Management (EVM)* Effective Vaccine Management (EVM) Initiative ; WHO . Assessment Framework Criteria*). The questions were translated to Arabic. During the interview, the tool assessment of cold chain system was done through nine criteria. For an assessment at the sub-national and lower levels the criteria of vaccine arrival were excluded.

1) Vaccine arrival: adopted pre-shipping and arrival procedures ensure that every single shipment from the vaccine producer arrives to the receiving store in a convenient condition and with the correct recording sheets which is named as vaccine arrival (VAR) documents.

    - Evaluate vaccine arrival reports (VARs) received.
    - For damaged vaccine, follow up with manufacturer, how many received in damaged or exposed condition.
    - Follow up of incomplete documents.
    - Vaccine manufacturers & viability of Lot Certificate from.

2) Temperature control: vaccines are stored and monitored within the WHO recommended temperature range across the cold chain system.

    - Temperature mapping.
    - Correct storage temperature ranges for the vaccine on the schedule, wither a health. worker can keep.
    - Knowledge of Health worker when vaccine can be damaged by temperatures change.
    - Knowledge of health worker on correct reading of temperature recording device & all types of thermometer used in the facility.
    - Refrigeration temperatures recorded.

- Manually, temperature record sheets completed.
- Refrigerated vehicles.
- Alarm & Temperature record sheets.
- Events formally reviewed at least once a month.

3) Storage capacity: cold storage, dry storage and transport capacity will suffice to accommodate all vaccines needed for the schedule.

    - Sufficiency of storage at -20°C Capacities available/ required.
    - Sufficient transport capacity.
    - Sufficient capacity for freezing or storing them.
    - Sufficient passive containers.
    - Contingency plan.

4) Cold chain equipment and transport

    - Cold chain equipment and vehicles for vaccine distribution is acceptable.
    - Vaccine store building status.
    - Enough space to maintain and vaccine store well-ventilated.
    - Cold boxes and passive containers.
    - Refrigerated / insulated vehicles.
    - Vaccine vehicles.
    - Warm clothing and training on working inside.
    - Generator is required and is installed.
    - Deep freezers temperature.
    - Monitoring equipment checklist.
    - Temperature alarm equipment.
    - Telecommunications links sufficient.
    - If vaccine transport is directly operated by this store.
    - Refrigerated vehicle.
    - Transport container.

5) Maintenance: systems to maintain cold chain equipment and vehicles are satisfactory.

    - Building, equipment, vehicle exists and is followed - Reports availability
    - Operation status.

- Cancellation of deliveries due to transport problem or delay.

6) Stock management: effective stock management policies and adherence to procedures are in place.

   - Computer software, system, backup, are adequate.
   - All transactions updated in 1 day
   - Routine reports on internal vaccine distributions, the program prepare work.
   - Summarize the details of every transaction
   - Vaccine is issued based on the 'closest expiry first' principle,
   - Stock records demonstrate that vaccine request forms are used for ordering and receiving vaccines.
   - Arrival checks were carried out correctly by the receiving store, sample of these completed arrival documents.
   - In accordance with standing orders is damaged or expired stock is properly recorded and disposed of
   - Disposal facility in accordance with national / WHO policies.
   - Discard records
   - Internal review of vaccine loss
   - Peak and minimum levels are defined. Stocks were kept within the peak and minimum level.
   - Instances of Stock-outs or short
   - Shipments
   - Delivery which took place during the review period, Records from the receiving store for every

7) Distribution: the distribution of vaccine between storing and service levels in the cold chain is in an effective manner.

   - Distribution reports shows adherence with the planned delivery timetable.
   - Correct positioning and status of ice packs and packing of Cold Boxes
   - Correct transport using refrigerated Vehicle
   - Freeze indicators recording compliance with every Transport
   - Distribution emergency planning
   - Timetable & destination of all outreach activities should be recorded.

8) Vaccine management: proper and efficient vaccine management policies are in place & implemented at all levels of the vaccine supply chain.

- Knowledge and use of shake test, instructions on the use of VVMs, posters and stickers are available to health workers
- Health workers know how to read VVM
- VVMs on all vaccines in the store or vaccine center refrigerator.
- Health workers apply VVM practice to achieve vaccine management purposes
- If Open Vial Policy has been adopted.
- Immunization reports
- To calculate the vaccine wastage at the store, standard reporting forms present or not.

9) Information systems and management: related information systems and supportive management functions are convenient.

- Copy of SOP.
- Standard operating procedures (SOP) following WHO Recommendations.
- Vaccine needs forecasting.
- Cold chain equipment inventory.
- Vaccine transport service operation by the store.
- Outsourced Transport services.
- Training materials for vaccine management.
- Clear and correct Training materials are consistent with WHO recommendations, standard, operating procedures for health workers.
- Staff training

4.8.Data Analysis.

Data were analyzed using the WHO & UNICEF'S EVM1 assessment and analysis tool by a specialist. It is comprehensive tool excel-based developed by WHO for data analysis based on individual indicator scoring. Each indicator scoring is comprised of subset of indicators formulated as questions within the application in the form of a questionnaire, the tool conducts the evaluation process as a standalone questionnaire, which is used in this study and requires no authorization. The questionnaire in this setting is structured based on the questions constructed in the tool, the responses to the questions of the questionnaire has to be entered accordingly. Results and scoring is generated automatically based on the analysis of the different sets of questions in the tool in relation to different indicators and sub indicators intended for analysis. The evaluation conducted for each service level and each criterion scores were compared against the minimum score of 80% that is recommended by the WHO for assessment of the strength of the cold chain indicators. Excel sheets were used for further processing of data and graphic representation.

4.9.Ethical Considerations.

Ethical aspect of the study was fulfilled, approval to conduct the study was obtained from the Palestinian MoH (Appendix). The participants were informed of the purpose of the study, besides that their participation is voluntarily and confidential, anonymity is maintained and they can opt out any moment during the study, they were informed that MoH will be communicated the data.

5. CHAPTER FIVE

RESULTS

Tables below & Figures demonstrate the assessment scores across the involved governorate's storage levels in Palestinian MoH. Results were varying among different levels from national to sub-national and service delivery points and vaccination centers and mobile outreach services, criteria scoring were variable, some scored above recommended of 80% while others scored below.

Table 5.1: EVM Criteria Scores in the governorate of Nablus National Central Store.

EVM CRITERION	NABLUS CENTRAL VACCINE STORAGE
Vaccine Arrival "VAR"	86%
Temperature Monitor	96%
Storage Capacity	95%
Cold Chain Equipment And Transport	98%
Maintenance	67%
Stock Management	N/A*
Distribution	87%
Vaccine Management	70%
Information System And Management	75%

N/A*: Service is not Provided in this facility

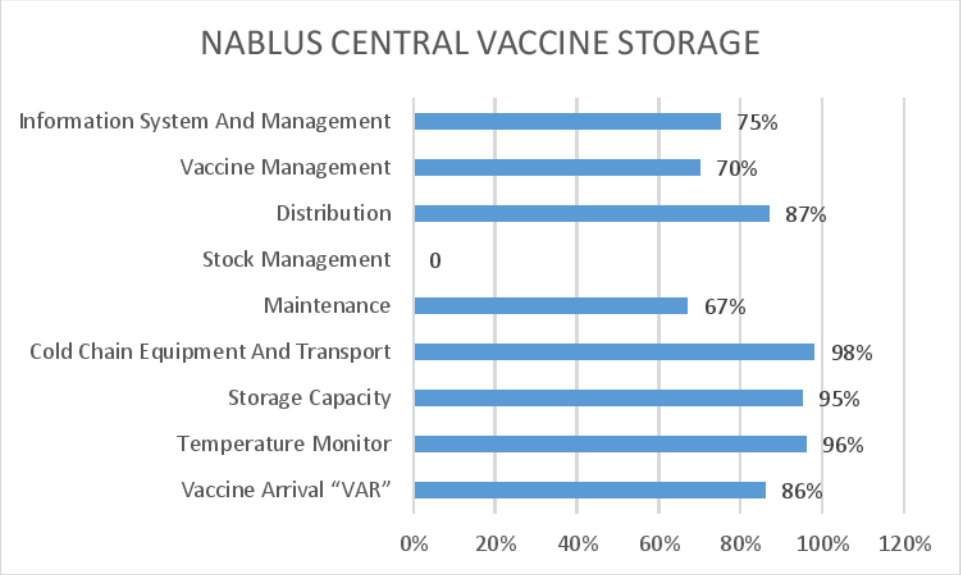


Figure 5.1: EVM Criteria Scores in the governorate of Nablus National Central Store.

0 = N/A*: Service is not Provided in this facility

Table 5.2: EVM Criteria Scores in the governorate of Bethlehem Sub-National and lower levels.

EVM CRITERION	PHC Directorate Of Bethlehem	Obadiah Clinic	Outreach Mobile Clinic
Vaccine Arrival	N/A*	N/A*	N/A*
Temperature Monitor	75%	90%	87%
Storage Capacity	73%	87%	N/A*
Cold Chain Equipment And Transport	89%	85%	89%
Maintenance	64%	57%	N/A*
Stock Management	83%	87%	N/A*
Distribution	77%	N/A*	N/A*
Vaccine Management	74%	94%	94%
Information System And Management	57%	85%	87%

N/A*: Service is not Provided in this facility.

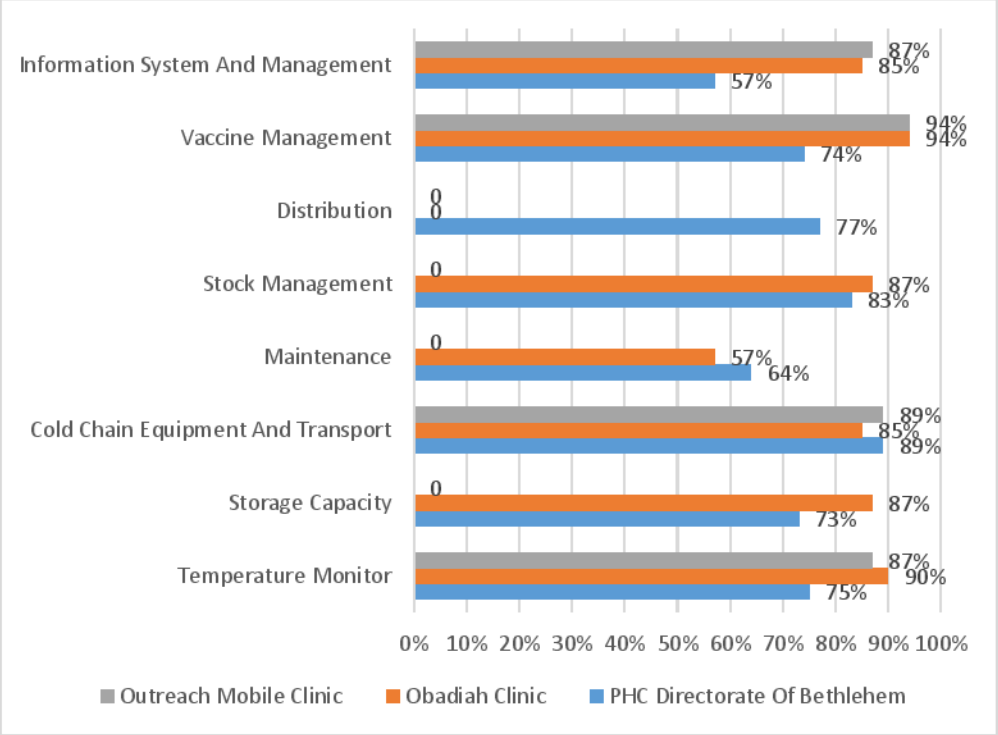


Figure 5.2: EVM Criteria Scores in the governorate of Bethlehem Sub-National and lower levels, 0 = N/A in reciprocal Table: Service is not Provided in this facility

Table 5.3: EVM Criteria Scores in the governorate of Hebron Sub-National and lower levels.

