Republic of Iraq

Ministry of Higher Education and Scientific Research

University of Diyala - College of Medicine

Efficacy of Measles Vaccine and the Attributable Factors among Vaccinees in Diyala Province

A thesis

Submitted to the council of the College of Medicine-University of Diyala in partial fulfillment for the requirements of the degree of Master of Science in Medical Microbiology

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(وَقُل رَّبِّ زِدۡنِي عِلۡمٗا)

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سورة طه

الآية 114

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Dedication

To…..

My first teacher, my first love, the most precious blessing in my life, who gave me encouragement, love and tranquility and who would have no life for me without her ….. my dear mother

To…..

The one who supporting and gave me strength when I thought of giving up ….my dear father

To…..

The shining stars in the sky of my life….. my sister Hadeel

To….

My eyes…….my brothers Mohammed and Mofk

Raghad

Acknowledgements

Praise be to Allah

Iam express my thankful, to my esteemed supervisor, advisor, and mentor, Prof. Dr. Abdulrazak SH. Hasan for suggesting the subject and his scientific guidance throughout the study. Iam greatly grateful to his help, which helped me present this work in the right perspective,

Iam express my deepest gratitude to my co-advisor Prof. Dr. Nadhim Ghazal Noaman for his encouragement, inspiring advice and moral support in carrying out this thesis work.

Iam would also like to take this opportunity to thank the deanship College of Medicine , University of Diyala ; and the staff members of Microbiology Department.

Iam very much thankful to Assist. Lec. Hiba Hadi Rashid

Iam offer a personal expression of gratitude to all staff members of Al-Abara Healthcare Center / Diyala Directory of Health, for their kind help in collecting samples.

A final word, I would like to thank each and every person who have been a source of support and encouragement and helped me to achieve my goal and complete my thesis work successfully.

Summary

Measles is a very contagious respiratory disease caused by measles virus that spreads through respiratory droplets. It is a vaccine preventable disease that can cause serious illness, lifelong complications and death. Measles virus (MeV), is a single-stranded, negative-sense, enveloped, non-segmented RNA virus of the genus *Morbillivirus* within the family *Paramyxoviridae*. Humans are the natural hosts of the virus; Measles virus vaccine is a live attenuated was developed since 1963. One vaccine dose is about 93% effective while two doses are about 97% effective at preventing measles. However, measles remains an important cause of child morbidity and mortality worldwide despite the availability of a safe and efficacious vaccine.

Measles cases surged in 2017, as multiple countries experienced severe and prolonged outbreaks of measles due to gaps in vaccination coverage. The resurgence of measles is of serious concern, with extended outbreaks occurring across regions, and particularly in countries that had achieved, or were close to achieving, measles elimination.

Therefore, this study aimed to explore the rate of measles cases among unvaccinated children in Diyala province through detection of anti-measles IgM. Beside the determination of the efficacy of measles vaccine in vaccinated children through detection of anti-measles IgG.

This is a cross sectional study conducted in Diyala province from 1stNovember 2020 to 20th October 2021 . A total of 425 blood samples were collected from children (1-14) years of age including; children clinically suspected as having measles, vaccinated and unvaccinated groups as well as apparently healthy control. Those participants were allocated from primary health care centers. A special questionnaire form was pre-constructed for this purpose. The human privacy was respected by obtaining a child's parents' verbal consent. Furthermore, the study project was approved by the Scientific and Ethical Committee in the College of

Medicine- University of Diyala as well as the Scientific Committee of Diyala Health Directorate . Blood samples were collected from participants, the sera were separated. Anti-measles IgG(CD Creative Diagnostics) and IgM antibodies (MyBioSource-USA) were done using ELISA technique. Statistical analysis was done using SPSS version 27 and p values ≤ 0.05 were considered significant

The results showed that the rate of anti-measles IgM positivity rate among sick children was 15.6%. the majority of patients (23.3%) had 1.0 mIU/ml IgM concentration, while 8.9% of the patients had 4.0 mIU/ml IgM concentration. the highest mean ± SD of IgM concentration was among children 5 years old. Furthermore, the mean ± SD of IgM was unsignificantly higher in male (P = 0.600). Unsignificantly higher mean ± SD of IgM was found among ruralees (P= 0.902).

