

# Assessment Of Immune Response Of Children Vaccinated Against Viral Diseases: A Meta-Analysis Of Egyptian Studies In The Last Ten Years

Thesis submitted for fulfillment of PhD In Medical Childhood Studies (Special Needs)

#### BY

#### **May Mohamed Abdel Hamid**

Msc. Pediatric, Cairo University

Under supervision of

## Dr. Omar El Sayed El Shourbagy

**Gamal**Professor of Pediatrics, Medical

Dr. Hanan Abd-Allah El-

Professor of Preventive Medicine and Epidemiology, Medical Studies Department for Children, Faculty of Postgraduate Childhood Studies, Ain Shams University

Professor of Pediatrics, Medical Studies Department for Children Faculty of Postgraduate Childhood Studies, Ain Shams University

#### Dr. Ola Mostafa Ibrahim

Professor of Child Health Child Health Department, National Research Center

#### Dr. Reham Sabrey Tarkhan

Lecturer of Pediatrics, Medical Studies Department for Children, Faculty of Postgraduate Childhood Studies, Ain Shams University

#### **ACKNOWLEDGEMENT**

I would like to thank **Dr. Omar El Shourbagy** professor of preventive medicine and epidemiology in medical studies department for children, Faculty of Postgraduate Childhood Studies, Ain Shams University for his remarkable effort, guidance and patience.

I would like to express my sincere thanks, deep gratitude and extreme appreciation to **Dr. Hanan El-Gamal** professor of pediatrics in Medical Studies Department for Children, Faculty of Postgraduate Childhood Studies, Ain Shams University for her supervision, valuable guidance and encouragement throughout the work.

It is a great honor to express my gratitude to **Dr. Ola Mostafa,** professor of Child Health in Child Health department, National Research Center for her remarkable help and her kind supervision she offered me during this work.

I am very grateful to **Dr Reham Sabrey**, lecturer of Pediatrics in Medical Studies Department For Children, Faculty Of Postgraduate Childhood Studies, Ain Shams University for her kind assistance and cooperation.

Also, I would like to show my gratitude to **Dr Maged Elwakeel**, Assistant Professor Of Child Health, National Research Center for his great help and support in this study.

I wish to thank all the members of the central digital library of Ain Shams for their unlimited cooperation during searching for thesis and papers needed for this work.

#### **ABSTRACT**

# Assessment Of Immune Response Of Children Vaccinated Against Viral Diseases: A Meta-Analysis Of Egyptian Studies In The Last Ten Years

May Mohamed A.Hamid, Omar El Shourbagy, Hanan El-Gamal, Ola Mostafa and Reham Sabrey Medical Studies Department for Children, Faculty of Postgraduate Childhood Studies, Ain Shams University

#### **Abstract:**

**Background:** Vaccines are considered the most cost-effective health investment.

**Objective:** is to provide the first meta-analysis of immune response of Egyptian children to viral vaccines, factors affecting it and duration of sero-protection of each viral vaccine.

**Methodology:** The researcher reviewed the Egyptian theses, papers, journals, in English language, searching for the eligible studies published in the last ten years. Meta-analysis was done using MedCalc software ver. 12.7.7.0. The pool consists of 43 studies.

**Results:** In this meta-analysis, regarding hepatitis B virus vaccine, 33 studies were included with a total number of 9611 healthy Egyptian vaccinated child, the proportion of seroprotected Egyptian children is 66.13%., the proportion of children with positive HBc antibodies is 2.81%, the proportion of children with positive HBs antigen is 0.64%. The mean HBsAb titer increases after booster dose by 267.96±232.95 mIU/ml. Regarding MMR vaccine, 10 studies were included, with 1141 cases, the proportions of seroprotected Egyptian

children against measles, mumps and rubella respectively are 80.74%, 45.06 and 90.21%.

**Conclusion:** The vaccination program in Egypt seems to be highly effective. The age related immunity waning after vaccination suggests the need of booster dose.

#### **Recommendations:**

Further studies need to be done to study the cellular immune response, also the immune response of other vaccines especially the non-obligatory vaccines.

Additional follow up study are needed to determine the duration of immunological memory.

**Key words:** vaccine, immune response, polio vaccine, Rotavirus vaccine, hepatitis B vaccine, hepatitis A vaccine, measles, mumps, rubella, influenza vaccine and varicella vaccine.