EVM CRITERION	PHC Directorate Of Hebron	Al-Salam Clinic	Outreach Mobile Clinic
Vaccine Arrival	N/A*	N/A*	N/A*
Temperature Monitor	93%	81%	94%
Storage Capacity	94%	83%	N/A*
Cold Chain Equipment And Transport	89%	91%	87%
Maintenance	71%	63%	N/A*
Stock Management	87%	91%	N/A*
Distribution	75%	N/A*	N/A*
Vaccine Management	93%	87%	91%
Information System And Management	78%	87%	87%

N/A*: Service is not Provided in this facility

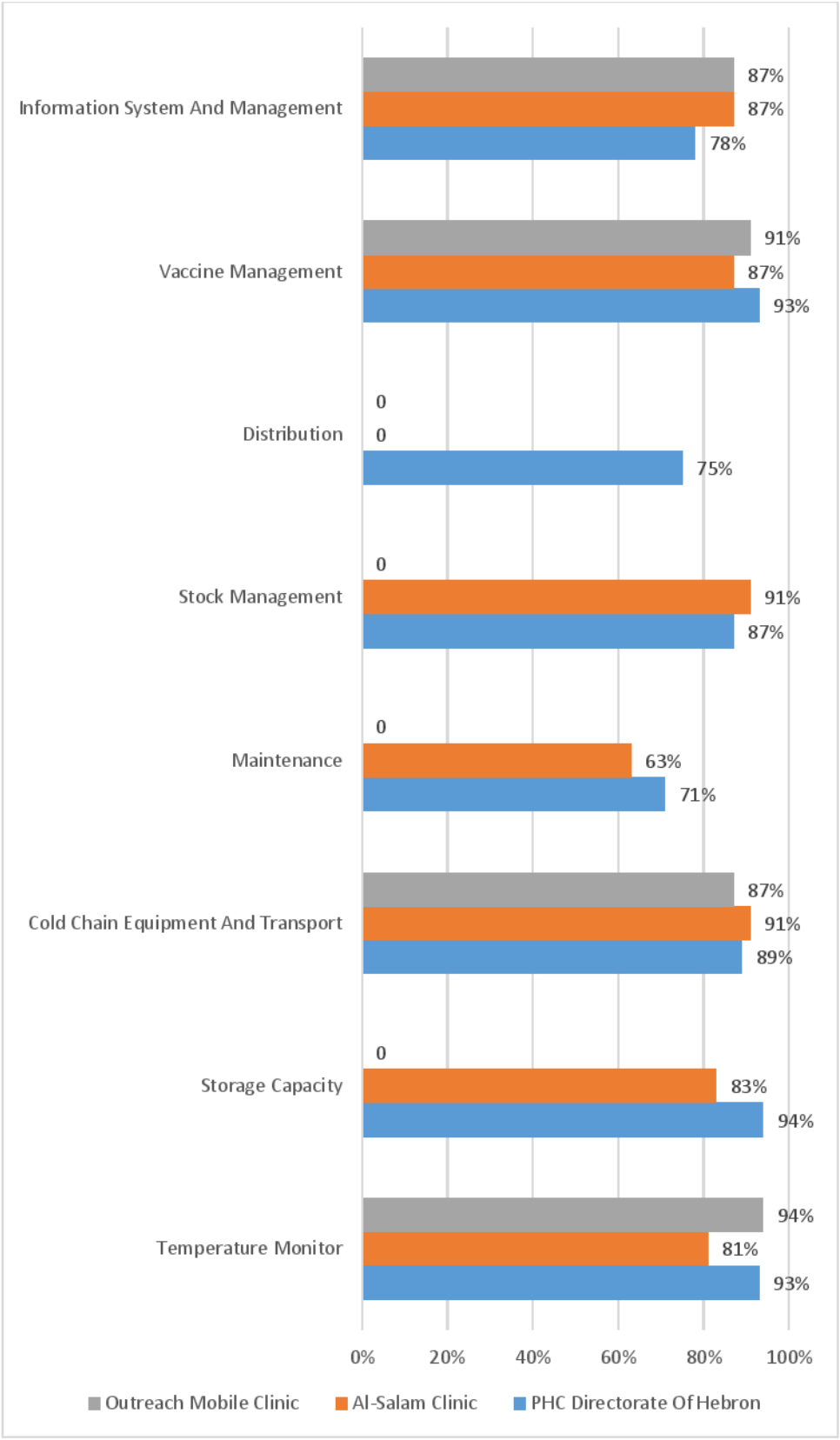


Figure 5.3: EVM Criteria Scores in the governorate of Hebron Sub-National and lower levels. 0 = N/A* in reciprocal Tables: Service is not Provided in this facility

5.1. Vaccine Arrival

The national level "central store of Nablus" is the only store that performs vaccine arrival services, provide VAR documentation upon receiving vaccine from manufactures or suppliers and scored above the average of 86% (Table.5.1), the two sub-national levels in the governorates of Bethlehem and Hebron PHC directorate do not have this service.

5.2. Temperature Monitoring

Figure.5.4 demonstrates a variation of scoring, however, the central store of Nablus scored 96% which is above the recommended score (Table.5.1), whereas the governorates of Bethlehem (Table.5.2) scored 75% at the sub-national level, which is below the recommended score, on the other hand the vaccine center of Obadiah and mobile outreach services performed better and scored 90% and 87% respectively, above the recommended score. The governorate of Hebron (Table.5.3) scored at the sub-national level 93% above the recommended, as well as the vaccine center of Al-Salam and the mobile outreach service scored 81% and 94% respectively.

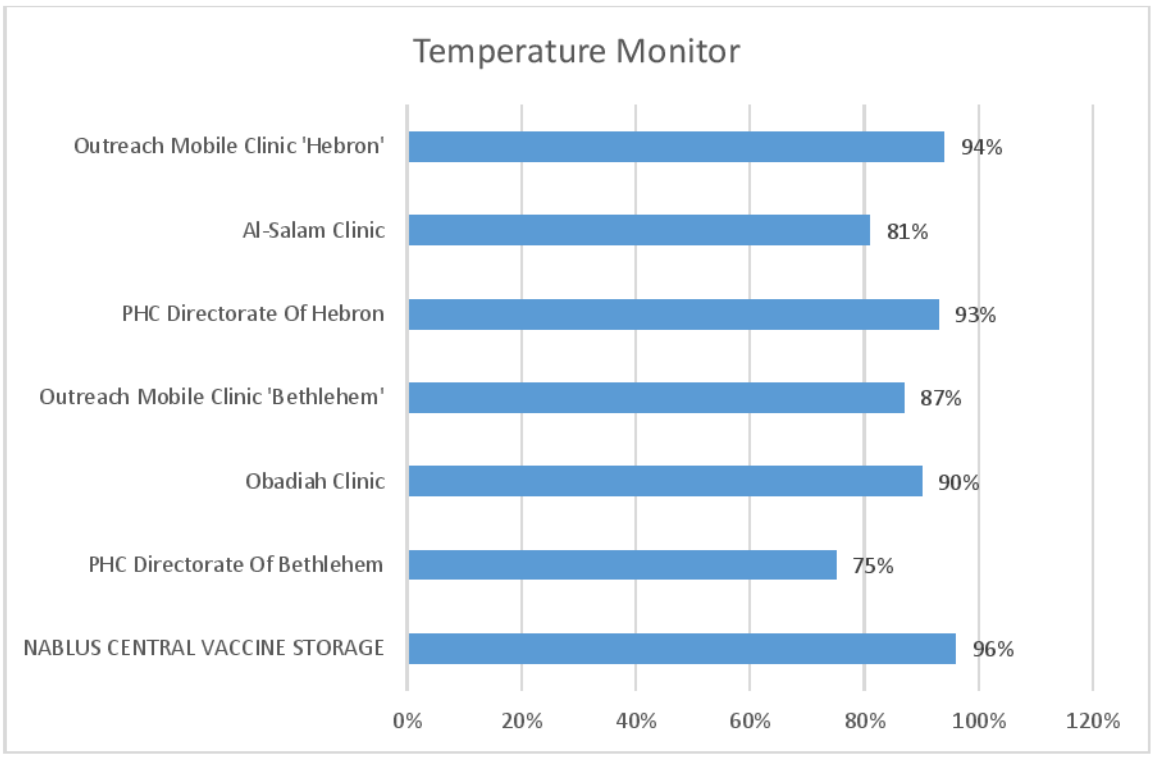


Figure 5.4: Temperature monitor scoring among all cold chain levels.

In the figure.5.5 Below demonstrated that the knowledge and experience of the health workers is obviously considered in practice. However, temperature mapping performance was perfect among employees of the central store of Nablus were 100% are adherent whereas other service points in the governorates of Bethlehem and Hebron did not have an organized file for archiving, therefor the workers who are performing the temperature

mapping in the PHC directorate of Bethlehem and Al-Salam clinic are 57% and 37% respectively, alternatively the mobile outreach teams do not have standard procedures for temperature mapping.

The refrigerated vehicles are well deployed in the central store of Nablus 91% as all vehicles are well-maintained and owned by the Palestinian MoH, other clinics and service points in the governorates of Bethlehem and Hebron running a hired contractor vehicle for vaccine delivery, hence, most of clinics reported the issue of non-refrigerated vehicles. The mobile clinics teams on the contrary in Bethlehem and Hebron were better at 77% and 67% respectively.

The workers were knowledgeable across all levels in the perspective of the correct vaccine temperature range for freezing at -20°C and during mobilization of 2-8°C and higher temperatures for a set period of time, besides knowledge to the adverse event of vaccine damage due to temperature change, however, some reported a power interruption due to main power supply issues.

Alarms integrated into the cold chain cold rooms and deep freezers are well deployed in the central store of Nablus and PHC directorate of Hebron 87%, the alarm runs off when temperature change through notifying the responsible personnel by text messaging their cellphones.

The particularly important aspect of worker's experience and knowledge besides the worker's qualifications was comforting since the vast majority of workers are qualified nurses and received multiple sessions of training in which the mobile outreach workers scored 91% and 93% in Bethlehem and Hebron respectively, whereas the workers of the central store of Nablus are not nurses and a few are newly employed under supervision who received no training yet 71%.

