

A Prospective Study on Evaluating the Long-Term Effects of Childhood Vaccination from Birth to 13 Years Old in Kuwait

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Abstract

Background: To prevent infectious diseases and deaths of children, vaccinations play a crucial role in public health strategies in Kuwait. However, it remained uncertain to demonstrate the potential long-term health outcomes of vaccination, including neurodevelopmental disorders (NDD) and autism. This study aimed to evaluate the long-term health outcomes of vaccination among Kuwait children from birth to thirteen years old. **Objectives:** This study included the significant objectives: (1) to compare long-term health effects, including chronic and acute conditions for unvaccinated, partially vaccinated, and vaccinated children, and (2) to evaluate the association of vaccination with the neurodevelopmental disorders (NDD) and autism, and the preventable illnesses. **Methods:** This prospective study involved a sample of 976 children from Kuwait based on mothers' reporting. Data collection about the vaccination status of children and various health outcomes relevant to chronic and acute illnesses was performed based on structured questionnaires through an online survey. However, participants were classified into unvaccinated (n = 40), partially vaccinated (n = 222), and fully vaccinated (n = 714). Statistical analyses, including the chi-square test, Odds Ratios (OR), 95% Confidence Interval (CI), and logistic regression, were performed using SAS (Version 9.4) to determine the associations between vaccination status and health outcomes among children. **Results:** The study disclosed that vaccinated children showed an increased diagnosis of chronic (allergic rhinitis, allergies, autism spectrum, eczema, neuro-developmental disorders, learning disability, ADHD, and any chronic condition) and acute (whooping cough, pneumonia, rubella, hepatitis A or B, measles, mumps, meningitis, influenza, rotavirus, cancer, chronic fatigue, Crohn's disease, inflammatory bowel disease, conduct disorder, diabetes type 1 or 2, rheumatoid arthritis, obesity, seizures, hearing loss, polio, diphtheria, tetanus, and depression) illnesses than unvaccinated

children. The fully vaccinated children showed an increased prevalence of influenza diagnosis, while partially vaccinated children were more likely to be diagnosed with rheumatoid arthritis than unvaccinated children. In contrast, unvaccinated were more likely to have been diagnosed with chickenpox and encephalopathy than fully and partially vaccinated. Males with chronic and acute conditions had a lower incidence of allergies and pneumonia, respectively, whereas females had a reduced prevalence of acute illnesses, such as whooping cough, inflammatory bowel disease, and hepatitis A or B among vaccinated (n = 936; combination of partially vaccinated and fully vaccinated) children. Regarding medication use and health service applications, vaccinated children were more likely to use medications for fever, antibiotics, and allergies. In addition, they showed an increased rate of sick visits and emergency visits in the past twelve months. On the other hand, factors like age (2 - 5 years, 6 - 9 years, and 10 - 13 years), birth type (cesarian), and mother suffering during pregnancy (gestational diabetes) were significantly associated with NDD (learning disability, autism spectrum, and attention deficient hyperactivity disorder) in the adjusted analysis. In the interaction model of age and birth type, age (6 - 9 years; OR 5.3, 95% CI: 1.1, 25.3) and mother suffering (gestational diabetes; OR 2.5, 95% CI: 1.2, 5.2) during pregnancy were associated with NDD. **Conclusion:** The findings of this study showed that there are some cases where the infection rate is higher among the vaccinated compared to unvaccinated children, or there are no significant differences between the two groups in Kuwait. Upon controlling the factors in the interaction model, the age of 6 to 9 years and gestational diabetic mothers during pregnancy were associated with the synergistic increment of odds with NDD. These data findings are recommended to verify a larger and diverse group of samples to optimize the vaccination on health outcomes in Kuwait children.

Keywords

Vaccination, Partial Vaccination, Neurodevelopmental Disorders, Long-Term Health Impacts, Autism, Chronic Conditions, Acute Conditions, Kuwait

1. Introduction

Vaccination contributes to preventing and controlling infectious diseases worldwide. In Kuwait, childhood vaccination programs maintain national public health. In alignment with global health standards, the Ministry of Health in Kuwait has developed a vaccination schedule for children from birth to thirteen years old to protect them from vaccine-preventable diseases. There was a recognition of the need to determine the vaccination and its long-term implications on health outcomes in children in Kuwait. It would assist in understanding the health outcomes, including disease prevention and sustained immunity while determining any adverse effects in the prevalence of health outcomes that may arise with the comparison of groups like vaccinated and unvaccinated children. This research

contributed valuable insights into the vaccination programs with a broader understanding of assessing the impact of vaccination on health outcomes by considering the factors, including long-term effects of vaccination and overall impact on health outcomes, including acute and chronic conditions.

Vaccine hesitancy appears to be a global issue. In Mumbai, India, there is 7.4% hesitancy of parents toward vaccination mostly concerned about side effect [1]. While in Pakistan, there were 6 reasons for defaulting some children immunization including child illness, perceived vaccine side effects, caregiver-related factors, myths, vaccinator attitudes and inadequate immunization services [2].

The VAERS (Vaccine Adverse Event Reporting System) contains certain limitations in obtaining all adverse circumstances, resulting in possible underreporting of several vaccine-based reactions and death. However, mandatory vaccination seems essential to confirm high rates of immunization coverage, particularly in some populations where people are specifically susceptible to the reactions of fatal vaccines [3]. In the USA, an estimated 90% of population possess the rates of immunization coverage, directing a high people ratio getting vaccines. After receiving such vaccines, infants have a high risk of unexpected death, with an extreme number of deaths of infants happening within days of such post-vaccination. It is obtained that approximately 58% of the deaths of such infants informed to VAERS happen in 3 days of such post-vaccination, underscoring the requirement to improve and monitor vaccine safety [4]. While in the Republic of Congo, 63.46% of measles vaccinated patients were exposed to the virus [5].

Vaccination also contains certain risks, consisting adverse impacts such as gastrointestinal disorders, ear infections, asthma, and developmental delays. Ethical concerns hinder researches on diverse vaccination impacts, restricting a complete assessment of health effects. Before the age of one year, vaccination was integrated with extreme odds of ear infections, asthma, and developmental delays [6]. Whereas, 0 out of 561 patients, those were unvaccinated possess ADHD (Attention Deficit Hyperactivity Disorder), differentiated to 5.3% of fully and partially vaccinated peoples. The entire autism spectrum disorder rate in the research was 0.361% that considered as one-fifth of the 1.851% of the US national rate.

Batista and others [7] review various common side effects associated with childhood vaccines. It analyzes data from studies published between 2018 and 2023, identifying adverse reactions such as nausea, fever, diarrhea, rash, and, in rare cases, neurological events and severe allergic reactions.

In Kuwait, there were two studies which showed the 13-valent pneumococcal conjugate vaccine (PCV13) does not appear to provide much protection [8] [9].

In general, the potential factors causing vaccine hesitancy include: Fear of side effects, religious and philosophical beliefs, distrust in medical institutions and the influence of anti-vaccine movements in social media and other platforms.

Comparative studies have not been investigated across Gulf regions regarding the health outcomes in vaccinated and unvaccinated children. The studies were required to investigate the linkage between vaccination and health outcomes,

including chronic and acute illnesses among children. It was necessary to address the long-term effects of vaccination on children health outcomes through a balanced approach and evidence-based practices to enhance vaccination programs in Kuwait.

Recently, the incidence of neuro-developmental disorders (NDD) has been reduced with the growing awareness of autism and other sensitive tools [10]. It remained uncertain to discuss the role of vaccines in the increased diagnoses of NDD due to the lack of data about health outcomes by comparing unvaccinated and vaccinated children. A significant association was not found between autism and vaccination based on various epidemiological studies [11].

Kuwait does not have VAERS (Vaccine Adverse Event Reporting System), so there is no way to know the side effects regarding vaccinations.

The paper seeks to analyse the childhood vaccination's long-term effects from birth to 13 years old children in the context of Kuwait, concentrating on both vaccine coverage and health outcomes.

It was required to investigate the impact of vaccination on the development of NDD among children in Kuwait, while considering other measured factors.

The study aims were:

- 1) to compare fully vaccinated, partially vaccinated, and unvaccinated children to explore the long-term effects of vaccination on health outcomes, including chronic and acute conditions, medication use, and health service applications, and
- 2) to evaluate the association between vaccination and NDD based on unadjusted and adjusted analyses.

2. Methods

2.1. Study Planning

The study evaluated the long-term effects of vaccination on children from birth to 13 years old in Kuwait. The target group of the study was chosen as mothers who could access their children's records regarding vaccination to provide accurate data findings. Initially, we identified the online groups focused on local communities in Kuwait, and a careful invitation message was shared across emails and WhatsApp to reach out to the potential participants. The invitation messages included a brief introduction, purpose, and importance of the research along with the link for an online questionnaire. The online questionnaire was developed using Google Forms to provide the questions and allow the participants to answer the questions regarding demographic data, health outcomes, and vaccination status. To fill out the questionnaire, clear instructions or guidelines should be provided for each section.

2.2. Study Design

The selection criteria of this study included mothers who had their children's vaccination certificates and were interested in sharing their opinions voluntarily. A questionnaire link was distributed to mothers through WhatsApp, and emails to

collect the data. This approach allowed an efficient collection of data from a diverse group of the population in Kuwait.

In the initial stage, the researcher continued the study by choosing several key segments for the survey within Kuwait. To gather comprehensive data, an online questionnaire was designed for collecting the data regarding the health outcomes and vaccination history of children. In the second stage, the second mail was sent, demonstrating the research background and purpose, that the institutional heads were instructed to send further to all the respective mothers. Therefore, a link was facilitated to a questionnaire where no personally determining details or information was demanded. The researcher pursued to acquire maximum responses from mothers of children aged from 0 to 13 years old by including questions about the demographics of children and mothers, birth history of children, vaccination history, and health outcomes. However, the demographics of children included age and gender, while mothers' demographics included education, social status, and pregnancy-related factors such as medications and suffering. Furthermore, the age group of 0 - 13-year-old children was chosen as the majority recommended vaccination or immunization was intended to be received. Regarding vaccination history, we collected the details about the partially vaccinated, fully vaccinated, and unvaccinated statuses of a child. In addition, the children's health was also gathered relevant to the incidence of chronic and acute illnesses and emergency room visits.