TABLE OF CONTENTS	
Content	Page
Acknowledgment	I
Abstract	П
Contents	IV
List of Abbreviations	VI
List of Tables	VII
List of Figures	X
Introduction	1
Aim of the study	3
Review of literature	5
Chapter 1: Vaccine overview	6
Chapter 2: Future of immunization	17
Chapter 3: Viral Vaccines6	22
Polio Vaccine	22
Hepatitis B Vaccine	25
Measles Mumps Rubella Vaccine	27

Rota Vaccine	28
Hepatitis A Vaccine	30
Varicella Vaccine	30
Viral Influenza Vaccine	32
Human Papilloma Virus vaccination	32
Rabies vaccine	33
Yellow Fever vaccine	34
Japanese Encephalitis	35
Meta-Analysis	36
Methodology	43
Results	47
Discussion	116
Conclusion & Recommendation	127
Summary	130
References	133
Appendices	149
Arabic Summary	1-4

# List of abbreviations

APC	Antigen presenting cells
CDC	Center of Disease Control and Prevention
CI	Confidence index
DC	Dendritic cells
DTP	Diphtheria-tetanus- pertussus vaccine
HBc Ab	Hepatitis B core antibodies
HBs Ab	Hepatitis B surface antibodies
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
Нер	Hepatitis vaccine
Hib	Hemophilus influenza virus vaccine
IgG	Immunoglobulins G
IPV	Inactivated polio vaccine
MMR	Measles – mumps – rubella vaccine
MMRV	Measles – mumps – rubella- varicella vaccine
МОНР	Ministry of Health and Population
NIP	National Immunization Program
OPV	Oral polio vaccine
WHO	World Health Organization

# **List of Tables**

No	Tables	Page
1	Types of vaccines	12
2	Recommendations for routine immunization according	15
	to WHO	
3	In Egypt, the schedule of basic obligatory vaccination	16
	according to ministry of health & population in 2019	
4	Additional recommended vaccine adopted from	16
	vacsera schedule in Egypt	
5	Meta-analysis: proportion of non protected cases with	49
	HBs antibodies < 10 mIU in all groups	
6	Meta-analysis: proportion of protected cases with HBs	53
	antibodies ≥ 10 mIU in all groups	
7	Meta-analysis: proportion of cases with positive	58
	hepatitis b core antibody in all age groups	
8	Meta-analysis: proportion of cases with positive	61
	hepatitis BsAg in all age groups	
9	The mean HBsAb level before and booster dose in all	65
	age groups	
10	Meta-analysis: proportion of non protected cases with	66
	HBs antibodies < 10 mIU in children less than 5 years	
11	Meta-analysis: proportion of protected cases with HBs	68
	antibodies ≥ 10 mIU in in children less than 5 years	

No	Tables	Page
12	Meta-analysis: proportion of cases with positive	70
	hepatitis b core antibody in children less than 5 years	
13	Meta-analysis: proportion of cases with positive	72
	hepatitis BsAg in children less than 5 years	
14	The mean HBsAb level in children less than 5 years	74
15	The mean HBsAb level before and booster dose in	75
	children less than 5 years	
16	Meta-analysis: proportion of non protected cases with	77
	HBs antibodies < 10 mIU in children aged from 5-10	
	years	H
17	Meta-analysis: proportion of protected cases with HBs	80
	antibodies $\geq 10 \text{ mIU}$ in in children aged from 5-10	
	years	
18	Meta-analysis: proportion of cases with positive	83
	hepatitis b core antibody in children aged from 5-10	
	years	
19	Meta-analysis: proportion of cases with positive	85
	hepatitis BsAg in children aged from 5-10 years	
20	The mean HBsAb level in children aged from 5-10	88
	years	
21	The mean HBsAb level before and booster dose in	90
	children aged from 5-10 years	

No	Tables	Page
22	Meta-analysis: proportion of non protected cases with	91
	HBs antibodies < 10 mIU in children aged >10 years	
23	Meta-analysis: proportion of protected cases with HBs	93
	antibodies ≥ 10 mIU in in children aged > 10 years	
24	Meta-analysis: proportion of cases with positive	96
	hepatitis b core antibody in children aged >10 years	
25	Meta-analysis: proportion of cases with positive	98
	hepatitis BsAg in children aged > 10 years	
26	The mean HBsAb level in children aged >10 years	100
27	The mean HBsAb level before and booster dose in	102
	children aged > 10 years	
28	Meta-analysis: Proportion of non protected cases of	104
	measles vaccine	
29	Meta-analysis: Proportion of protected cases of	106
	measles vaccine	
30	Meta-analysis: Proportion of non protected cases of	108
	mumps vaccine	
31	Meta-analysis: Proportion of protected cases of mumps	110
	vaccine	
32	Meta-analysis: Proportion of non protected cases of	112
	rubella vaccine	
33	Meta-analysis: Proportion of protected cases of rubella	114
	vaccine	