Regarding the anti-measles IgG, the positivity rate among vaccinated children was 92.6% which was significantly higher compared to control 4.5% (P= 0.0001). Furthermore, the majority (41.5%) of vaccinated children had 30.0 mIU/ml IgG concentration, while 4.8% of vaccinated children had => 40.0 mIU/ml IgG concentration. the mean concentration ± SD of IgG was significantly higher among children ≥ 6 years old (P= 0.0001). The mean concentration ± SD IgG was unsignificantly higher in male (P = 0.655). It was also unsignificantly higher among ruralees (P= 0.143). Furthermore, the mean ± SD of IgG concentration (32.601±4.682) was significantly higher among children received 4 vaccine doses.

The mean ± SD of platelets counts in measles vaccinated children (247.652±47.172) was significant higher compared to patients and control groups (P=0.0001). The mean ± SD of Hb (g/dL) of vaccinated children 12.931±0.842 was significantly higher (P=0.0001). Also, the mean ± SD of WBC count (Cell/CC x 10^3) in vaccinated children 7.101±1.327 was significant lower compared to others (P= 0.0001). As well as the lymphocytes count (Cell/CC x 10^3), results found that the mean ± SD of vaccinated children was significantly higher compare to other groups (P= 0.0001). This study concluded that measles cases actually occurred among unvaccinated children that may be alarming emergence of outbreaks in these

areas. However, the protection rate of measles vaccine among fully vaccinated children was efficacious.

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List of abbreviations

Abbreviation	Meaning
AAFP	American Academy of Family Physicians
AAP	American Academy of Pediatrics
Abs	Antibodies
ACIP	Advisory Committee on Immunization Practices
arbU/ml	Arbitrary units per milliliter
CBC	Complete blood count
CD	Cluster of differentiation
CDC	Center for Disease Control and Prevention
EDTA	Ethylene diamine tetraacetic acid
ELISA	Enzyme-Linked Immunosorbent Assay
EPI	Expanded Program on Immunization
F	Fusion protein
H	Hemagglutinin protein
HRP	Horseradish peroxidase
IFN	Interferon
IgG	Immunoglobulin (G)
IgM	Immunoglobulin (M)
L	Large protein
M	Matrix protein
MCV	Measles-containing vaccine
MeV	Measles virus
MMR	Measles-Mumps-Rubella vaccine
N	Nucleoprotein
P	Phosphoprotein
RNP	Ribonucleoprotein
SD	Standard deviation
SLAM	Signaling lymphocyte activation molecule
WHO	World Health Organization

CHAPTER ONE

Introduction

Chapter One

1. Introduction

1.1.Overview:

Despite the availability of a safe and effective attenuated measles vaccine for more than 50 years, measles is still a major causes of children morbidity and mortality. In recent years, it has become a global public health problem, attributed to low vaccination coverage observed in different countries (Fadic and Repetto, 2019; Julik and Valle, 2017). According to 2017 estimates, measles resulted in approximately 110.000 deaths annually (Portnoy *et al.*, 2019). In 2019 there was measles virus resurgence causing more than 200,000 deaths, the deaths occurred mostly in children under 5 years of age, also those whom are most susceptible to complications of pneumonia, diarrhea and dehydration (Ikegame *et al.*, 2021).

Measles is a highly contagious systemic viral illness (Griffin, 2018).The causative agent of illness is Measles virus (MeV), which is a member of genus *Morbillivirus* within the *Paramyxoviridae* family, it has a negative-sense, single-stranded RNA genome (Coughlin *et al.*, 2017). The length of genome is16 kilobase, comprises six genes that encode eight viral proteins. The viral genome encapsidated by nucleoprotein **(N)**, phosphoprotein **(P)** and large protein **(L)** forming the ribonucleoprotein complex **(RNP)**, which surrounded by matrix **(M)** protein. Two of the proteins are non-structural proteins **V and C**, which expressed from an alternative RNA transcript of the P gene. Their function is primarily implicated in the prevention of type 1 interferon **(IFN)**-induced immune responses. Measles virus envelope glycoproteins include hemagglutinin **(H)** and fusion **(F)** proteins (Aref *et al.*, 2016). **H** protein mediated adsorption of virus to receptors on the host cell and **F** protein is

responsible for the membrane fusion of virus and host cell and for the penetration of virus into the host cell (Ha *et al.*, 2017).