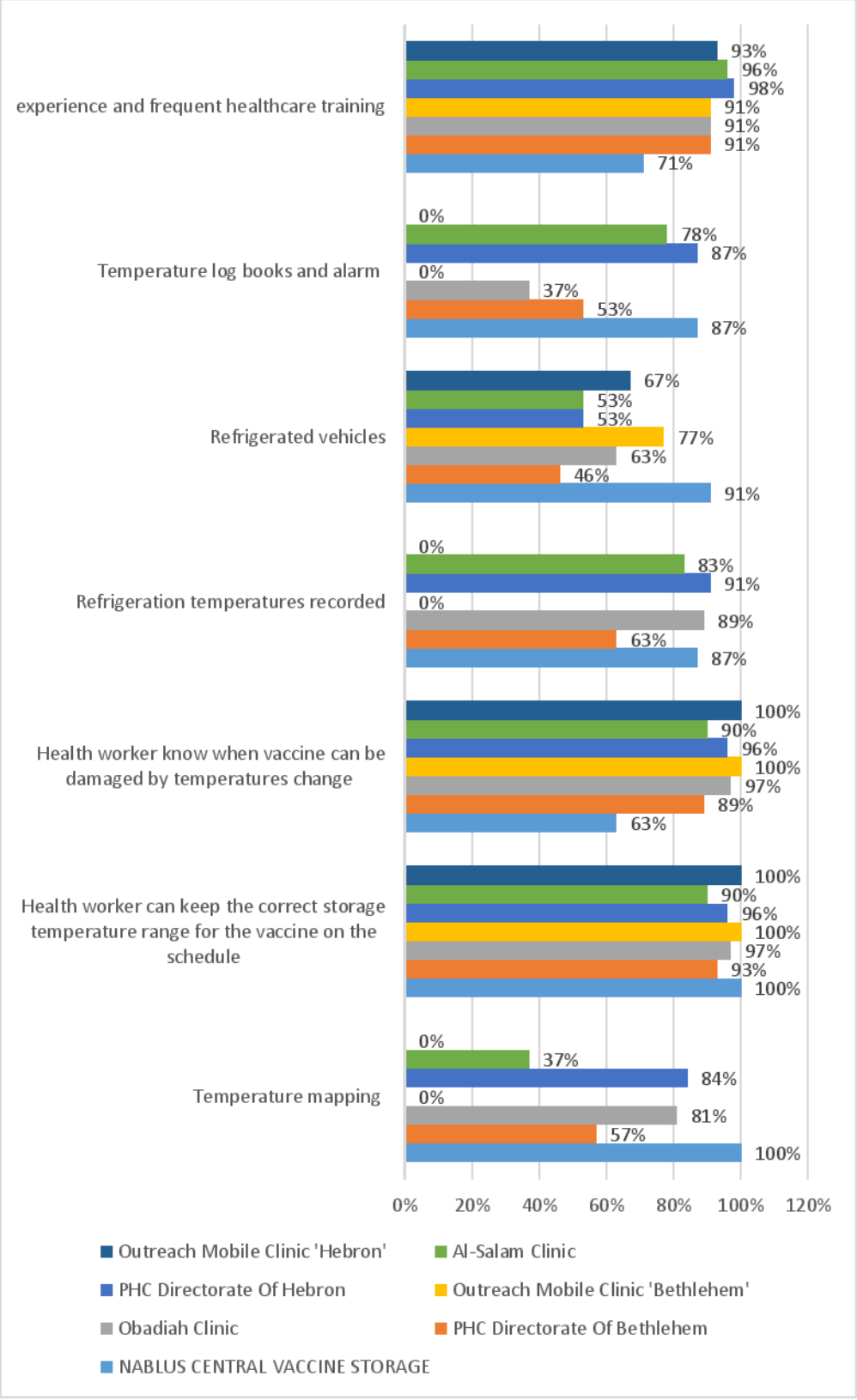


Figure 5.5: Scores of a selected indicators of temperature monitor.

0 = N/A: Service is not Provided in this facility

5.3.Storage Capacity

In Figure.5.6 which demonstrates scoring generally above the recommendations within recommended temperature range of -20 °C, however, the central store of Nablus scored 95% which is above the recommended score and is the highest (Table.5.1), whereas the governorates of Bethlehem (Table.5.2) scored 73% at the sub-national level, which is below the recommended score due to main cold room being out of service but the informants reported enough cold storage for a month, alternatively the vaccine center of Obadiah scored 87% whereas mobile outreach services do not have storing service. The governorate of Hebron (Table.5.3) scored at the sub-national level 94% above the recommended, as well as the vaccine center of Al-Salam scored 83% and the mobile outreach service have no such service.

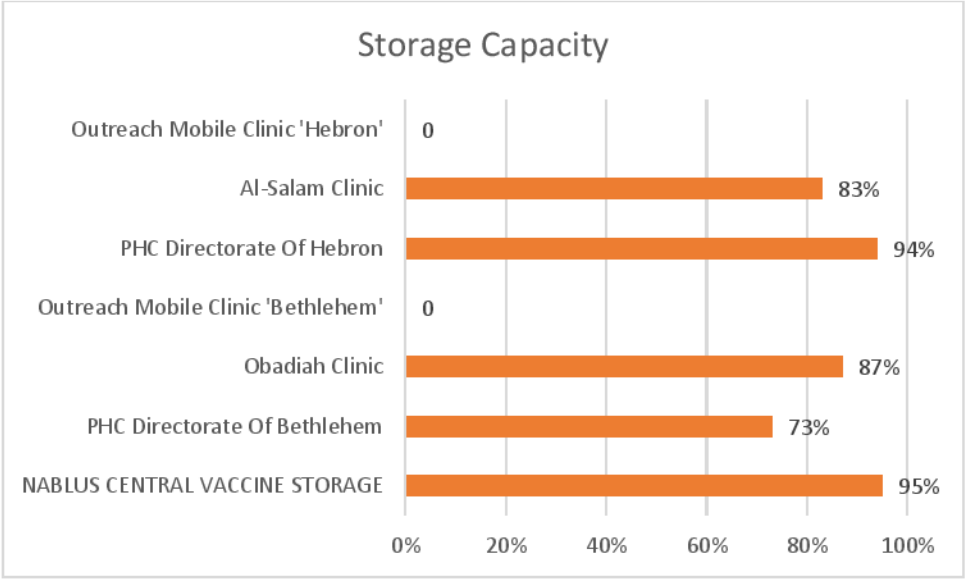


Figure 5.6: Scores of storage capacity across all levels.

0 = N/A in reciprocal Tables: Service is not Provided in this facility

5.4.Building, Cold Chain Equipment and Transport.

The scoring in Figure.5.7 of this indicator for the equipment and transport was above the recommended score, however, the central store of Nablus scored 98% which is above the recommended score (Table.5.1), whereas the governorates of Bethlehem (Table.5.2) scored 89%, & 85%,89% in the sub-national level PHC directorate and Obadiah and mobile service respectively, which is above the recommended score. The governorate of Hebron (Table.5.3) scored 89%, 91%, 87% in the sub-national level PHC directorate and Al-Salam, mobile service respectively. On the other hand, the building scoring in (Figure.5.8) the central store of Nablus was 57%, In Bethlehem PHC directorate scored

76% below the recommended score, vaccine center of Obadiah performed better and scored 83% above the recommended score. The governorate of Hebron scored at the sub-national level PHC directorate 79% below the recommended, as well as the vaccine center of Al-Salam scored 88% above the recommendation, the mobile outreach services has no building indicators as the settings of services is variable.

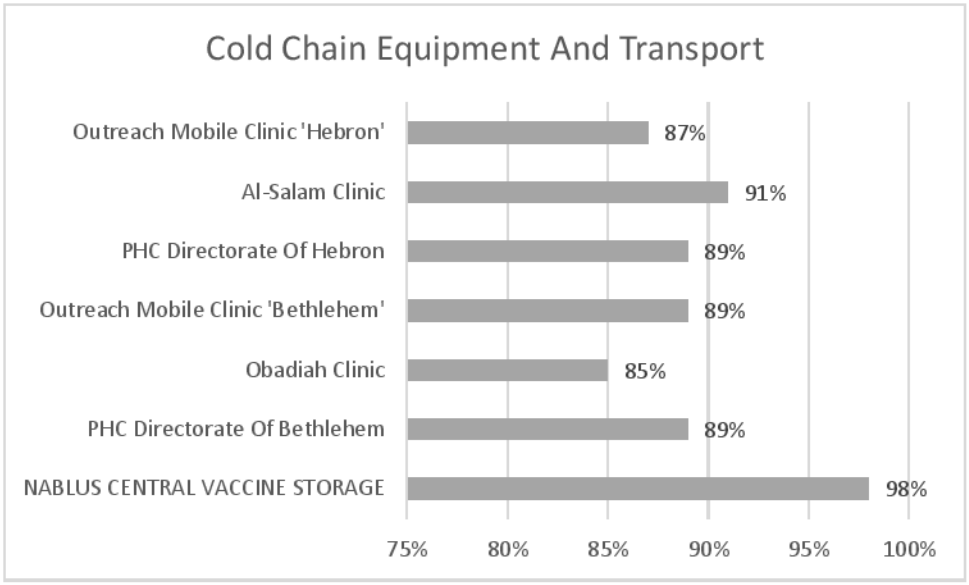


Figure 5.7: Cold chain equipment & transport indicator across Palestinian MoH.

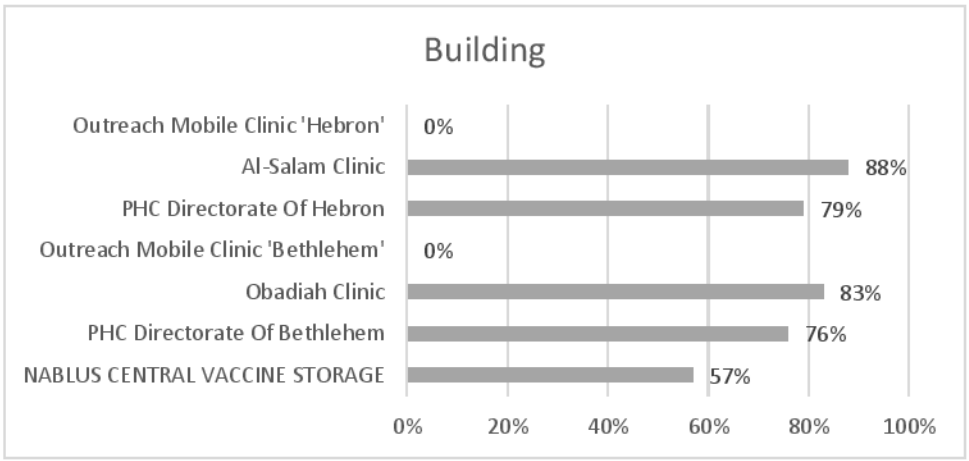


Figure 5.8: Building Criteria acores across MoH facilities.