2.3. Recruitment and Informed Consent

Multiple reminders were sent to the participants to encourage their participation. The survey questionnaire contained only "close-ended questions" with single answers or responses, with the goal of developing both completion rates and responses. Moreover, the online survey remained open for four months during the spring of 2024.

Before accessing the online questionnaire link, this study was presented a consent form for participants to ensure that the collected data would be kept as confidential and maintained data anonymity. The participation was entirely voluntary and they could be allowed to withdraw from the questionnaire at any time. However, participants needed to answer for questionnaire, including their demographics, health status of children, and vaccination history of children. The designed questionnaire was expected to take 10 to 15 minutes of time to complete the answers to questions.

2.4. Definitions and Measures

Health outcomes: All the mothers were informed to direct on a particular list of above 40 chronic and acute diseases all those factors for that their children suffered from diagnosis by respective physician. Major outcomes contained the vaccine-preventable diseases' including hepatitis B, polio, tetanus, pertussis, diphtheria, rubella, mumps, and measles. In the survey, other questions contained the

application of health procedures and services, hospitalizations, medications used, sick visits to doctors or physicians, social status (married, separated, or divorced), and the education level of the mother. Particularly for the mother, the questions included birth history and pregnancy-related conditions, medications application during pregnancy, and contact with a contrary environment (stated as living near communication tower/electrical tower less than 300 meters).

Vaccination status: Differentiated as fully vaccinated (obtained all suggested age-appropriate vaccines), partially vaccinated (obtained few suggested vaccinations and not all), and unvaccinated (such as no past vaccinations) as investigated by mothers. Such diversifications were made on the segment that the vaccines' long-term impact would seem more authentic among fully-vaccinated instead of the partially-vaccinated infants and children and absent or rare among the unvaccinated. However, all the mothers were informed to apply their vaccination records of their child to direct the suggested doses and vaccines their children received. Moreover, vaccination dates were not demanded to decrease the inaccurate reporting's likelihood and ignore the overburdening participants.

2.5. Statistical Methods

The research followed “unadjusted bivariate analysis” applying chi-square tests primarily to analyze the null hypothesis of particularly no relationship between health outcomes and vaccination status, such as health services' application, medications, physician-diagnosed chronic and acute illnesses, and vaccine-preventable diseases' prevalence rates. In the majority of analyses, fully and partially vaccinated children and infants were associated together as the group of vaccinated, with all the unvaccinated children and infants as the “control group.” However, the second goal of this research was to ascertain whether any integration is there between health outcomes and vaccination, which stands as significant after measuring for other assumed aspects, such as the socio-demographic variables. In this research, descriptive statistics were measured on all variables to ascertain percentages and frequencies for categorical means and variables for such continuous variables. However, the strength of the relationship between health outcomes and vaccination status was analyzed by applying 95% CI (Confidence Intervals) and OR (Odds Ratios). Odds ratios demonstrate the strength of the relationship between two simultaneously measured categorical variables and are suitable procedures for that association in such cross-sectional research. Finally, adjusted and unadjusted analyses of logistic regression were followed in this research applying SAS (Version 9.4) to ascertain the factors integrated with vaccination adherence and health outcomes.

3. Results

3.1. Socio-Demographic Characteristics

The information provided the data for 976 children in this study. **Table 1** shows the demographic characteristics of respondents (mothers) and children. Mothers

mostly held college degrees (61%) and were married (93%). However, the majority of respondents (77.4%) did not have gestational diabetes, pre-eclampsia, or other conditions during their pregnancy. In addition, many of them (74.1%) did not take any medications during pregnancy.

Table 1. Socio-demographics of participants.

Socio-Demographics		Frequency (Percent)
Mothers' Demographic Information		
Education	High School or lower	140 (14.3%)
	Diploma	191 (19.6%)
	College Degree	595 (61%)
	Higher Education	50 (5.1%)
	Total	976 (100%)
Suffering of mothers during pregnancy	Gestational diabetes	109 (11.2%)
	Pre-eclampsia	18 (1.8%)
	Others	94 (9.6%)
	None of the above	755 (77.4%)
	Total	976 (100%)
Medications taken by mothers during pregnancy	Antibiotics	186 (19.1%)
	Vaccines	67 (6.8%)
	None of the above	723 (74.1%)
	Total	976 (100%)
Social status	Married	908 (93%)
	Divorced	51 (5.2%)
	Widow	17 (1.8%)
	Total	976 (100%)
Children's Demographic Information		
Gender of the child	Male	500 (48.8%)
	Female	476 (51.2%)
	Total	976 (100%)
Age of the child (in Years)	Less than 2	176 (18%)
	2 - 5	316 (32.4%)
	6 - 9	191 (19.6%)
	10 - 13	146 (15%)

Regarding demographic characteristics of children, many of them (51.2%) were female compared to male (48.8%) (**Table 1**). They were mostly aged (32.4%) between two and five years old. Based on these findings, this study targeted female children between two to five years old.

3.2. Birth History and Health Information of Children

Table 2 presents the birth history of children, including the birth type, birth time, and type of feeding in the first three months and health information, including vaccination, emergency visits, sick visits, in the past year, spent nights in the hospital, used medications for fever, antibiotics, allergy, and ADHD, and COVID vaccine status. However, the results depicted that most of the children (69.2%) were born naturally with full-term (88.9%) birth time and mixed-feeding of both breast milk and bottle feeding (43.8%) in the first three months of their birth. The distribution of children for vaccination status was fully vaccinated (73.2%), partially vaccinated (22.7%), and unvaccinated (4.1%). Many children did not take the COVID-19 vaccine (83.7%). Out of them, most children did not have any emergency visits (57.7%) during the past year and did not spend one or more nights (84.6%) at the hospital. The children were mostly had sick visits (64.2%) during the last twelve months. Regarding medications for different health conditions, many children used antibiotics (54.1%) and medicines for fever (84.4%). On the contrary, most of them did not use medications for allergies (64.6%) and ADHD (95.9%) as well.

Table 2. Birth history and health information of children.

Birth History and Health Information of Children		Frequency (Percent)
Birth History		
Birth type	Natural	675 (69.2%)
	Cesarean	301 (30.8%)
	Total	976 (100%)
Birth time	Full Term	868 (88.9%)
	Pre-term	108 (11.1%)
	Total	976 (100%)
Type of feeding in the first three months	Breast Milk	334 (34.2%)
	Bottle Feeding	215 (22%)
	Mixed Feeding	427 (43.8%)
	Total	976 (100%)
Health Information		
Vaccination status	Fully Vaccinated	714 (73.2%)
	Partially Vaccinated	222 (22.7%)
	Unvaccinated	40 (4.1%)
	Total	976 (100%)
Emergency visits during the last 12 months	Yes	413 (42.3%)
	No	563 (57.7%)
	Total	976 (100%)

Continued

Sick visits during the last 12 months	Yes	627 (64.2%)
	No	349 (35.8%)
	Total	976 (100%)
Spent one or more nights at the hospital	Yes	150 (15.4%)
	No	826 (84.6%)
	Total	976 (100%)
Used medications for allergy	Yes	346 (35.4%)
	No	630 (64.6%)
	Total	976 (100%)
Used antibiotics	Yes	528 (54.1%)
	No	448 (45.9%)
	Total	976 (100%)
Used medications for fever	Yes	824 (84.4%)
	No	152 (15.6%)
	Total	976 (100%)
Used medications for ADHD	Yes	40 (4.1%)
	No	936 (95.9%)
	Total	976 (100%)
Children given COVID-19 vaccine	Yes	159 (16.3%)
	No	817 (83.7%)
	Total	976 (100%)

3.3. Vaccination Status and Chronic Illness

Vaccinated children were more likely to have been diagnosed than unvaccinated children for different chronic conditions, such as allergic rhinitis (9.9% vs. 7.5%, $p = 0.61$; OR 1.4, 95% CI: 0.4, 4.5), allergies (16.3% vs. 10%, $p = 0.28$; OR 1.8, 95% CI: 0.6, 5), and neuro-developmental disorders (0.7% vs. 0%, $p = 0.58$; OR 1.01, 95% CI: 1, 1.01), autism spectrum (1.2% vs. 0%, $p = 0.49$; OR 1.01, 95% CI: 1, 1.02), eczema (13.7% vs. 10%, $p = 0.51$; OR 1.4, 95% CI: 0.5, 4.1), learning disability (2.9% vs. 0%, $p = 0.28$; OR 1.03, 95% CI: 1.02, 1.04), ADHD (2.9% vs. 2.5%, $p = 0.89$; OR 1.2, 95% CI: 0.2, 8.8), and any chronic condition (2.8% vs. 0%, $p = 0.29$; OR 1.03, 95% CI: 1.02, 1.04). On the contrary, unvaccinated children were more likely to be diagnosed with none of these chronic conditions than vaccinated children (80% vs. 65.9%, $p = 0.065$; OR 0.5, 95% CI: 0.2, 1.1) (Table 3). However, no significant differences were observed for all these conditions, including allergic rhinitis, allergies, neuro-developmental disorders, autism spectrum, ADHD, learning disability, eczema, any chronic conditions, and none of the above.

Table 3. Vaccination status and health outcomes, chronic conditions.

Chronic Disease	Vaccinated (n = 936)	Unvaccinated (n = 40)	Chi-square	P-value	Odds Ratio (95% CI)
Allergic Rhinitis					
Yes	93 (9.9%)	3 (7.5%)	0.26	0.61	1.4 (0.4 - 4.5)
No	843 (90.1%)	37 (92.5%)			
Allergies					
Yes	153 (16.3%)	4 (10%)	1.14	0.28	1.8 (0.6 - 5.0)
No	783 (83.7%)	36 (90%)			
Neuro-Developmental Disorder (NDD)					
Yes	7 (0.7%)	0 (0%)	0.3	0.58	1.01 (1.0 - 1.01)
No	929 (99.3%)	40 (100%)			
Autism Spectrum					
Yes	11 (1.2%)	0 (0%)	0.48	0.49	1.01 (1.0 - 1.02)
No	925 (98.8%)	40 (100%)			
Eczema					
Yes	128 (13.7%)	4 (10%)	0.44	0.51	1.4 (0.5 - 4.1)
No	808 (86.3%)	36 (90%)			
Learning Disability					
Yes	27 (2.9%)	0 (0%)	1.19	0.28	1.03 (1.02 - 1.04)
No	909 (97.1%)	40 (100%)			
ADHD					
Yes	27 (2.9%)	1 (2.5%)	0.02	0.89	1.2 (0.2 - 8.8)
No	909 (97.1%)	39 (97.5%)			
Any Chronic Condition					
Yes	26 (2.8%)	0 (0%)	1.14	0.29	1.03 (1.02 - 1.04)
No	910 (97.2%)	40 (100%)			
None of the Above					
Yes	617 (65.9%)	32 (80%)	3.414	0.065	0.5 (0.2 - 1.1)
No	319 (34.1%)	8 (20%)			

Figure 1 compares the percentages of chronic diseases between vaccinated and unvaccinated participants. You can see the slight differences between the two groups in different conditions.