Transmission of measles virus occurs via person-to-person contact, as well as airborne spread. Infectious droplets from the respiratory secretions of a patient with measles can remain airborne for up to two hours and thus the disease may be transmitted in public spaces, even in the absence of person-to-person contact (Gans *et al.*, 2018). The incubation period for disease usually lasts 10-14 days (from exposure to first symptoms appears), which generally consist of fever, cough, conjunctivitis, malaise and coryza. The characteristic morbilliform rash appears 2-4 days after onset of the prodrome. Usually, patients are contagious from about 4 days before eruption of the rash to 4 days after eruption, when the level of measles virus are highest in the respiratory tract. Prior to the appearance of the rash, bluish-white koplik's spots may be seen in the oral mucosa, which are pathognomonic for measles (Mondiale and de la Sante, 2017). Measles infects multiple systems and targets epithelial, white blood cell, and reticuloendothelial. Complications when they occur, largely arise by disruption of epithelial surface of different organ systems and immunosuppression. Approximately 30% of reported measles cases have one or more complications. In developed countries these include (7-9%) otitis media, (1-6%) pneumonia, (6%) diarrhea, blindness, and post-infectious encephalitis (1 per 1000 cases). The risk of serious measles complications is higher in adults and infants (Abad and Safdar, 2015).

Before the introduction of measles vaccine during 1960s, nearly every person had contracted measles during childhood (de Quadros *et al.*, 2008). With almost 30 million case of measles occurring every year globally (Zahoor, 2017). Person who was infected with measles acquired life-long immunity against measles (Adamo *et al.*, 2017). In the 1963, the live measles vaccine was introduced and consequently there was dramatical reduction of these

numbers. The vaccine was initially given as one dose; however, due to an epidemic in 1989 to 1990, a second dose became the standard care for children aged 4 to 6 years (Vassantachart *et al.*, 2020).

The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), recommended maintaining high levels of immunization through universal routine vaccination of all children with two doses of a combined measles, mumps and rubella (MMR) vaccine (Abu-Elyazeed *et al.*, 2018). The MMR is a live attenuated vaccines, which are used to stimulate the immune system to protect against measles, mumps and rubella (Bailey and Sapra, 2021). The first dose of MMR vaccine is routinely given at 12 to 15 months of age, and the second dose is routinely given at 4 to 6 years of age. The WHO considers 9 months as optimal timing for the first dose of measles vaccination for protection of susceptible infants against measles in countries with high measles prevalence and this dose does not count as part of the 2-dose regimen (Pawaskar *et al.*, 2021).

In Iraq, the measles immunization schedule recommends measles vaccine for infants at nine months of age (Al-Shamsi *et al.*, 2010). During 2019 measles cases in Iraq was 3.799 (Knoema, 2019).

Annual measles outbreaks typically occurs in late winter and early spring in temperate climates, influenced by both meteorological and social variables and by population density understood both in relation to the inhabited area and public place, such as school. Countries in which widely used measles vaccine have experienced a marked decrease in the incidence of disease (Misin *et al.*, 2020). Measles outbreaks occur predominantly in unvaccinated individuals and are facilitated by low coverage as well as the high transmissibility of measles virus (Berry *et al.*, 2017). To prevent recurrent outbreaks of measles, 95% of population must be immune. Several attenuated measles vaccine are available

worldwide, either as single-virus vaccines, or in combination with other vaccine viruses, commonly with rubella and mumps (Naji *et al.*, 2020).

Measles remains a common illness in many countries especially in part of Asia and Africa, People from both developed and developing countries are seen to be targeted from this medical problem, but measles could be more perilous among children came from developing countries, and potentially leading to increase the mortality rate up to 15% (Aljothery *et al.*, 2020). Several factors can contribute to the severity of measles in developing countries, including poor nutrition, exposure to high doses of virus in crowded conditions, and an early age at which infants are exposed to the community at large (WHO, 2019). In addition to vitamin A deficiency, poor hygiene, inadequate immunization, and decreased immunity (Labib *et al.*, 2019).

2.1. Aims of the study:

For the best of our knowledge this is the first study in Diyala in this regard. Therefore, it was designed to achieve the following goals.

1. Determination of the efficacy of measles vaccine among vaccinated children in Diyala province.
2. Explore the rate of measles cases among children in Diyala community.
3. Assessing of effect of certain socio-demographic factors on vaccine efficacy.