0 = N/A: No Building for Mobile outreach services.

Figure.5.9 demonstrates selected indicators performance of the cold chain equipment and transportation, however, the scores on building status was variable across all levels, was in the central store 57% below the recommendations due to maintenance issues and humidity, whereas in the PHC directorate of Bethlehem was 76% below but close to the recommended score, the Obadiah clinic performed above the recommended score of 83% while the mobile services has no building due to outreach characteristic of service settings. The PHC directorate of Hebron scored 79% while the al-Salam clinic performed well with a score of 88% while mobile service has no building settings.

The cold boxes and carriers performed high in accordance to WHO policies which reflects a high compliance to the rules of keeping the vaccine cold, the central store of Nablus scored 98%, PHC directorate of Bethlehem 95%, Obadiah clinic 93%, mobile outreach service performed very well at 95%. The PHC directorate of Hebron scored 94%, Al-Salam clinic 93%, and the mobile service 94%. All scores were above the recommendations due to high adherence to the WHO regulations except for some operating procedure and place of collecting the carriers that might be exposed to sunrays.

Electric generator was installed in the national central store and the two sub-national stores and well equipped and maintained, the Obadiah clinic scored 83% and Al-Salam clinic 91% since they are equipped with small electric generators that are not connected to an automatically operated power grid during power interruption whereas the mobile services have no such power generators.

All levels scored on the deep freezer's temperature indicator completely perfect in adherence to the WHO regulations. The temperature alarm equipment were lower than recommended in some facilities, the central store scored 87% which is above the recommended score due to high technology alarm system and wireless alarming connected to employee's cell phones through text messaging, the score in the PHC directorate of Bethlehem was 53% due to an issue in the cold room at the time of assessment as the employees were on strike and no maintenance is being performed, the deep freezers showed an issue of their integrated alarms. The PHC directorate of Hebron performed better and scored 78%, the alarm is connected by wireless text messaging to the employee's cell phones but is not in good status of maintenance, the Al-Salam clinic performed high at 87% with good integrated alarm systems to the deep freezers and consistent follow up.

Telecommunication was sufficiently reflected at high scores. However, all employees are provided with cell phones to keep in connection where land lines are also available in some settings, the issue which has an impact on scoring was the compliance of the employee to use of the phone and reporting problems in addition to the limited use of the computers and spider network.

Refrigerated vehicles performed below the recommendation due to non-compliance to the WHO regulations, the contractor's vehicle deployed to the service line of the Palestinian MoH constitute the majority, however, the central store of Nablus owned their vehicles and scored 91%. The PHC directorate of Bethlehem, Obadiah clinic and mobile services scored 46%, 63%, 77% respectively in which their performance was all below the recommended score. The PHC directorate of Hebron, Al-Salam clinic and outreach service scored 53%, 53%, 67% respectively which is as well low performance and below the recommended score, obviously the drivers non-compliance had a great impact on scoring.

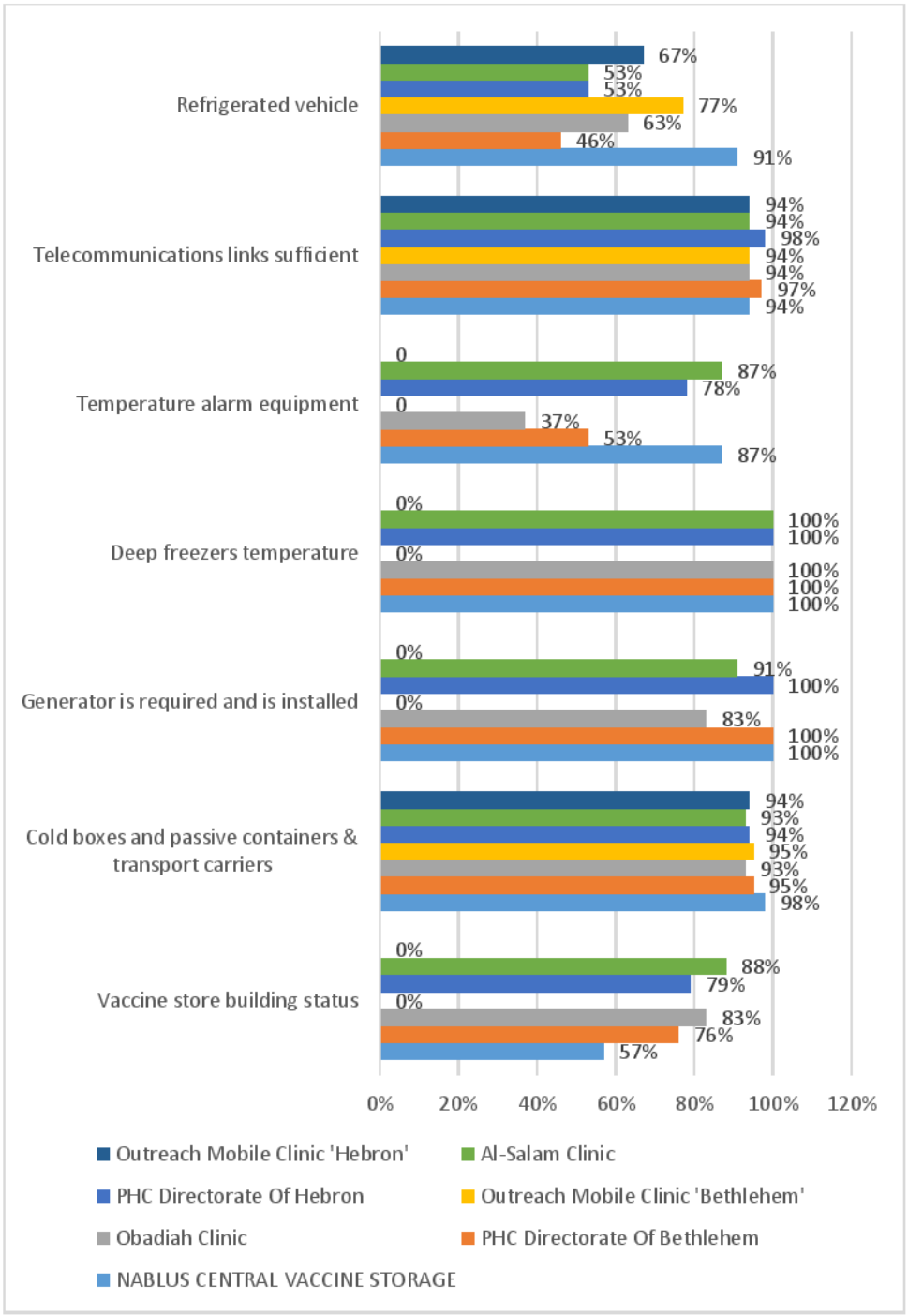


Figure 5.9: Cold chain equipment and transport selected indicators scores.

0 = N/A: Service is not Provided in this facility

5.5.Maintenance

Figure.5.10 demonstrates a global scoring below the recommended score across all Palestinian MoH levels. However, the central store of Nablus scored 67% which is below the recommended score (Table.5.1), whereas the governorates of Bethlehem (Table.5.2) scored 64% at the sub-national level, which is below the recommended score as well, besides the vaccine center of Obadiah scored 57%. The governorate of Hebron (Table.5.3) scored at the sub-national level 71% below the recommended, as well as the vaccine

center of al-Salam scored 63%. All informants reported a recurrent maintenance issues, reporting of problems is documented but the maintenance team do not respond in a timely manner most of the times in addition to the delay of service. The issue of unsatisfactory scores are attributed according to the informants, different factors including shortage of trained staff in addition to managers being unresponsive either being overwhelmed or short on budgets.

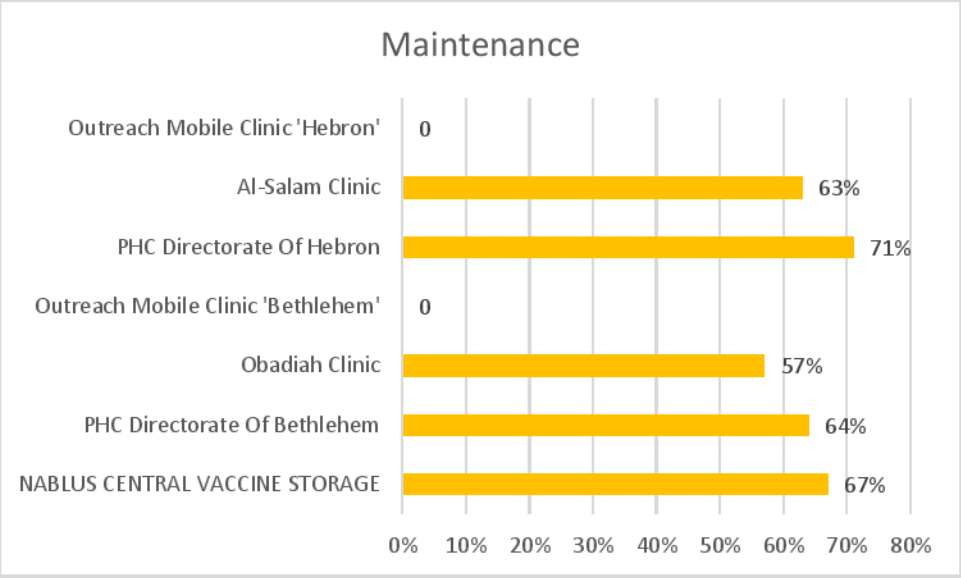


Figure 5.10: Maintenance indicator across Palestinian MoH.

0 = N/A in reciprocal Tables: Service is not Provided in this facility

5.6.Stock Management

Figure.5.11 demonstrates above the recommended scoring, however, the central store of Nablus does not provide the stock forecasting and management of disposal since all these services are taken care of at the PHC general directorate in Ramallah. On the other hand, the governorate of Bethlehem (Table.5.2) scored 83% at the sub-national level of PHC directorate, performing well above the recommended score, the vaccine center of Obadiah performed better and scored 87%, above the recommended score. The governorate of Hebron (Table.5.3) scored at the sub-national level of PHC directorate 87% above the recommended, as well as the vaccine center of Al-Salam scored 91% above the recommended score. The mobile service has no stock management indicators as the team sets the entire prepare process the headquarters of PHC facilities.