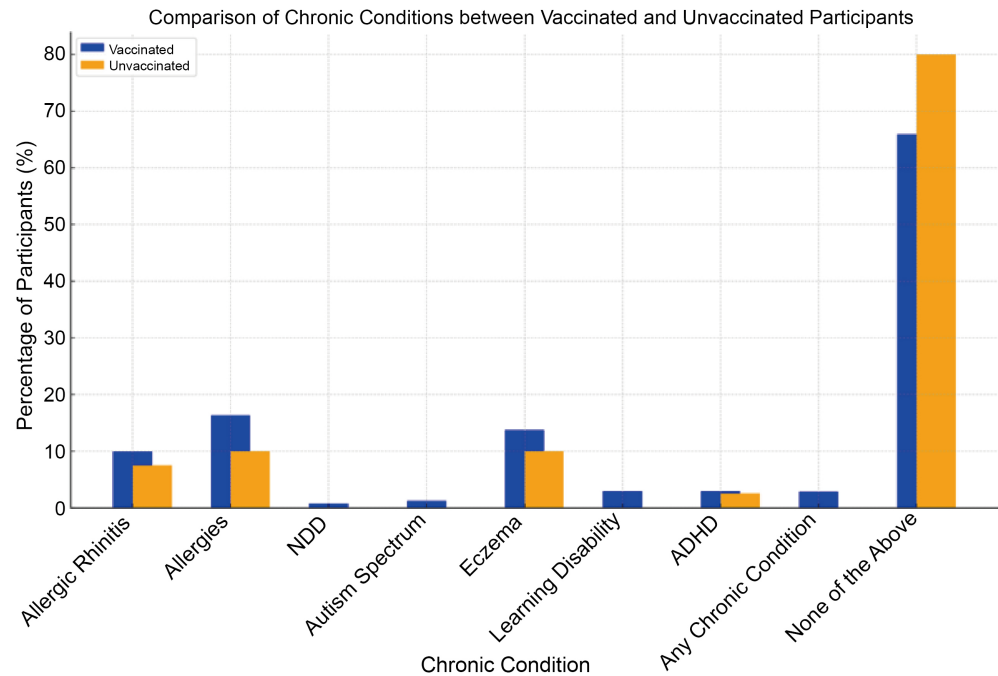


Figure 1. Comparing the percentages of chronic diseases between vaccinated and unvaccinated participants.

3.4. Vaccination Status and Acute Illness

Vaccinated children were more likely to be diagnosed with the acute conditions compared to unvaccinated children, such as whooping cough (1.1% vs. 0%, $p = 0.511$; OR 1.01, 95% CI: 1, 1.02), pneumonia (4.9% vs. 0%, $p = 0.151$; OR 1.1, 95% CI: 1.04, 1.07), rubella (0.8% vs. 0%, $p = 0.557$; OR 1.01, 95% CI: 1.0, 1.01), hepatitis A or B (0.4% vs. 0%, $p = 0.678$; OR 1, 95% CI: 1.0, 1.01), measles (1.3% vs. 0%, $p = 0.471$; OR 1, 95% CI: 1.0, 1.02), mumps (0.8% vs. 0%, $p = 0.557$; OR 1, 95% CI: 1.0, 1.01), meningitis (0.1% vs. 0%, $p = 0.836$; OR 1, 95% CI: 0.99, 1), influenza (28.2% vs. 20%, $p = 0.257$; OR 1.6, 95% CI: 0.7, 3.5), Rota virus (0.8% vs. 0%, $p = 0.583$; OR 1, 95% CI: 1.0, 1.01), cancer (0.2% vs. 0%, $p = 0.77$; OR 1, 95% CI: 0.99, 1.0), chronic fatigue (0.2% vs. 0%, $p = 0.77$; OR 1, 95% CI: 0.99, 1.0), Crohn’s disease (0.1% vs. 0%, $p = 0.836$; OR 1, 95% CI: 0.99, 1.0), inflammatory bowel disease (0.5% vs. 0%, $p = 0.643$; OR 1, 95% CI: 1.0, 1.01), conduct disorder (1.1% vs. 0%, $p = 0.511$; OR 1.01, 95% CI: 1.01, 1.02), diabetes type 1 or 2 (1% vs. 0%, $p = 0.533$; OR 1.01, 95% CI: 1.0, 1.02), Rheumatoid arthritis (0.2% vs. 0%, $p = 0.77$; OR 1, 95% CI: 0.99, 1), obesity (3.4% vs. 0%, $p = 0.234$; OR 1.04, 95% CI: 1.0, 1.04), seizures (0.3% vs. 0%, $p = 0.72$; OR 1, 95% CI: 0.99, 1.01), hearing loss (0.3% vs. 0%, $p = 0.72$; OR 1, 95% CI: 0.99, 1.01), depression (1.3% vs. 0%, $p = 0.471$; OR 1, 95% CI: 1.0, 1.02), polio (0.3% vs. 0%, $p = 0.72$; OR 1, 95% CI: 0.99, 1.01), tetanus (0.1% vs. 0%, $p = 0.72$; OR 1, 95% CI: 0.99, 1.01), and diphtheria (0.1% vs. 0%, $p = 0.72$; OR 1, 95% CI: 0.99, 1.01). On the contrary, unvaccinated children were more likely to be diagnosed with acute conditions than the vaccinated children for chickenpox (20% vs. 14.8%, $p = 0.373$; OR 0.7, 95% CI: 0.3, 1.5), otitis media (5%

vs. 4.7%, $p = 0.93$; OR 0.9, 95% CI: 0.2, 4), encephalopathy (2.5% vs. 0.5%, $p = 0.119$; OR 0.2, 95% CI: 0.02, 1.8), and none of the above (65% vs. 57.9%, $p = 0.373$; OR 0.7, 95% CI: 0.4, 1.4) (Table 4). Although the vaccinated and unvaccinated children showed likely diagnoses for those mentioned above respective acute conditions, they did not provide significant differences since their p -values were above 0.5. Therefore, no significant differences were found between vaccinated and unvaccinated children under acute conditions.

Table 4. Vaccination status and health outcomes, acute conditions.

Acute Disease	Vaccinated (n = 936)	Unvaccinated (n = 40)	Chi-square	P-value	Odds Ratio (95% CI)
Chickenpox					
Yes	139 (14.8%)	8 (20%)	0.795	0.373	0.7 (0.3 - 1.5)
No	797 (85.2%)	32 (80%)			
Whooping Cough (Pertussis)					
Yes	10 (1.1%)	0 (0%)	0.432	0.511	1.01 (1.0 - 1.02)
No	926 (98.9%)	40 (100%)			
Pneumonia					
Yes	46 (4.9%)	0 (0%)	2.063	0.151	1.1 (1.04 - 1.07)
No	890 (95.7%)	40 (100%)			
Rubella					
Yes	8 (0.8%)	0 (0%)	0.345	0.557	1.01 (1.0 - 1.01)
No	928 (99.2%)	40 (100%)			
Otitis Media					
Yes	44 (4.7%)	2 (5%)	0.008	0.93	0.9 (0.2 - 4.0)
No	892 (95.3%)	38 (95%)			
Hepatitis A or B					
Yes	4 (0.4%)	0 (0%)	0.172	0.678	1.0 (1.0 - 1.01)
No	932 (99.6%)	40 (100%)			
Measles					
Yes	12 (1.3%)	0 (0%)	0.519	0.471	1.0 (1.0 - 1.02)
No	924 (98.7%)	40 (100%)			
Mumps					
Yes	8 (0.8%)	0 (0%)	0.345	0.557	1.0 (1.0 - 1.01)
No	928 (99.2%)	40 (100%)			
Meningitis					
Yes	1 (0.1%)	0 (0%)	0.043	0.836	1.0 (0.99 - 1.0)
No	935 (99.9%)	40 (100%)			

Continued

Influenza					
Yes	264 (28.2%)	8 (20%)	1.285	0.257	1.6 (0.7 - 3.5)
No	672 (71.8%)	32 (80%)			
Rota Virus					
Yes	7 (0.8%)	0 (0%)	0.301	0.583	1.0 (1.0 - 1.01)
No	929 (99.2%)	40 (100%)			
Cancer					
Yes	2 (0.2%)	0 (0%)	0.086	0.77	1.0 (0.99 - 1.0)
No	934 (99.8%)	40 (100%)			
Chronic Fatigue					
Yes	2 (0.2%)	0 (0%)	0.086	0.77	1.0 (0.99 - 1.0)
No	934 (99.8%)	40 (100%)			
Crohn's Disease					
Yes	1 (0.1%)	0 (0%)	0.043	0.836	1.0 (0.99 - 1.0)
No	935 (99.9%)	40 (100%)			
Inflammatory Bowel Disease					
Yes	5 (0.5%)	0 (0%)	0.215	0.643	1.0 (1.0 - 1.01)
No	931 (99.5%)	40 (100%)			
Conduct Disorder					
Yes	10 (1.1%)	0 (0%)	0.432	0.511	1.01 (1.0 - 1.02)
No	926 (98.9%)	40 (100%)			
Diabetes Type 1 or 2					
Yes	9 (1%)	0 (0%)	0.388	0.533	1.01 (1.0 - 1.02)
No	927 (99%)	40 (100%)			
Rheumatoid Arthritis					
Yes	2 (0.2%)	0 (0%)	0.086	0.77	1.0 (0.99 - 1.0)
No	934 (99.8%)	40 (100%)			
Obesity					
Yes	32 (3.4%)	0 (0%)	1.414	0.234	1.04 (1.0 - 1.04)
No	904 (96.6%)	40 (100%)			
Seizures					
Yes	3 (0.3%)	0 (0%)	0.129	0.72	1.0 (0.99 - 1.01)
No	933 (99.7%)	40 (100%)			
Hearing Loss					
Yes	3 (0.3%)	0 (0%)	0.129	0.72	1.0 (0.99 - 1.01)
No	933 (99.7%)	40 (100%)			