# **List of Figures:**

No	Title	Page
1.	Distribution of the estimated deaths among children under 5 years of age, from diseases that are preventable by vaccination in 2008	7
2.	Mechanism of action of vaccines	11
3.	Routes of administrations	13
4.	Current vaccines for rotavirus	29
5.	Evidence base medicine hierarchy	38
6.	Meta-analysis: proportion of non protected cases with HBs antibodies < 10 mIU in all groups	52
7.	Meta-analysis: proportion of protected cases with HBs antibodies ≥ 10 mIU in all groups	57
8.	Meta-analysis: proportion of cases with positive hepatitis b core antibody in all age groups	60
9.	Meta-analysis: proportion of cases with positive hepatitis BsAg in all age groups	64
10.	Meta-analysis: proportion of non protected cases with HBs antibodies < 10 mIU in children less than 5 years	64
11.	Meta-analysis: proportion of protected cases with HBs antibodies ≥ 10 mIU in in children less than 5 years	69

No	Title	Page
12.	Meta-analysis: proportion of cases with positive hepatitis b core antibody in children less than 5 years	71
13.	Meta-analysis: proportion of cases with positive hepatitis BsAg in children less than 5 years	73
14.	The mean HBsAb level in children less than 5 years	74
15.	The mean HBsAb level before and booster dose in children less than 5 years	76
16.	Meta-analysis: proportion of non protected cases with HBs antibodies < 10 mIU in children aged from 5-10 years	79
17.	Meta-analysis: proportion of protected cases with HBs antibodies ≥ 10 mIU in in children aged from 5-10 years	82
18.	Meta-analysis: proportion of cases with positive hepatitis b core antibody in children aged from 5-10 years	84
19.	Meta-analysis: proportion of cases with positive hepatitis BsAg in children aged from 5-10 years	87
20.	The mean HBsAb level before and booster dose in children aged from 5-10 years	89
21.	Meta-analysis: proportion of non protected cases with HBs antibodies < 10 mIU in children aged >10 years	92

No	Title	Page
22.	Meta-analysis: proportion of protected cases with HBs antibodies ≥ 10 mIU in in children aged > 10 years	95
23.	Meta-analysis: proportion of cases with positive hepatitis b core antibody in children aged >10 years	97
24.	Meta-analysis: proportion of cases with positive hepatitis BsAg in children aged > 10 years	100
25.	The mean HBsAb level before and after booster dose in children ages > 10 years	102
26.	The mean HBsAb level in children aged >10 years	103
27.	Meta-analysis: Proportion of non protected cases of measles vaccine	106
28.	Meta-analysis: Proportion of protected cases of measles vaccine	108
29.	Meta-analysis: Proportion of non protected cases of mumps vaccine	110
30.	Meta-analysis: Proportion of protected cases of mumps vaccine	112
31.	Meta-analysis: Proportion of non protected cases of rubella vaccine	114
32.	Meta-analysis: Proportion of protected cases of rubella vaccine	116



# INTRODUCTION



# **INTRODUCTION**

### **Introduction**

The invention of vaccination was a turning point in the war between microbes and humans. Vaccines represent the most cost-effective life-saving device in history. Despite their success, one of the great ironies of vaccines is that the vast majority of vaccines have been developed empirically, with little or no understanding of the immunological mechanisms by which they induce protective immunity (**Pulendran and Ahmed**, **2011**).

Viral vaccines can be classified into two broad groups, live attenuated vaccines and subunit vaccines. Many of these are live viruses that have been cultivated under conditions that disable their virulent properties. They typically provoke more durable immunological responses. Examples of these viral diseases are measles, rubella, and mumps. Attenuated vaccines have some advantages and disadvantages. They have the capacity of transient growth so they give prolonged protection, and no booster dose is required. But they may get reverted to the virulent form and cause the disease (Steel, et al, 2009).

The subunit vaccines (the vaccine against recombinant hepatitis B, usually contain substances called adjuvants, which enhance the magnitude and modulate the quality of the immune response (**Plotkin**, et al. 2012).