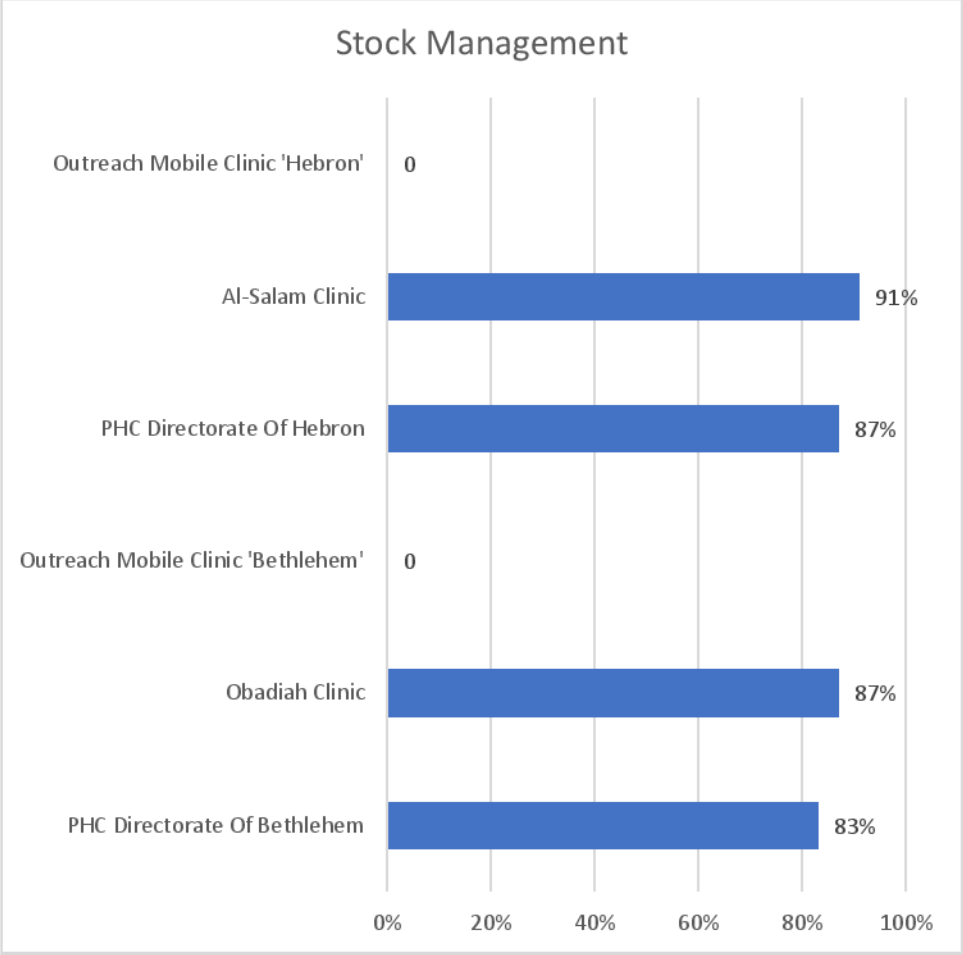


Figure 5.11: Stock management indicator across Palestinian MoH.

0 = N/A in reciprocal Tables: Service is not Provided in this facility

5.7.Distribution

Figure.5.12 shows a scoring of the central store of Nablus 87% which is above the recommended score (Table.5.1), whereas the governorates of Bethlehem (Table.5.2) scored 77% at the sub-national level of the PHC directorate, which is below the recommended score. The governorate of Hebron (Table.5.3) scored at the sub-national level 75% below the recommended, the clinics of Obadiah and Al-Salam vaccine centers and the mobile services have no distribution service provided.

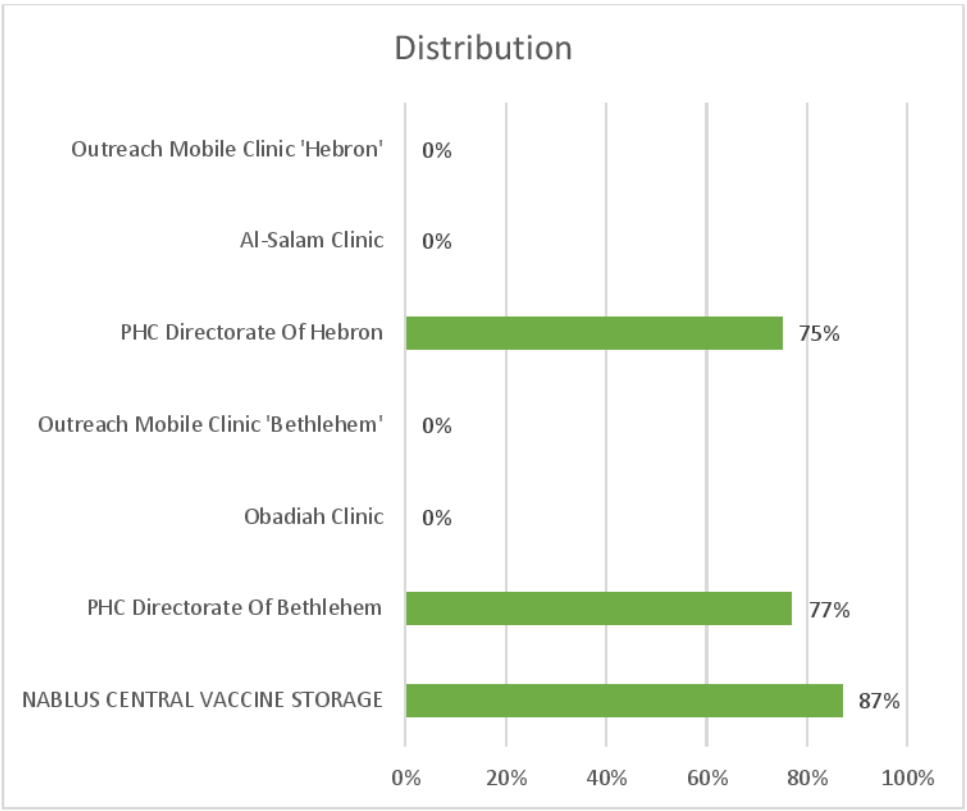


Figure 5.12: Distribution indicator across Palestinian MoH.

0 = N/A in reciprocal Tables: Service is not Provided in this facility

Figure.5.13 shows a variable performance on the distribution sub-indicators assessed, the distribution reports and compliance to schedule of vaccine distribution in the central store of Nablus performed above the recommended score with 85%, while the PHC directorate of Bethlehem scored below the recommended score with 68%, as well as the PHC directorate of Hebron which scored 73%, due to non-compliance practice of scheduled delivery and documentation scores were lower than recommended. Alternatively, the scoring and performance was above recommendation in regard of correct conditioning of ice packs and packing of cold boxes, scores were 94% for the central store, 86% for the PHC directorate of Bethlehem, 95% for the PHC directorate of Hebron. Variations were obvious among scoring in regard of the use of freezing indicators with every transport of vaccine, virtually the mobile outreach recording of activities performed well in the PHC directorate of Bethlehem with a score of 83% above the average, on the contrary to mobile outreach service that scored 71% due to loss of documentations, the PHC directorate of Hebron scored 65% below the recommended score for non-compliance with documentations in addition to no reporting to mobile service since it has been taken into an account of other close vaccine center.

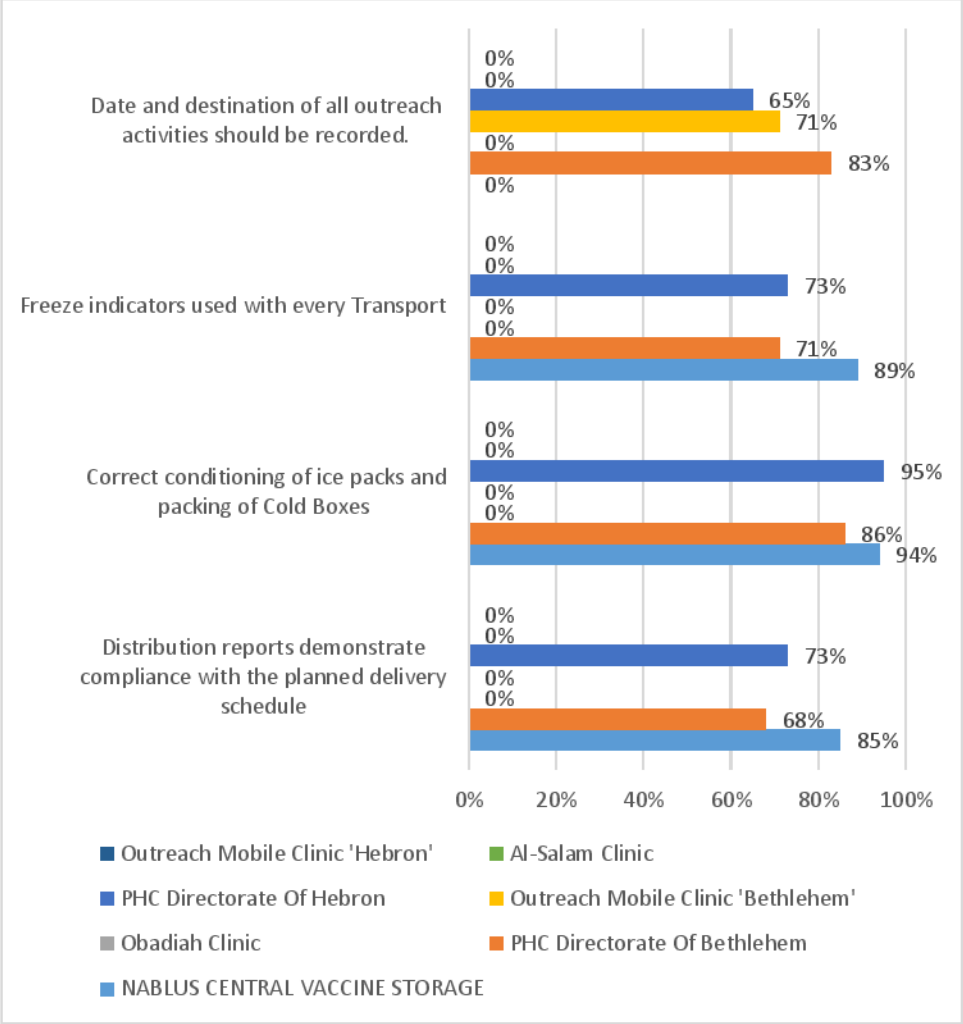


Figure 5.13: Performance indicators of distribution across Palestinian MoH.

0 = N/A: Service is not Provided in this facility

5.8. Vaccine Management

Figure.5.14 shows that the central store of Nablus scoring is 70% (Table.5.1), the low score is attributed to the lack of knowledge of the employees of the Vaccine Vial Monitor (VVM) and lack of standard operating procedure, whereas the governorates of Bethlehem (Table.5.2) scored 74% at the sub-national level of PHC directorate, which is below the recommended score due to lack of standard operating procedures and mismanagement of the wastage of vaccine, on the other hand the vaccine center of Obadiah and mobile outreach services performed better and scored 94% and 94% respectively, above the recommended score. The governorate of Hebron (Table.5.3) scored at the sub-national level PHC directorate 93% above the recommended, as well as the vaccine center of Al-Salam and the mobile outreach service scored 87% and 91% respectively.