Continued

Depression					
Yes	12 (1.3%)	0 (0%)	0.519	0.471	1.0 (1.0 - 1.02)
No	924 (98.7%)	40 (100%)			
Encephalopathy					
Yes	5 (0.5%)	1 (2.5%)	2.426	0.119	0.2 (0.02 - 1.8)
No	931 (99.5%)	39 (97.5%)			
Polio					
Yes	3 (0.3%)	0 (0%)	0.129	0.72	1.0 (0.99 - 1.01)
No	933 (99.7%)	40 (100%)			
Tetanus					
Yes	1 (0.1%)	0 (0%)	0.043	0.836	1.0 (0.99 - 1.0)
No	935 (99.9%)	40 (100%)			
Diphtheria					
Yes	1 (0.1%)	0 (0%)	0.043	0.836	1.0 (0.99 - 1.0)
No	935 (99.9%)	40 (100%)			
None of the above					
Yes	542 (57.9%)	26 (65%)	0.794	0.373	0.7 (0.4 - 1.4)
No	394 (42.1%)	14 (35%)			

Figure 2 indicates that there were small differences in the incidence of acute diseases between the two groups, with no statistically significant differences in most cases.

3.5. Partial versus Full Vaccination, Chronic Health Conditions

As shown in **Table 5**, an intermediate position was taken by partially vaccinated children between fully and not vaccinated children for some chronic health outcomes, such as allergic rhinitis, neuro-developmental disorder, autism spectrum, learning disability, and any chronic condition. Thus, the partially vaccinated group had taken an intermediate position in terms of allergic rhinitis, NDD, learning disability (LD), autism spectrum (ASD), and any chronic condition without any significant differences.

The results show allergic Rhinitis incidence was slightly higher among fully vaccinated (10.4%) than among partially vaccinated (8.6%) and unvaccinated (7.5%).

- Allergies incidence was similar between the partially vaccinated (16.7%) and fully vaccinated (16.3%) groups, and was lower among the unvaccinated (10%).
- Neurodevelopmental Disorders (NDD) and Autism Spectrum rates were very low in all groups, with no cases among the unvaccinated.

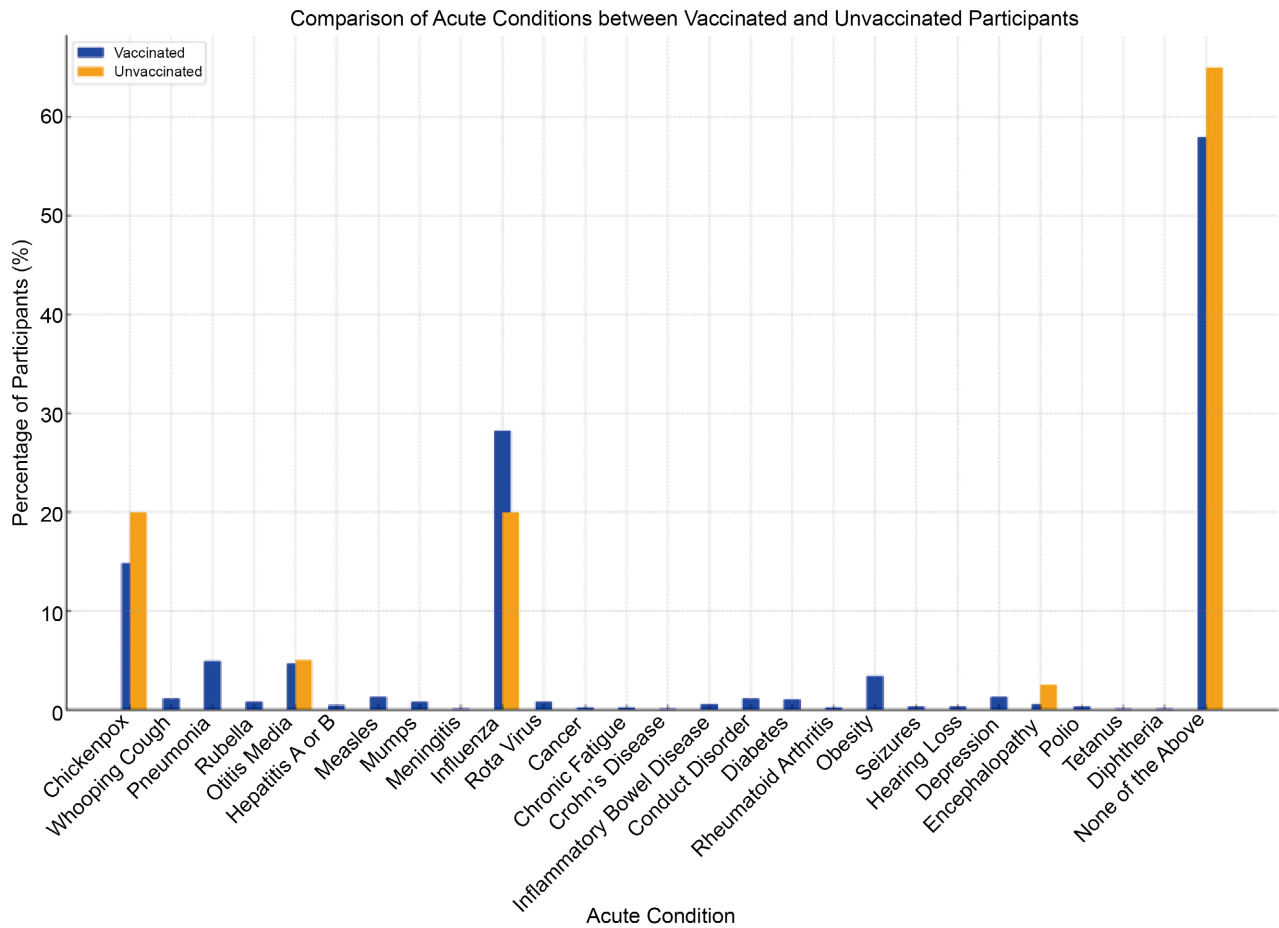


Figure 2. A comparison of different acute cases between vaccinated and unvaccinated participants.

Table 5. Partial versus full vaccination for chronic health conditions.

Chronic Disease	Unvaccinated (n = 40)	Partially Vaccinated (n = 222)	Fully Vaccinated (n = 714)	Total (n = 976)	Chi-square	P-value
Allergic Rhinitis						
Yes	3 (7.5%)	19 (8.6%)	74 (10.4%)	96 (9.8%)	0.879	0.644
No	37 (92.5%)	203 (91.4%)	640 (89.6%)	880 (90.2%)		
Allergies						
Yes	4 (10%)	37 (16.7%)	116 (16.3%)	157 (16.1%)	1.167	0.558
No	36 (90%)	185 (83.3%)	598 (83.7%)	819 (83.9%)		
Neuro-Developmental Disorder (NDD)						
Yes	0 (0%)	3 (1.4%)	4 (0.6%)	7 (0.7%)	1.79	0.409
No	40 (100%)	219 (98.6%)	710 (99.4%)	969 (99.3%)		
Autism Spectrum						
Yes	0 (0%)	2 (0.9%)	9 (1.3%)	11 (1.1%)	0.672	0.715
No	40 (100%)	220 (99.1%)	705 (98.7%)	965 (98.9%)		

Continued

Eczema						
Yes	4 (10%)	34 (15.3%)	94 (13.2%)	132 (13.5%)	1.112	0.573
No	36 (90%)	188 (84.7%)	620 (86.8%)	844 (86.5%)		
Learning Disability						
Yes	0 (0%)	6 (2.7%)	21 (2.9%)	27 (2.8%)	1.223	0.542
No	40 (100%)	216 (97.3%)	693 (97.1%)	949 (97.2%)		
ADHD						
Yes	1 (2.5%)	4 (1.8%)	23 (3.2%)	28 (2.9%)	1.245	0.536
No	39 (97.5%)	218 (98.2%)	691 (96.8%)	948 (97.1%)		
Any Chronic Condition						
Yes	0 (0%)	4 (1.8%)	22 (3.1%)	26 (2.7%)	2.211	0.331
No	40 (100%)	218 (98.2%)	692 (96.9%)	950 (97.3%)		
None of the Above						
Yes	32 (80%)	151 (68%)	466 (65.3%)	649 (66.5%)	3.99	0.136
No	8 (20%)	71 (32%)	248 (34.7%)	327 (33.5%)		

- Eczema incidence rate was highest among partially vaccinated individuals (15.3%), followed by fully vaccinated individuals (13.2%), and then unvaccinated individuals (10%).
- Any Chronic Condition incidence rate was highest among fully vaccinated individuals (3.1%) compared to the other groups.

Overall, **Figure 3** indicates that there are some differences in the rates between the different groups, but most of the differences are not large enough to be statistically significant, as shown in **Table 5** by the p-values.

3.6. Partial versus Full Vaccination, Acute Health Conditions

Similar to chronic conditions, partially vaccinated children had taken an intermediate position between fully and unvaccinated children for some acute health outcomes but not all health outcomes. They included influenza, Rotavirus, inflammatory bowel disease, conduct disorder, diabetes type 1 or 2, obesity, and depression. However, unvaccinated children were significantly more likely to be diagnosed compared to partially and fully vaccinated children for chickenpox (20% vs. 5.9% vs. 17.7%; $p < 0.001$) and encephalopathy (2.5% vs. 1.8% vs. 0.1%; $p < 0.01$). Partially vaccinated children were significantly more likely to be diagnosed than unvaccinated and fully vaccinated children for rheumatoid arthritis (0.9% vs. 0% vs. 0%; $p = 0.033$), and none of the above (67.6% vs. 65% vs. 54.9%; $p < 0.01$). Fully vaccinated children were significantly more likely to be diagnosed compared to partially vaccinated and unvaccinated children with influenza (30.1% vs. 22.1% vs. 20%; $p = 0.035$) (**Table 6**). Therefore, significant differences in acute health

conditions among unvaccinated, partially vaccinated, and fully vaccinated children were found for chickenpox, influenza, rheumatoid arthritis, encephalopathy, and none of the above.