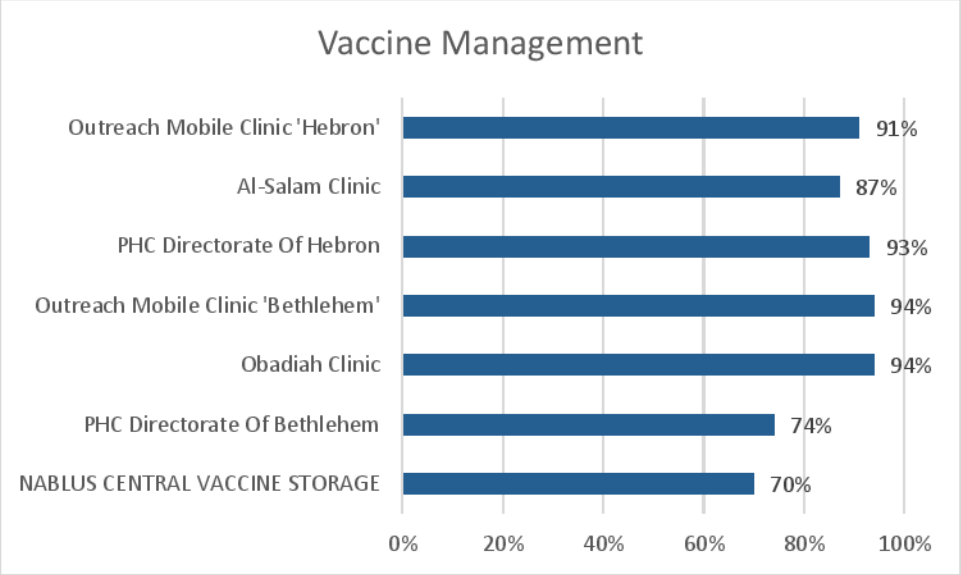


Figure 5.14: Vaccine management indicator across Palestinian MoH.

5.9.Information System and Management

Figure.5.15 display the scoring of the central store of Nablus 75% which is below the recommended score (Table.5.1), the lack of standard operating procedure booklet and no adherence to SOP'S recommended by the WHO, newly employed personnel was not subjected to full training in addition to the vaccine quantity forecasting and planning which is carried out by the PHC general directorate in Ramallah, whereas the governorates of Bethlehem (Table.5.2) scored 57% at the sub-national level of PHC directorate, which is below the recommended score, since they were unable to demonstrate the vaccine orders and forecasting at the time of assessment, document were scattered and non-organized, besides no SOP'S booklet is available which demonstrated non-compliance to WHO recommendations, on the other hand the vaccine center of Obadiah and mobile outreach services performed better and scored 85% and 87% respectively above the recommendations. Hence, demonstrated an experience and were subjected to frequent training and adherent to the WHO recommendations in regard of operating procedures. The governorate of Hebron (Table.5.3) scored at the subnational level of PHC directorate 78% below the recommended. Nonetheless, the SOP'S booklet was not provided, vaccine forecasting was not well organized and not archived electronically, on the other hand the vaccine center of al-Salam and the mobile outreach service scored 87% and 87% respectively and were above the recommended score. Vaccine schedule and documentation is strictly adhered to by the vaccine centers and mobile services, all children were vaccinated fully according to schedule and documented and computerized.

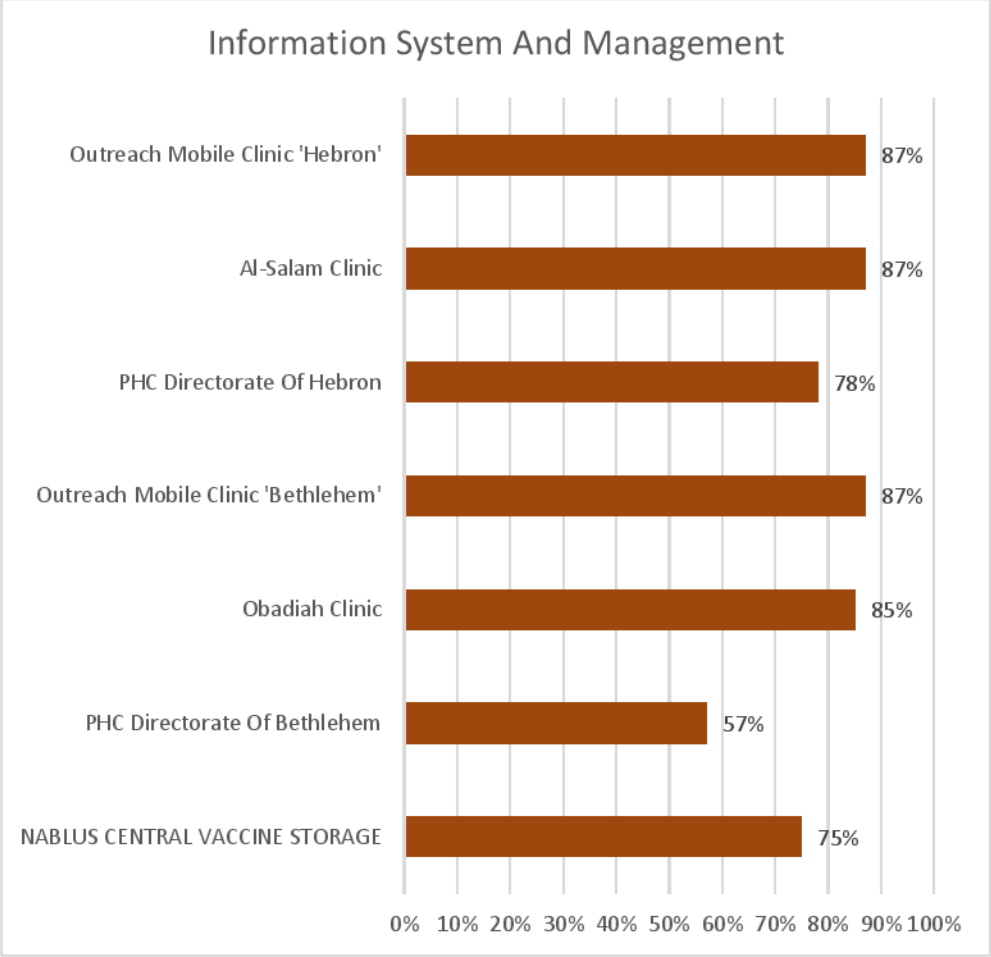


Figure 5.15: Information system and management indicator across Palestinian MoH.

6. CHAPTER SIX
DISCUSSION

6.1.Overview

The results of this analysis demonstrated a high performance and strength among most indicators of the Palestinian MoH cold chain, which have scored above the recommended standard scores while low scoring indicators reason was attributed to many factors including management issues, lack of financial resources and maintenance craftsmen lack of knowledge and professionalism. Besides the computerization of data and old building's structure. However, the vaccine arrival indicator which has been assessed in the national level of the central store of Nablus where the supplied vaccine from manufacturer is directed for storage, scored 86% which is highly performing in accordance with WHO policies and regulations(WHO, 2005). It is performing very well in contrast to other countries cold chains such as Gujarat in India assessed 2011 and scored 44%(UNICEF, 2011).

Temperature monitoring indicator on the other hand, demonstrates across major facilities assessed a high performance above the global standardized scoring, which means a strict adherence to WHO regulations(Kartoglu & Milstien, 2014), however, it has demonstrated that the knowledge and experience of the health workers is obviously considered in practice, the central store of Nablus scored in temperature monitoring 96% while in employees knowledge scored 71%, governorates of Bethlehem scored 75% at the sub-national level, which is below the recommended score due to maintenance and documentations issues, whereas the mobile outreach service scored 87% in temperature monitoring and 91% in health workers knowledge. The frequently trained and experienced health workers played a major role in the high performing scoring of this indicator. Additionally, it is highly performing in contrast to Gujarat in India which has scored 39% in the national level(UNICEF, 2011). And to Tolon District in West Ghana which scored 77%(Osei et al., 2019).

The mobile outreach services' workers were knowledgeable in the perspective of the correct vaccine temperature range and the adverse event of vaccine damage due to temperature change, were adherent to the WHO regulations in both directorates of Bethlehem and Hebron.

Generally, the passive storage of vaccine at the national and sub-national levels within recommended temperature range of -20 °C performance is optimum, however, the central store of Nablus scored 95% The governorate of Hebron scored 94% whereas Bethlehem has a maintenance issue of the cold room.

Cold chain equipment and transport indicator scoring was above the recommended score for all facilities, however, the criteria of building scoring were variable and was far below the recommendations and WHO regulations, obviously the old structure and poorly maintained and humidity of buildings in terms of quality assurance and regulations contributed to low scoring. The central store of Nablus was 57%, vaccine center of Obadiah performed better and scored 83% above the recommended score, as well as the vaccine center of Al-Salam scored 88% above the recommendation, which is attributed to

newly constructed buildings and continuously house kept. It is performing well when compared to Gujarat in India with 49% score(UNICEF, 2011).

In the perspective of mobile services, the cold boxes and carriers are an important tool for vaccine transportation, thereafter, they performed high in accordance to WHO policies which reflects a high compliance to the rules of keeping the vaccine cold, mobile outreach service performed very well at 95% in Bethlehem, 94% in Hebron.

Telecommunication is well represented, however, all employees are provided with cell phones to keep in connection despite the issue of availability of service from providers, in addition to the internet service issues.

Refrigerated vehicles comprise the biggest part of dilemma to the Palestinian MoH, the service is based on two types of vehicle, one type is owned by the MoH and is in most is well maintained and refrigerated and cooled for vaccine transport, the other type is a rented contractor's vehicles that is non-compliant to the WHO regulations, the contractor's vehicle deployed to the service line of the Palestinian ministry of health constitute the majority. thus, the central store of Nablus owned their vehicles and scored 91%. The PHC directorate of Bethlehem scored 46%, the PHC directorate of Hebron scored 53, which is low performance and below the recommended score where the deployed vehicles are contractor's and rented type.

Maintenance indicator comprised an overwhelming low scoring trend to the MoH cold chain in the process of assessment, a universal below the recommended score across all Palestinian MoH levels, however, the central store of Nablus scored 67%, governorates of Bethlehem scored 64% at the sub-national level. The governorate of Hebron scored at the sub-national level 71% below the recommended. The process of reporting of problems is documented well established but the maintenance team is undertrained and do not respond in a timely manner most of the times in addition to the delay of service. This performance is almost close to the performance in Gujarat in India with 64% score(UNICEF, 2011).

Stock management is basically carried out in the MoH headquarter of the general directorate of PHC such as vaccine forecasting, shipment tracking and communicating with manufacturers and suppliers. On the other hand, the governorate of Bethlehem scored 83% at the sub-national level of PHC directorate, performing well above the recommended score. The governorate of Hebron scored at the sub-national level of PHC directorate 87% above the recommended.

Distribution performance on the distribution indicators were below the recommended standardized scoring in some facilities due to un organized distribution reports and the events of non-compliance to schedule of vaccine distribution. The PHC directorate of Bethlehem scored below the recommended score with 68%, as well as the PHC directorate of Hebron which scored 73%. Despite the low score in this indicator it is higher than Gujarat score of 22%(UNICEF, 2011), and Tolo District in Ghana with 43%(Osei et al., 2019).