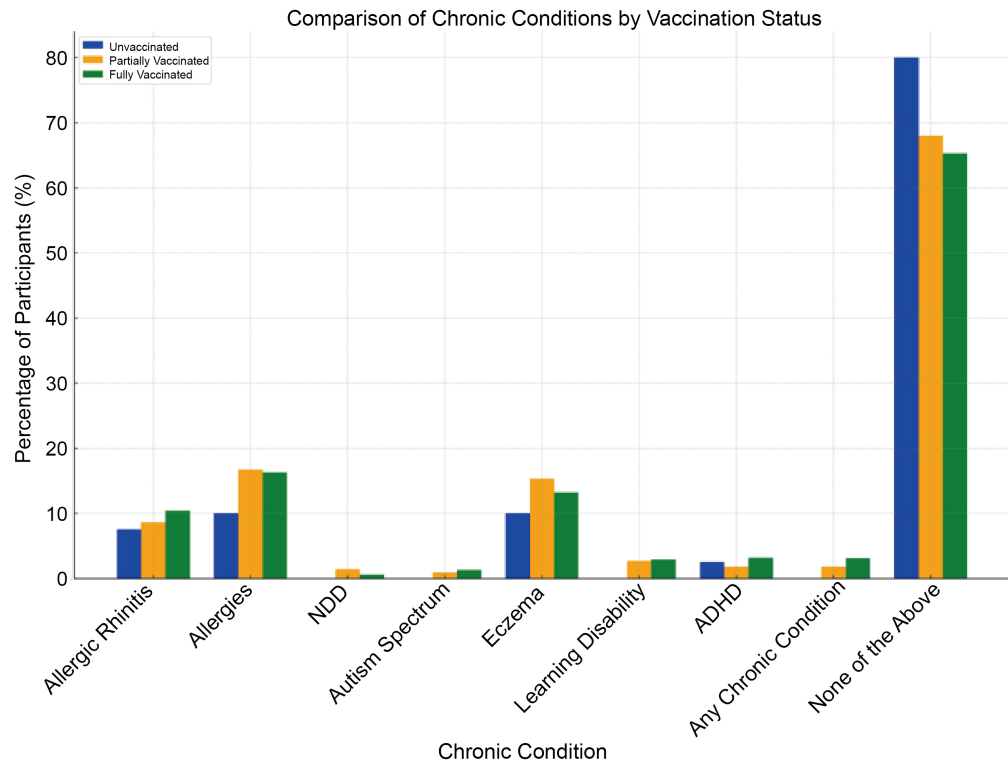


Figure 3. Compares the percentages of chronic health conditions between three groups: unvaccinated, partially vaccinated, and fully vaccinated.

Table 6. Partial versus full vaccination for acute health conditions.

Acute Disease	Unvaccinated (n = 40)	Partially Vaccinated (n = 222)	Fully Vaccinated (n = 714)	Total (n = 976)	Chi-square	P-value
Chickenpox						
Yes	8 (20%)	13 (5.9%)	126 (17.7%)	147 (15.1%)	19.2***	<0.001
No	32 (80%)	209 (94.1%)	588 (82.3%)	829 (84.9%)		
Whooping Cough (Pertussis)						
Yes	0 (0%)	3 (1.3%)	7 (1%)	10 (1%)	0.662	0.718
No	40 (100%)	219 (98.7%)	707 (99%)	966 (99%)		
Pneumonia						
Yes	0 (0%)	12 (5.4%)	34 (4.8%)	46 (4.7%)	2.219	0.33
No	40 (100%)	210 (94.6%)	680 (95.2%)	930 (95.3%)		

Continued

Rubella						
Yes	0 (0%)	3 (1.3%)	5 (0.7%)	8 (0.8%)	1.228	0.541
No	40 (100%)	219 (98.7%)	709 (99.3%)	968 (99.2%)		
Otitis Media						
Yes	2 (5%)	9 (4.1%)	35 (4.9%)	46 (4.7%)	0.279	0.87
No	38 (95%)	213 (95.9%)	679 (95.1%)	930 (95.3%)		
Hepatitis A or B						
Yes	0 (0%)	1 (0.4%)	3 (0.4%)	4 (0.4%)	0.175	0.916
No	40 (100%)	221 (99.6%)	711 (99.6%)	972 (99.6%)		
Measles						
Yes	0 (0%)	6 (2.7%)	6 (0.8%)	12 (1.2%)	5.356	0.069
No	40 (100%)	216 (97.3%)	708 (99.2%)	964 (98.8%)		
Mumps						
Yes	0 (0%)	2 (0.9%)	6 (0.8%)	8 (0.8%)	0.352	0.839
No	40 (100%)	220 (99.1%)	708 (99.2%)	968 (99.2%)		
Meningitis						
Yes	0 (0%)	1 (0.4%)	0 (0%)	1 (0.1%)	3.4	0.183
No	40 (100%)	221 (99.6%)	714 (100%)	975 (99.9%)		
Influenza						
Yes	8 (20%)	49 (22.1%)	215 (30.1%)	272 (27.9%)	6.73*	0.035
No	32 (80%)	173 (77.9%)	499 (69.9%)	704 (72.1%)		
Rota Virus						
Yes	0 (0%)	1 (0.4%)	6 (0.8%)	7 (0.7%)	0.663	0.718
No	40 (100%)	221 (99.6%)	708 (99.2%)	969 (99.3%)		
Cancer						
Yes	0 (0%)	1 (0.4%)	1 (0.1%)	2 (0.2%)	0.884	0.643
No	40 (100%)	221 (99.6%)	713 (99.9%)	974 (99.8%)		
Chronic Fatigue						
Yes	0 (0%)	1 (0.4%)	1 (0.1%)	2 (0.2%)	0.884	0.643
No	40 (100%)	221 (99.6%)	713 (99.9%)	974 (99.8%)		
Crohn's Disease						
Yes	0 (0%)	1 (0.4%)	0 (0%)	1 (0.1%)	3.4	0.183
No	40 (100%)	221 (99.6%)	714 (100%)	975 (99.9%)		
Inflammatory Bowel Disease						
Yes	0 (0%)	1 (0.4%)	4 (0.6%)	5 (0.5%)	0.255	0.88
No	40 (100%)	221 (99.6%)	710 (99.4%)	971 (99.5%)		

Continued

Conduct Disorder						
Yes	0 (0%)	2 (0.9%)	8 (1.1%)	10 (1%)	0.512	0.774
No	40 (100%)	220 (99.1%)	706 (98.9%)	966 (99%)		
Diabetes Type 1 or 2						
Yes	0 (0%)	2 (0.9%)	7 (1%)	9 (0.9%)	0.4	0.819
No	40 (100%)	220 (99.1%)	707 (99%)	967 (99.1%)		
Rheumatoid Arthritis						
Yes	0 (0%)	2 (0.9%)	0 (0%)	2 (0.2%)	6.807*	0.033
No	40 (100%)	220 (99.1%)	714 (100%)	974 (99.8%)		
Obesity						
Yes	0 (0%)	4 (1.8%)	28 (3.9%)	32 (3.3%)	3.813	0.149
No	40 (100%)	218 (98.2%)	686 (96.1%)	944 (96.7%)		
Seizures						
Yes	0 (0%)	2 (0.9%)	1 (0.1%)	3 (0.3%)	3.328	0.189
No	40 (100%)	220 (99.1%)	713 (99.9%)	973 (99.7%)		
Hearing Loss						
Yes	0 (0%)	1 (0.4%)	2 (0.3%)	3 (0.3%)	0.289	0.87
No	40 (100%)	221 (99.6%)	712 (99.7%)	973 (99.7%)		
Depression						
Yes	0 (0%)	2 (0.9%)	10 (1.4%)	12 (1.2%)	0.867	0.648
No	40 (100%)	220 (99.1%)	704 (98.6%)	964 (98.8%)		
Encephalopathy						
Yes	1 (2.5%)	4 (1.8%)	1 (0.1%)	6 (0.6%)	10.08**	<0.01
No	39 (97.5%)	218 (98.2%)	713 (99.9%)	970 (99.4%)		
Polio						
Yes	0 (0%)	1 (0.4%)	2 (0.3%)	3 (0.3%)	0.289	0.87
No	40 (100%)	221 (99.6%)	712 (99.7%)	973 (99.7%)		
Tetanus						
Yes	0 (0%)	1 (0.4%)	0 (0%)	1 (0.1%)	3.4	0.183
No	40 (100%)	221 (99.6%)	714 (100%)	975 (99.9%)		
Diphtheria						
Yes	0 (0%)	1 (0.4%)	0 (0%)	1 (0.1%)	3.4	0.183
No	40 (100%)	221 (99.6%)	714 (100%)	975 (99.9%)		
None of the above						
Yes	26 (65%)	150 (67.6%)	392 (54.9%)	568 (58.2%)	11.96**	<0.01
No	14 (35%)	72 (32.4%)	322 (45.1%)	408 (41.8%)		

***Significant at 0.001 level; **Significant at 0.01 level; *Significant at 0.05 level.

Figure 4 shows differences in some acute cases between different vaccination statuses, and the statistical significance varies between cases.

3.7. Gender Differences in Chronic Illnesses

This study showed that males were more likely to be diagnosed with chronic conditions for allergic rhinitis (11.6% vs. 8.1%, $p = 0.073$; OR 1.5, 95% CI: 1, 2.3), allergies (20% vs. 12.5%, $p < 0.01$; OR 1.7, 95% CI: 1.2, 1.5), autism spectrum (1.5% vs. 0.9%, $p = 0.414$; OR 1.7, 95% CI: 0.5, 5.7), eczema (13.9% vs. 13.4%, $p = 0.816$; OR 1, 95% CI: 0.7, 1.5), and ADHD (3.5% vs. 2.2%, $p = 0.222$; OR 1.6, 95% CI: 0.7, 3.6) among vaccinated children ($n = 936$; combination of both fully and partially vaccinated groups) (Table 7). On the contrary, females were more likely to be diagnosed than males, but not significantly for some chronic conditions, such as NDD (1.1% vs. 0.4%, $p = 0.225$; OR 0.4, 95% CI: 0.1, 1.9), learning disability (3.5% vs. 2.3%, $p = 0.261$; OR 0.6, 95% CI: 0.3, 1.4), any chronic condition (3.5% vs. 2.1%, $p = 0.181$; OR 0.6, 95% CI: 0.3, 1.3), and none of the above (68.6% vs. 63.4%, $p = 0.096$; OR 0.8, 95% CI: 0.6, 1.0) (Table 7). The significant differences between male and female groups for chronic outcomes, specifically in terms of allergies, indicate that males were significantly more likely to be diagnosed with allergic chronic conditions compared to females among vaccinated children.

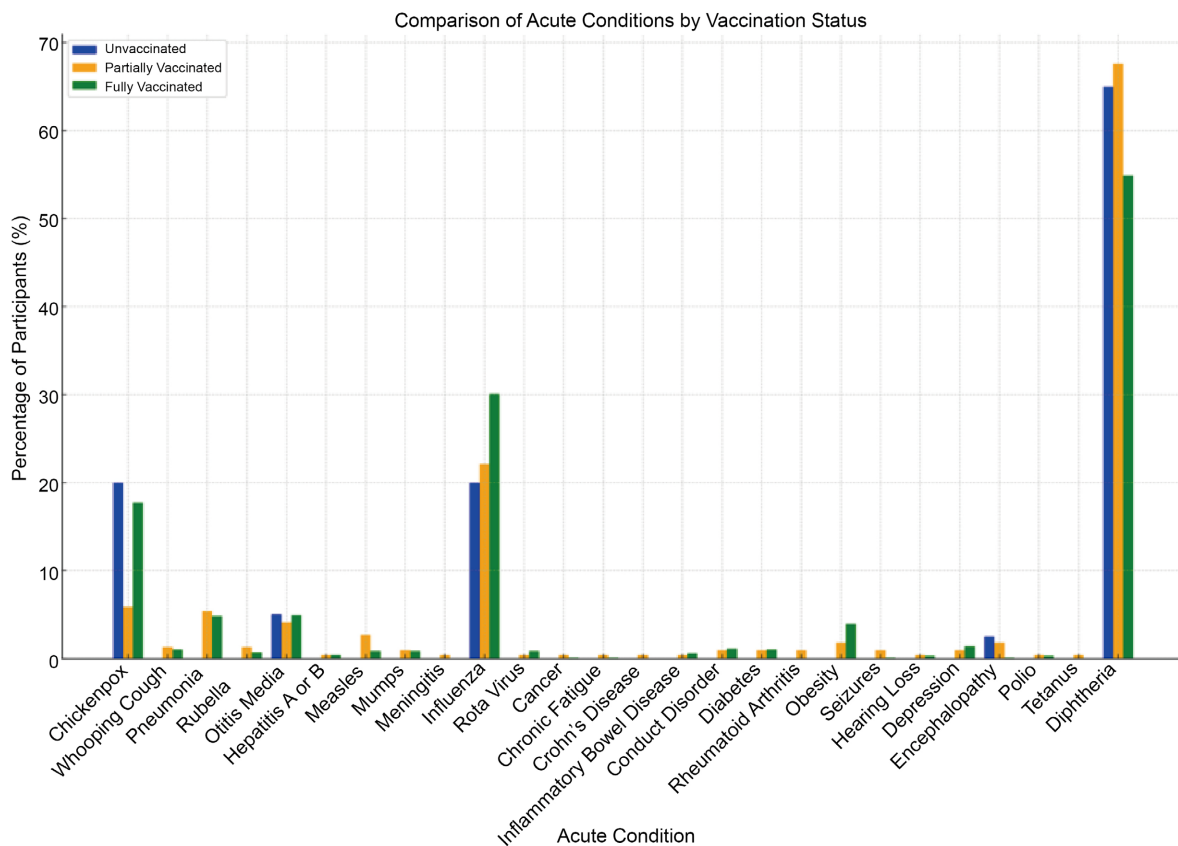


Figure 4. A comparison of the percentages of acute cases among unvaccinated, partially vaccinated, and fully vaccinated participants.

Table 7. Chronic health conditions and gender among vaccinated children.

	Male (n = 481)	Female (n = 455)	Total (n = 936)	Chi-square	P-value	Odds Ratio (95% CI)
Allergic Rhinitis						
Yes	56 (11.6%)	37 (8.1%)	93 (9.9%)	3.22	0.073	1.5 (1.0 - 2.3)
No	425 (88.4%)	418 (91.9%)	843 (90.1%)			
Allergies						
Yes	96 (20%)	57 (12.5%)	153 (16.3%)	9.442**	<0.01	1.7 (1.2 - 2.5)
No	385 (80%)	398 (87.5%)	783 (83.7%)			
Neuro-Developmental Disorder (NDD)						
Yes	2 (0.4%)	5 (1.1%)	7 (0.8%)	1.47	0.225	0.4 (0.1 - 1.9)
No	479 (99.6%)	450 (98.9%)	929 (99.3%)			
Autism Spectrum						
Yes	7 (1.5%)	4 (0.9%)	11 (1.2%)	0.668	0.414	1.7 (0.5 - 5.7)
No	474 (98.5%)	451 (99.1%)	925 (98.8%)			
Eczema						
Yes	67 (13.9%)	61 (13.4%)	128 (13.7%)	0.054	0.816	1.0 (0.7 - 1.5)
No	414 (86.1%)	394 (86.6%)	808 (86.3%)			
Learning Disability						
Yes	11 (2.3%)	16 (3.5%)	27 (2.9%)	1.262	0.261	0.6 (0.3 - 1.4)
No	470 (97.7%)	439 (96.5%)	909 (97.1%)			
ADHD						
Yes	17 (3.5%)	10 (2.2%)	27 (2.9%)	1.491	0.222	1.6 (0.7 - 3.6)
No	464 (96.5%)	445 (97.8%)	909 (97.1%)			
Any Chronic Condition						
Yes	10 (2.1%)	16 (3.5%)	26 (2.8%)	1.789	0.181	0.6 (0.3 - 1.3)
No	471 (97.9%)	439 (96.5%)	910 (97.2%)			
None of the Above						
Yes	305 (63.4%)	312 (68.6%)	617 (65.9%)	2.773	0.096	0.8 (0.6 - 1.0)
No	176 (36.6%)	143 (31.4%)	319 (34.1%)			

**Significant at 0.01 level.

Figure 5 shows there were some differences between males and females in some chronic health conditions, but the differences were not statistically significant in most cases except for allergies.

3.8. Gender Differences in Acute Illnesses

In the vaccinated children (n = 936, combination of both fully and partially vaccinated groups), females were significantly more likely to be diagnosed with acute

illnesses than males, such as whooping cough (1.8% vs. 0.4%, $p = 0.046$; OR 0.2, 95% CI: 0.04, 1.1), hepatitis A or B (0.9% vs. 0%, $p = 0.039$; OR 1, 95% CI: 0.98, 0.99), and inflammatory bowel disease (1.1% vs. 0%, $p = 0.021$; OR 1, 95% CI: 0.98, 0.99). In the opposite, males were significantly more likely to be diagnosed than females with pneumonia (6.4% vs. 3.3%, $p = 0.026$; OR 2, 95% CI: 1.1, 3.8) (Table 8). The remaining acute health conditions, such as chickenpox, rubella, otitis media, measles, mumps, meningitis, rotavirus, influenza, chronic fatigue, cancer, chron's disease, conduct disorder, rheumatoid arthritis, diabetes type 1 or type 2, depression, obesity, hearing loss, seizures, encephalopathy, polio, diphtheria, tetanus, and none of the above were not showed gender differences significantly (Table 8).

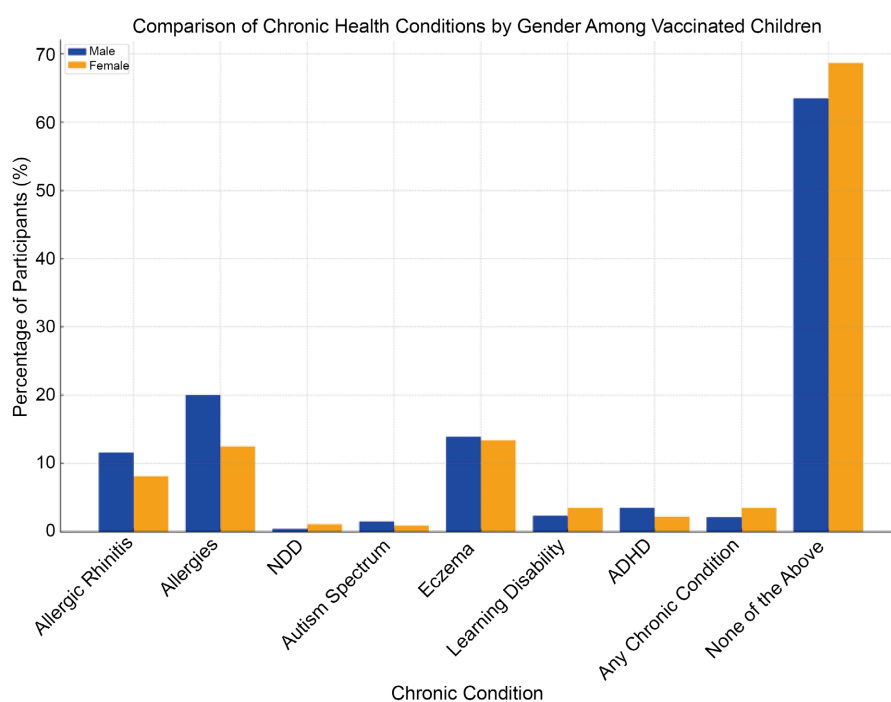


Figure 5. A comparison of the percentages of chronic health conditions among males and females of vaccinated children.

Table 8. Acute health conditions and gender among vaccinated children.