Information system and management demonstrated a universal lack of standard operating procedure booklets, vaccine orders and documents were scattered and non-organized, besides no adherence to SOP'S recommended by the WHO across higher levels but not in lower levels, newly employed personnel was not subjected to full training in some instances, the scoring of the central store of Nablus 75%, governorates of Bethlehem and

Hebron scored 57%, 78%, respectively at the sub-national level of PHC directorates. The lower levels of vaccine centers of Obadiah 85% and Al-Salam 87%, mobile outreach services in both governorates performed well and scored 87%. This will simply imply the experienced employees who were subjected to frequent training and adherent to the WHO recommendations in regard of operating procedures despite the lack of SOP's. It is performing better than the scores in Gujarat which was 25%(UNICEF, 2011), and Tolo District of West Ghana 26%(Osei et al., 2019).

6.2.Limitations

Research is often subjected to limitations. Nevertheless, this study results have to be seen in the light of limitations encountered throughout the process of the study and data collection.

The limitations shortlisted as follows:

- Focus of the study on the southern West Bank
- Timing of the study
- Facilities evaluated under particular circumstances at time of evaluation.
- Employees interviewed
- Financial resources to Palestinian MoH
- Information Technology

The primary limitation was that the study has focused on the southern area of West Bank, instead of assessing the entire West Bank and Gaza Strip. However, taking into consideration the political partition of Palestine and the frequent recurrent clashes and confrontations taking place of the Israeli occupation's armed forces against the Palestinian civilians limit the freedom of transportation and personal safety. Fortunately, the area of southern West Bank dwelled by half the population of West Bank and approximately one third the health care facilities of the Palestinian MoH.

The process of evaluation and data collection took place in the season of high climate temperatures and not throughout the year, taking into considerations the winter season obstacles. virtually the climate index in terms of Temperature in the area of Palestine is high most of the year except for the months of winter when the RV infections season kicks in.

During data collection during the visit to the facility of PHC of Bethlehem, unfortunately some employees were going into strike from their posts against their employer, who is the Palestinian Governments. Management employees who could have been of assistance to overlook every single detail that belongs to the surveying process where unavailable, cold chain maintenance teams as well were out of their posts and the vaccines' walk in cold room was out of service. Eventually, their scores in some indicators were below recommended.

The employees of the vaccination services in the facilities of the Palestinian MoH are healthcare workers who are specialized in the medical field, nurses in particular with long time experience and frequent training in vaccinations technique & cold chain system. On the contrary, the central store of vaccines contained personnel who are not educated in the

medical field to work in warehousing of vaccines. This has had an impact on knowledge and experience of those personnel to manipulate issues breakout.

Limited financial resources to the Palestinian MoH have a tremendous impact on the buildings of some health care facilities and services, buildings of some facilities are ancient and poorly maintained. Transporting vehicles in most facilities are contracted in from the private sector to conduct transportation services of the employees, vaccines and dry medical goods. Drivers are not medically knowledgeable and non-compliant to MoH instructions. Employment of professional crew is limited and impacted the healthy status of cold chain.

The world is transforming to the era of spider network and computerization of important documents, hence, the need for information technology specialist is increasing. Due to the limited number of information technology specialist in the Palestinian MoH, despite the abundancy of computer devices across MoH facilities, data access and integrity was challenging in some settings.

Further future studies to have a comprehensive evaluation to the Palestinian MoH cold chain are required to take these limitations into consideration, to expand the sample frame to include facilities across all geographic areas of West Bank & Gaza Strip. Consider various evaluation processes throughout the year across different seasons.

6.3.Conclusion

The results of this study demonstrated a high performance and strength among most indicators of the Palestinian MoH cold chain, which have scored above the recommended standard scores of 80, particularly the temperature monitoring indicator and storage capacity indicator, the cold chain equipment and transport indicator scored high as well as the stock management indicator. Nevertheless, the sub-indicator of health worker knowledge and experience besides the frequent training scored high. The sub-indicator of deep freezers temperature as well as cold boxes and carriers scored above 80 as well which are performing well. Other indicators showed variable performance among various service levels, the National, Sub-national and lower service levels. The building indicator did not perform well in all levels and show variable results, this was attributed to factors with management issues and maintenance craftsmen, the indicator of distribution performed variably among various levels, some scored high and some scored low as well as the maintenance indicator which has scored low across all service levels. The distribution task is performed in participation between Palestinian MoH owned vehicles and contracted corporate of private sector vehicles. The information system indicator scored variably among various service levels which obviously attributed to the computerization of data and further documentation issues.

The study concluded that the Palestinian vaccine cold chain is generally performing well among all levels. It is in a good standing when compared to other countries cold chain assessment according to studies in the literature, particularly Tolo District of West Ghana in Africa according to study conducted 2019 & Gujarat of India in Asia in a study conducted by UNICEF (Delhi Office) 2011. Mobile outreach services performance was

adequately effective and compliant to the global recommendations despite the limited resources and various influencing factors of sun exposure and transportation issues.

Ultimately, effectiveness of the Palestinian MoH cold chain is in a good standing that renders the RV vaccine efficacious and safe, all children in the areas assessed are fully vaccinated according to schedule and data is completely computerized and documented.

6.4. Recommendations

It is strongly recommended to:

- Implement an action plan to an expanded study to cover the various geographic areas of West Bank & Gaza Strip.
- Improve the weak cold chain system indicators and amend the defects.
- Conduct an annual evaluation of cold chain system to spot weaknesses and carry out improvement
- Conduct timely and efficacious maintenance of cold chain equipment and recruit professionals in the field of cold chain system and information technology specialists.
- Management endorsement in terms of SOP's and computerization of documents.
- Annual training of healthcare workers upon updated cold chain SOP in harmony with WHO standards.
- Palestinian MoH required to extend its partnership with the international foundation such as Gavi besides the WHO & UNICEF to invest in the current updated cold chain devices, further sponsor into the buildings' setting.

References

- Abu Elamreen, F. H., Abed, A. A., & Sharif, F. A. (2007). Detection and identification of bacterial enteropathogens by polymerase chain reaction and conventional techniques in childhood acute gastroenteritis in Gaza, Palestine. International Journal of Infectious Diseases, 11(6), 501–507. https://doi.org/10.1016/j.ijid.2007.01.010

- Anderson, E. J., & Weber, S. G. (2004). Rotavirus infection in adults. Lancet Infectious Diseases, 4(2), 91–99. https://doi.org/10.1016/S1473-3099(04)00928-4

- Angel, J., Franco, M. A., & Greenberg, H. B. (2012). Rotavirus immune responses and correlates of protection. Current Opinion in Virology, 2(4), 419–425. https://doi.org/10.1016/J.COVIRO.2012.05.003

- Badur, M., Latha, N., Kumar, P., Dudala, S., Shaik, S., Kang, G., & Kumar, C. (2015). Prevalence of Rotavirus diarrhea among under-5 hospitalized children in a Government tertiary hospital, Tirupati. Journal of Dr. NTR University of Health Sciences, 4(2), 112. https://doi.org/10.4103/2277-8632.158589

- Bhutta, Z. A., Ahmed, T., Black, R. E., Cousens, S., Dewey, K., Giugliani, E., Haider, B. A., Kirkwood, B., Morris, S. S., Sachdev, H., & Shekar, M. (2008). What works? Interventions for maternal and child undernutrition and survival. The Lancet, 371(9610), 417–440. https://doi.org/10.1016/S0140-6736(07)61693-6

- Bishara, R. H. (2006). Cold chain management - An essential component of the global pharmaceutical supply chain. American Pharmaceutical Review, 9(1), 105–109.

- Bresee, J. S., Glass, R. I., Ivanoff, B., & Gentsch, J. R. (1999). Current status and future priorities for rotavirus vaccine development, evaluation and implementation in developing countries. Vaccine, 17(18), 2207–2222. https://doi.org/10.1016/S0264-410X(98)00376-4

- Cascio, A., Vizzi, E., Alaimo, C., & Arista, S. (2001). Rotavirus gastroenteritis in Italian children: Can severity of symptoms be related to the infecting virus? Clinical Infectious Diseases, 32(8), 1126–1132. https://doi.org/10.1086/319744

- Chan, M. C. W. (2022). Return of Norovirus and Rotavirus Activity in Winter 2020-21 in City with Strict COVID-19 Control Strategy, China. Emerging Infectious Diseases, 28(3), 713–716. https://doi.org/10.3201/eid2803.212117

- Chow, J., Darley, S., & Laxminarayan, R. (2007). Cost-effectiveness of disease interventions in India. Washington DC: Resources for the Future. http://www.rff.org/RFF/documents/RFF-DP-07-53.pdf

- Crawford, S. E., Ramani, S., Tate, J. E., Parashar, U. D., Svensson, L., Hagbom, M., Franco, M. A., Greenberg, H. B., O'Ryan, M., Kang, G., Desselberger, U., & Estes, M. K. (2017). Rotavirus infection. Nature Reviews Disease Primers, 3. https://doi.org/10.1038/nrdp.2017.83

- Di Pasquale, A., Preiss, S., Da Silva, F. T., & Garçon, N. (2015). Vaccine adjuvants: From 1920 to 2015 and beyond. Vaccines, 3(2), 320–343. https://doi.org/10.3390/vaccines3020320

- Dongdem, J. T., Adjimani, J., & Armah, G. (2010). Detection and characterization of human rotavirus in tap water by multiplex RT-PCR. Journal of Medicine and Medical Sciences, 1(6), 223–230. http://interesjournals.org/JMMS/Pdf/2010/July/Dongdem et al.pdf

- Fischer, T. K., Valentiner-Branth, P., Steinsland, H., Perch, M., Santos, G., Aaby, P., Mølbak, K., & Sommerfelt, H. (n.d.). Protective Immunity after Natural Rotavirus Infection: A Community Cohort Study of Newborn Children in Guinea-Bissau, West Africa. https://academic.oup.com/jid/article/186/5/593/2191062

- Gazmararian, J. A., Oster, N. V, Green, D. C., Schuessler, L., Howell, K., Davis, J., Krovisky, M., & Warburton, S. W. (2002). Vaccine storage practices in primary care physician offices. American Journal of Preventive Medicine, 23(4), 246–253. https://doi.org/10.1016/s0749-3797(02)00512-3

- Glass, R. I., Parashar, U. D., Bresee, J. S., Turcios, R., Fischer, T. K., Widdowson, M. A., Jiang, B., & Gentsch, J. R. (2006). Rotavirus vaccines: current prospects and future challenges. Lancet, 368(9532), 323–332. https://doi.org/10.1016/S0140-6736(06)68815-6

- Grimwood, K., & Lambert, S. B. (2009). Rotavirus vaccines: Opportunities and challenges. Human Vaccines, 5(2), 57–69. https://doi.org/10.4161/hv.5.2.6924

- Guardado, J. A. A., Clará W., A. W., Turcios, R. M., Fuentes, R. A. C., Valencia, D., Sandoval, R., De Figueroa, J. B., Bresee, J. S., & Glass, R. I. (2004). Rotavirus in El Salvador: An outbreak, surveillance and estimates of disease burden, 2000-2002. Pediatric Infectious Disease Journal, 23(10 SUPPL.), 2000–2002. https://doi.org/10.1097/01.inf.0000142464.83628.8e

- Hanson, C. M., George, A. M., Sawadogo, A., & Schreiber, B. (2017). Is freezing in the vaccine cold chain an ongoing issue? A literature review. Vaccine, 35(17), 2127–2133. https://doi.org/10.1016/j.vaccine.2016.09.070

- Henschke, N., Bergman, H., Hungerford, D., Cunliffe, N. A., Grais, R. F., Kang, G., Parashar, U. D., Wang, S. A., & Neuzil, K. M. (2022). The efficacy and safety of rotavirus vaccines in countries in Africa and Asia with high child mortality. Vaccine, 40(12), 1707–1711. https://doi.org/10.1016/j.vaccine.2022.02.003

- Hogan, D., & Gupta, A. (2023). Why Reaching Zero-Dose Children Holds the Key

to Achieving the Sustainable Development Goals.