	Male (n = 481)	Female (n = 455)	Total (n = 936)	Chi-square	P-value	Odds Ratio (95% CI)
Chickenpox						
Yes	70 (14.6%)	69 (15.2%)	139 (14.8%)	0.069	0.793	1.0 (0.7 - 1.4)
No	411 (85.4%)	386 (84.8%)	797 (85.2%)			
Whooping Cough (Pertussis)						
Yes	2 (0.4%)	8 (1.8%)	10 (1.2%)	3.987*	0.046	0.2 (0.04 - 1.1)
No	479 (99.6%)	447 (98.2%)	926 (98.8%)			

Continued

Pneumonia						
Yes	31 (6.4%)	15 (3.3%)	46 (4.9%)	4.959*	0.026	2.0 (1.1 - 3.8)
No	450 (93.6%)	440 (96.7%)	890 (95.9%)			
Rubella						
Yes	4 (0.8%)	4 (0.9%)	8 (0.8%)	0.006	0.937	0.9 (0.2 - 3.8)
No	477 (99.2%)	451 (99.1%)	928 (99.2%)			
Otitis Media						
Yes	22 (4.6%)	22 (4.8%)	44 (4.7%)	0.036	0.85	0.9 (0.5 - 1.7)
No	459 (95.4%)	433 (95.2%)	892 (95.3%)			
Hepatitis A or B						
Yes	0 (0%)	4 (0.9%)	4 (0.4%)	4.247*	0.039	1.0 (0.98 - 0.99)
No	481 (100%)	451 (99.1%)	932 (99.6%)			
Measles						
Yes	7 (1.5%)	5 (1.1%)	12 (1.3%)	0.235	0.628	1.3 (0.4 - 4.2)
No	474 (98.5%)	450 (98.9%)	924 (98.7%)			
Mumps						
Yes	3 (0.6%)	5 (1.1%)	8 (0.8%)	0.623	0.43	0.6 (0.1 - 2.4)
No	478 (99.4%)	450 (98.9%)	932 (99.2%)			
Meningitis						
Yes	0 (0%)	1 (0.2%)	1 (0.1%)	1.058	0.304	1.0 (0.99 - 1.0)
No	481 (100%)	454 (99.8%)	935 (99.9%)			
Influenza						
Yes	145 (30.2%)	119 (26.2%)	264 (28.2%)	1.84	0.175	1.2 (0.9 - 1.6)
No	336 (69.8%)	336 (73.8%)	672 (71.8%)			
Rota Virus						
Yes	3 (0.6%)	4 (0.9%)	7 (0.8%)	0.206	0.65	0.7 (0.2 - 3.2)
No	478 (99.4%)	451 (99.1%)	929 (99.2%)			
Cancer						
Yes	0 (0%)	2 (0.4%)	2 (0.2%)	2.119	0.146	1.0 (0.98 - 1.0)
No	481 (100%)	453 (99.6%)	934 (99.8%)			
Chronic Fatigue						
Yes	0 (0%)	2 (0.4%)	2 (0.2%)	2.119	0.146	1.0 (0.98 - 1.0)
No	481 (100%)	453 (99.6%)	934 (99.8%)			
Crohn's Disease						
Yes	0 (0%)	1 (0.2%)	1 (0.1%)	1.058	0.304	1.0 (0.99 - 1.0)
No	481 (100%)	454 (99.8%)	935 (99.9%)			
Inflammatory Bowel Disease						
Yes	0 (0%)	5 (1.1%)	5 (0.5%)	5.314*	0.021	1.0 (0.98 - 0.99)
No	481 (100%)	450 (98.9%)	931 (99.5%)			

Continued

Conduct Disorder						
Yes	6 (1.3%)	4 (0.9%)	10 (1.1%)	0.3	0.584	1.4 (0.4 - 5.1)
No	475 (98.7%)	451 (99.1%)	926 (98.9%)			
Diabetes Type 1 or 2						
Yes	5 (1.0%)	4 (0.9%)	9 (1%)	0.063	0.802	1.2 (0.3 - 4.4)
No	476 (99%)	451 (99.1%)	927 (99%)			
Rheumatoid Arthritis						
Yes	1 (0.2%)	1 (0.2%)	2 (0.2%)	0.002	0.969	0.9 (0.06 - 15.2)
No	480 (99.8%)	454 (99.8%)	934 (99.8%)			
Obesity						
Yes	18 (3.7%)	14 (3.1%)	32 (3.4%)	0.313	0.576	1.2 (0.6 - 2.5)
No	463 (96.3%)	441 (96.9%)	904 (96.6%)			
Seizures						
Yes	0 (0%)	3 (0.7%)	3 (0.3%)	3.182	0.075	1.0 (0.98 - 1.0)
No	481 (100%)	452 (99.3%)	933 (99.7%)			
Hearing Loss						
Yes	1 (0.2%)	2 (0.4%)	3 (0.3%)	0.393	0.531	0.5 (0.04 - 5.2)
No	480 (99.8%)	453 (99.6%)	933 (99.7%)			
Depression						
Yes	5 (1%)	7 (1.5%)	12 (1.3%)	0.46	0.498	0.7 (0.2 - 2.1)
No	476 (99%)	448 (98.5%)	924 (98.7%)			
Encephalopathy						
Yes	2 (0.4%)	3 (0.7%)	5 (0.5%)	0.261	0.609	0.6 (0.1 - 3.8)
No	479 (99.6%)	452 (99.3%)	931 (99.5%)			
Polio						
Yes	2 (0.4%)	1 (0.2%)	3 (0.3%)	0.281	0.596	1.9 (0.2 - 21)
No	479 (99.6%)	454 (99.8%)	933 (99.7%)			
Tetanus						
Yes	0 (0%)	1 (0.2%)	1 (0.1%)	1.058	0.304	1.0 (0.99 - 1.0)
No	481 (100%)	454 (99.8%)	935 (99.9%)			
Diphtheria						
Yes	0 (0%)	1 (0.2%)	1 (0.1%)	1.058	0.304	1.0 (0.99 - 1.0)
No	481 (100%)	454 (99.8%)	935 (99.9%)			
None of the above						
Yes	269 (55.9%)	273 (60%)	542 (57.9%)	1.593	0.207	0.8 (0.7 - 1.1)
No	212 (44.1%)	182 (40%)	394 (42.1%)			

*Significant at 0.05 significance level.

Figure 6 shows that there are some noticeable differences between the sexes in some acute cases, but most cases show similar proportions between males and females.

3.9. Use of Medications, Health Service Applications, and Living Conditions

The vaccinated (n = 936; a combination of both partially and fully vaccinated groups) children were significantly more likely to use medications than unvaccinated (n = 40) for allergies (36.5% vs. 10%, p < 0.001; OR 5.2, 95% CI: 1.8, 14.7), antibiotics (55.2% vs. 27.5%, p < 0.001; OR 3.3, 95% CI: 1.6, 6.6), and fever (85.8% vs. 52.5%, p < 0.001; OR 5.5, 95% CI: 2.9, 10.4) (Table 9). Regarding health service applications, vaccinated children were also significantly more likely to have emergency visits in the past year (43.3% vs. 20%, p < 0.01; OR 3.1, 95% CI: 1.4, 6.7) and sick visits in the past 12 months (65.3% vs. 40%, p < 0.01; OR 2.8, 95% CI: 1.5, 5.4). Vaccinated were more likely to have COVID vaccine than unvaccinated children (16.8% vs. 5%, p = 0.048; OR 3.8, 95% CI: 0.9, 1.6). No significant differences were observed between vaccinated and unvaccinated children regarding their living conditions, including living near electrical substations, electrical towers, communication towers, industrial areas, and waste dump areas (Table 9).

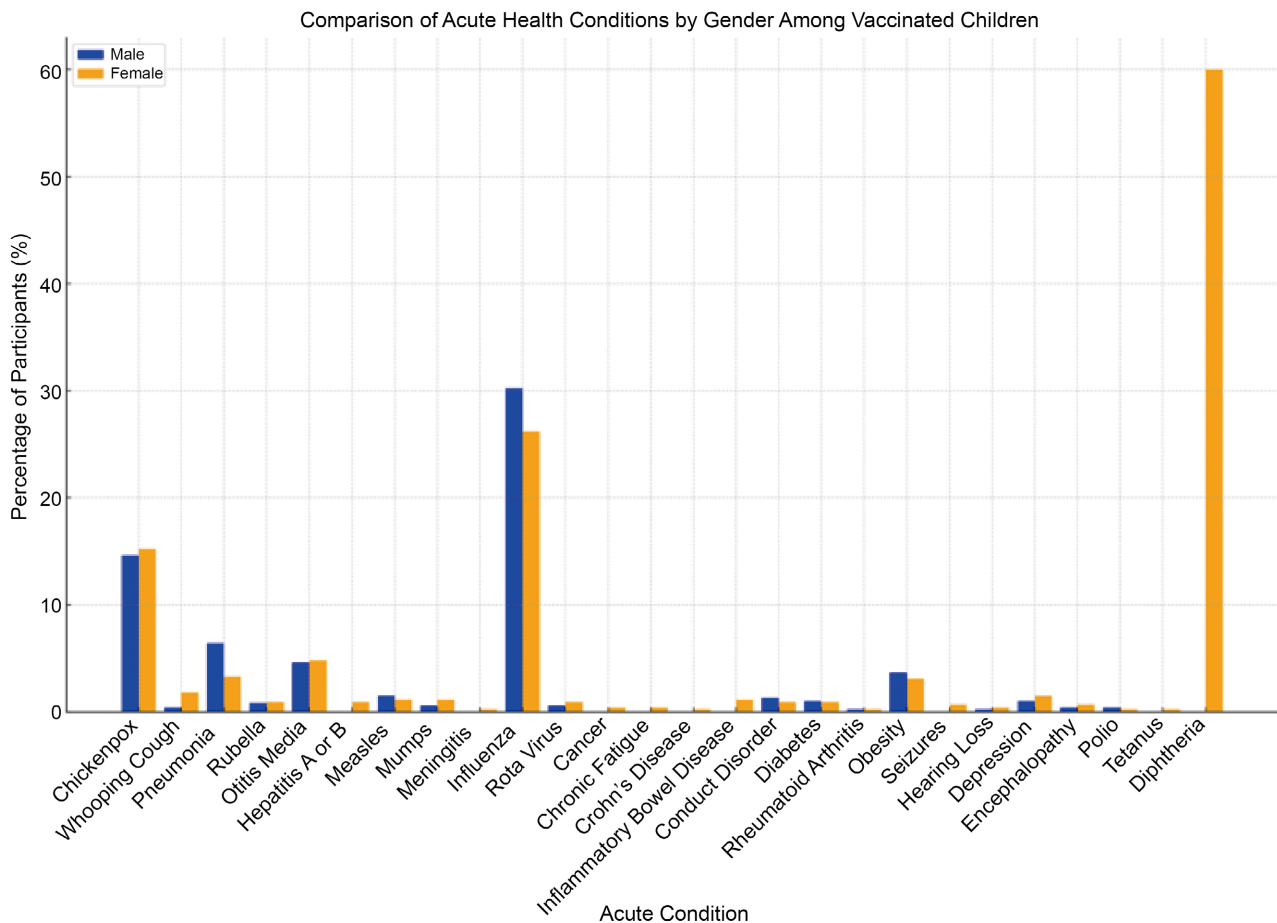


Figure 6. Comparison of acute health conditions among vaccinated male and female children.