- Hopkins, R. S., Gaspard, G. B., Williams, F. P., Karlin, R. J., Cukor, G., & Blacklow, N. R. (1984). A community waterborne gastroenteritis outbreak: Evidence for rotavirus as the agent. American Journal of Public Health, 74(3), 263–265. https://doi.org/10.2105/AJPH.74.3.263

- Hu, L., Crawford, S. E., Hyser, J. M., Estes, M. K., & Prasad, B. V. V. (2012). Rotavirus non-structural proteins: Structure and function. Current Opinion in Virology, 2(4), 380–388. https://doi.org/10.1016/j.coviro.2012.06.003

- Jiang, B., Gentsch, J. R., & Glass, R. I. (2002). The role of serum antibodies in the protection against rotavirus disease: An overview. Clinical Infectious Diseases, 34(10), 1351–1361. https://doi.org/10.1086/340103

- Josefsberg, J. O., & Buckland, B. (2012). Vaccine process technology. Biotechnology and Bioengineering, 109(6), 1443–1460. https://doi.org/10.1002/bit.24493

- Kartoglu, U., & Milstien, J. (2014). Tools and approaches to ensure quality of vaccines throughout the cold chain. Expert Review of Vaccines, 13(7), 843–854. https://doi.org/10.1586/14760584.2014.923761

- Kocabaş, E., & Dayar, G. T. (2015). Rotavirus aşıları. Cocuk Enfeksiyon Dergisi, 9(4), 166–174. https://doi.org/10.5152/ced.2015.2004

- Kurugöl, Z., Geylani, S., Karaca, Y., Umay, F., Erensoy, S., Vardar, F., Bak, M., Yaprak, I., Özkinay, F., & Özkinay, C. (2003). Rotavirus gastroenteritis among children under five years of age in İzmir, Turkey. Turkish Journal of Pediatrics, 45(4), 290–294.

- Lee, K. L., Romzi, P. N., Hanaysha, J. R., Alzoubi, H. M., & Alshurideh, M. (2022). Investigating the impact of benefits and challenges of IOT adoption on supply chain performance and organizational performance: An empirical study in Malaysia. Uncertain Supply Chain Management, 10(2), 537–550. https://doi.org/10.5267/j.uscm.2021.11.009

- Lopez-Quintero, C., Freeman, P., & Neumark, Y. (2009). Hand washing among school children in Bogotá, Colombia. American Journal of Public Health, 99(1), 94–101. https://doi.org/10.2105/AJPH.2007.129759

- Maglasang, P. L. F., Butalid, M. L. C., Pastoril, M. F., Pratama, A. N. W., & Tan, E. Y. (2018). A cross-sectional survey on cold chain management of vaccines in Cebu, Philippines. Pharmacy Practice, 16(2), 1–6. https://doi.org/10.18549/PharmPract.2018.02.1167

- Mangin, L. (2020). Covid-19 : le point sur les vaccins. Pour La Science, N° 518-

d(12), 6–7. https://doi.org/10.3917/pls.518.0006

- Matthias, D. M., Robertson, J., Garrison, M. M., Newland, S., & Nelson, C. (2007). Freezing temperatures in the vaccine cold chain: A systematic literature review. Vaccine, 25(20), 3980–3986. https://doi.org/10.1016/j.vaccine.2007.02.052

- McAdams, D., McDade, K. K., Ogbuoji, O., Johnson, M., Dixit, S., & Yamey, G. (2020). Incentivising wealthy nations to participate in the COVID-19 Vaccine Global Access Facility (COVAX): A game theory perspective. BMJ Global Health, 5(11), 1–7. https://doi.org/10.1136/bmjgh-2020-003627

- Naghipour, M., Nakagomi, T., & Nakagomi, O. (2008). Issues with reducing the rotavirus-associated mortality by vaccination in developing countries. Vaccine, 26(26), 3236–3241. https://doi.org/10.1016/j.vaccine.2008.04.004

- Narváez, C. F., Feng, N., Vásquez, C., Sen, A., Angel, J., Greenberg, H. B., & Franco, M. A. (2012). Human Rotavirus-Specific IgM Memory B Cells Have Differential Cloning Efficiencies and Switch Capacities and Play a Role in Antiviral Immunity In Vivo . Journal of Virology, 86(19), 10829–10840. https://doi.org/10.1128/jvi.01466-12

- Omatola, C. A., Ogunsakin, R. E., & Olaniran, A. O. (2021a). Prevalence, pattern and genetic diversity of rotaviruses among children under 5 years of age with acute gastroenteritis in south africa: A systematic review and meta-analysis. Viruses, 13(10). https://doi.org/10.3390/v13101905

- Omatola, C. A., Ogunsakin, R. E., & Olaniran, A. O. (2021b). viruses Prevalence, Pattern and Genetic Diversity of Rotaviruses among Children under 5 Years of Age with Acute Gastroenteritis in South Africa: A Systematic Review and Meta-Analysis. https://doi.org/10.3390/v13101905

- Ragiab El-Hamadi, M., Burshan, N. M., Abugalia, M. O., Mohamed, A., Azeem, A.-, & Mostafa Lapez, R. (2015). Cold Chain Status and Vaccination Activities At Vaccination Centers in Tripoli, Libya (2015). Mmsj, 1(2). www.misuratau.edu.ly

- Rotavirus immune responses and correlates of protection - ScienceDirect. Retrieved October 22, 2022, from https://www.sciencedirect.com/science/article/abs/pii/S1879625712000880

- Saha, A., Asadujjaman, M., & Asaduzzaman, M. (2017). A Mixed Integer Linear Programming Model for Solving Closed Loop Supply Chain Problems. Journal of Modern Science and Technology, 5(1), 125–134.

- Shea, J. O., & Prausnitz, M. R. (2021). Micro-needling dermal patch COVID-19

vaccine strategies. Vaccines, 1–9.

- Sinha, A. K., Verma, A. R., Chandrakar, A., Khes, S. P., Panda, P. S., & Dixit, S. (2017). Evaluation of cold chain and logistics management practice in Durg district of Chhattisgarh: pointer from Central India. International Journal Of Community Medicine And Public Health, 4(2), 390. https://doi.org/10.18203/2394-6040.ijcmph20170260

- Skansberg, A., Sauer, M., Tan, M., Santosham, M., & Jennings, M. C. (2021). Product review of the rotavirus vaccines ROTASIIL, ROTAVAC, and Rotavin-M1. Human Vaccines and Immunotherapeutics, 17(4), 1223–1234. https://doi.org/10.1080/21645515.2020.1804245

- Storeng, K. T. (2014). The GAVI Alliance and the 'Gates approach' to health system strengthening. Global Public Health, 9(8), 865–879. https://doi.org/10.1080/17441692.2014.940362

- Sustainable Radio Frequency Identification Solutions. (2012). Sustainable Radio Frequency Identification Solutions. https://doi.org/10.5772/174

- UNICEF Supply Department. (2018). Cold Chain Equipment - Solar Direct Drive and Mains Powered Refrigerator Systems: Product Profiles, Availability, and Guidance. July, 0–14.

- Velázquez, R. F., Linhares, A. C., Muñoz, S., Seron, P., Lorca, P., DeAntonio, R., & Ortega-Barria, E. (2017). Efficacy, safety and effectiveness of licensed rotavirus vaccines: A systematic review and meta-analysis for Latin America and the Caribbean. BMC Pediatrics, 17(1), 1–12. https://doi.org/10.1186/s12887-016-0771-y

- Who. (2005). Good distribution practices (GDP) for pharmaceutical products. World Health, 1–28.

- WHO, & UNICEF. (2017). Solar direct-drive vaccine refrigerators and freezers: evidence brief. World Health Organization Dept of Immunization, Vaccines and Biologicals, 1–10. https://apps.who.int/iris/handle/10665/254715

- Al-Khatib, I. A., Abusara, L. W., Odeh, Y. M., Sbeih, S. A., & Massoud, M. A. (2015). Hand washing among Palestinians in the West Bank and Gaza Strip: attitudes and practices. Journal of Environmental Health, 77(6), 50–56.

- Kumru, O. S., Joshi, S. B., Smith, D. E., Middaugh, C. R., Prusik, T., & Volkin, D. B. (2014). Vaccine instability in the cold chain: Mechanisms, analysis and formulation strategies. Biologicals, 42(5), 237–259. https://doi.org/10.1016/j.biologicals.2014.05.007

- Osei, E., Ibrahim, M., & Kofi Amenuvegbe, G. (2019). Effective Vaccine Management: The Case of a Rural District in Ghana. Advances in Preventive Medicine, 2019, 1–8. https://doi.org/10.1155/2019/5287287

- UNICEF Delhi Version, D. (2011). Effective Vaccine Management 1 |. September.

- WHO / UNICEF Effective Vaccine Management (EVM)* Effective Vaccine Management (EVM) Initiative ; WHO . Assessment framework Criteria.

Appendix

State of Palestine
Ministry of Health
Education in Health and Scientific Research
Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي
والبحث العلمي

Ref.: .....
Date:.....

الرقم: ٢٠٢٢/٤٤٠/١٦٤
التاريخ: ٢٠٢٢/٥/١٩

عطوفة الوكيل المساعد لشؤون الصحة العامة وصحة الاسرة المحترم،،،

تحية واحترام،،

الموضـــوع: تسهيل مهمة بحث

يرجى تسهيل مهمة الطالب: فهد طنينة– ماجستير الوقاية وضبط الامراض المعدية/ جامعة القدس، وباشراف د. أسعد رملاوي، في عمل بحث الرسالة بعنوان:

"Effectiveness of cold chain on rotavirus vaccine in Southern West Bank in Palestine"

من خلال السماح للطالب بجمع معلومات من خلال تعبئة استبانة الدراسة، وذلك في:

- **مديريات الصحة في: –بيت لحم – نابلس – الخليل (شمال وسط جنوب)**

على ان يتم الالتزام باساليب واخلاقيات البحث العلمي.
على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا.
على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، والتعهد بعدم النشر لحين الحصول على موافقة الوزارة على نتائج البحث.

مع التحية،،

د. عبد الله القواسمي
رئيس وحدة التعليم الصحي والبحث العلمي

نسخة: عميد كلية الصحة العامة المحترم/ جامعة القدس