Table 9. Vaccination status, use of medications, health service applications, and living conditions.

	Vaccinated (n = 936)	Unvaccinated (n = 40)	Total (n = 976)	Chi-square	P-value	Odds Ratio (95% CI)
Use of Medications						
Medication for Allergies						
Yes	342 (36.5%)	4 (10%)	346 (35.4%)	20.27***	<0.001	5.2 (1.8 - 14.7)
No	594 (63.5%)	36 (90%)	630 (64.6%)			
Antibiotics						
Yes	517 (55.2%)	11 (27.5%)	528 (54.1%)	11.88***	<0.001	3.3 (1.6 - 6.6)
No	419 (44.8%)	29 (72.5%)	448 (45.9%)			
Medication for Fever						
Yes	803 (85.8%)	21 (52.5%)	824 (84.4%)	32.334***	<0.001	5.5 (2.9 - 10.4)
No	133 (14.2%)	19 (47.5%)	152 (15.6%)			
Medication for ADHD						
Yes	38 (4.1%)	2 (5%)	40 (4.1%)	0.086	0.769	0.8 (0.2 - 3.5)
No	898 (95.9%)	38 (95%)	936 (95.9%)			
Health Service Applications						
Emergency visits in the past year						
Yes	405 (43.3%)	8 (20%)	413 (42.3%)	8.509**	<0.01	3.1 (1.4 - 6.7)
No	531 (56.7%)	32 (80%)	563 (57.7%)			
Sick visits in the past year						
Yes	611 (65.3%)	16 (40%)	627 (64.2%)	10.67**	<0.01	2.8 (1.5 - 5.4)
No	325 (34.7%)	24 (60%)	349 (35.8%)			
Hospitalized for one or more nights in the past year						
Yes	147 (15.7%)	3 (7.5%)	150 (15.4%)	1.986	0.159	2.3 (0.7 - 7.6)
No	789 (84.3%)	37 (92.5%)	826 (84.6%)			
Dentist visits in the past year						
Yes	401 (42.8%)	15 (37.5%)	416 (42.6%)	0.448	0.504	1.2 (0.7 - 2.4)
No	535 (57.2%)	25 (62.5%)	560 (57.4%)			
Covid Vaccine & Living Conditions						
Covid vaccine for a child						
Yes	157 (16.8%)	2 (5%)	159 (16.3%)	3.899*	0.048	3.8 (0.9 - 1.6)
No	779 (93.2%)	38 (95%)	817 (83.7%)			

Continued

Living near to communication							
Yes	249 (26.6%)	9 (22.5%)	258 (26.4%)	0.332	0.565	1.2 (0.6 - 2.7)	
No	687 (73.4%)	31 (77.5%)	718 (73.6%)				
Living near to electrical tower							
Yes	140 (15%)	7 (17.5%)	147 (15.1%)	0.194	0.66	0.8 (0.4 - 1.9)	
No	796 (85%)	33 (82.5%)	829 (84.9%)				
Living near to electrical substation							
Yes	384 (41%)	15 (37.5%)	399 (41%)	0.197	0.657	1.2 (0.6 - 2.2)	
No	552 (59%)	25 (62.5%)	577 (59%)				
Living near to industrial areas							
Yes	173 (18.5%)	6 (15%)	179 (18.3%)	0.311	0.577	1.3 (0.5 - 3.1)	
No	763 (81.5%)	34 (85%)	797 (81.7%)				
Living near to waste dump areas							
Yes	73 (7.8%)	3 (7.5%)	76 (7.8%)	0.005	0.945	1.0 (0.3 - 3.5)	
No	863 (92.2%)	37 (92.5%)	900 (92.2%)				

***Significant at 0.001 level; **Significant at 0.01 level; *Significant at 0.05 level.

Figure 7 indicates that there is an association between vaccination status and increased use of medicines and health services.

3.10. Factors Associated with Neurodevelopmental Orders

This study aimed to determine the associated factors of vaccination with neurodevelopmental disorders (NDD) by focusing on a particular health outcome and finding out whether it was associated with measured factors significantly after adjustment analysis. NDD was a combined diagnosis of learning disability (LD), autism spectrum (ASD), and ADHD due to the relatively smaller number of children with particular diagnoses. **Figure 8** shows the overlap and closer association of these diagnoses for NDD. However, the largest diagnoses group was noted for ADHD (n = 19), LD (n = 19), and ASD (n = 8), with smaller numbers for a combination of three diagnoses, such as ADHD and ASD (n = 5). ADHD, ASD, and LD (n = 3), and ADHD and LD (n = 1) (**Figure 1**).

3.11. Unadjusted Analysis

In unadjusted logistic regression analyses, the results depicted that factors associated with neuro-development disorders were age of the child (2 to 5 - OR 0.2, 95% CI: 0.1, 1.1; 6 to 9: OR 8.5, 95% CI: 1.9, 7.3; 10 to 13 - OR 0.1, 95% CI: 0.03,

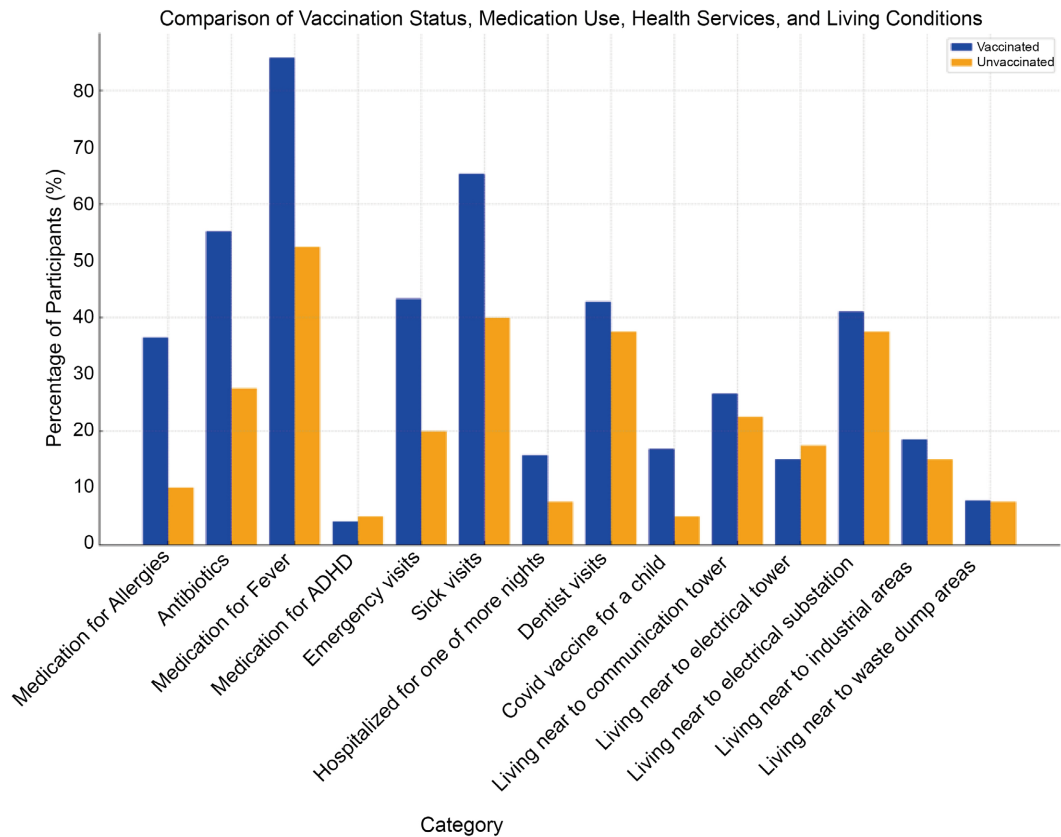


Figure 7. Compares the vaccinated and unvaccinated groups in terms of medication use, health services, and living conditions.

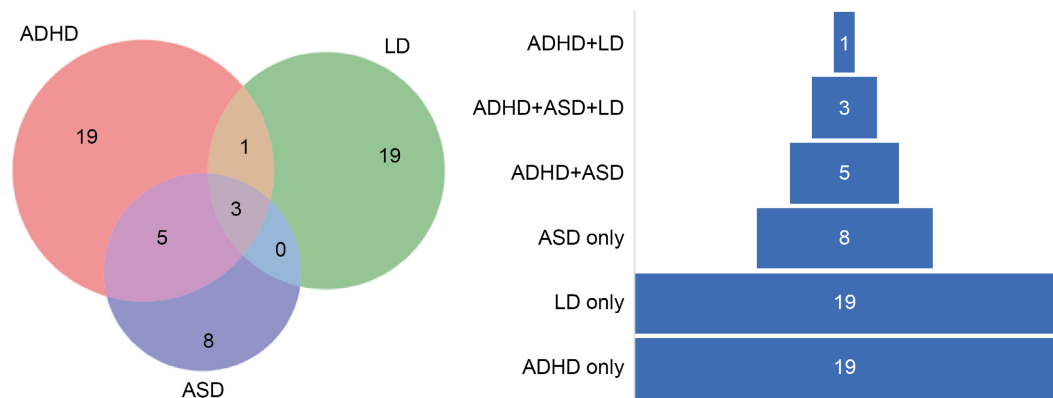


Figure 8. Overlap and distribution of neurodevelopmental disorders.

0.6; 13+– OR 0.2, 95% CI: 0.03, 0.7), birth type (OR 0.5, 95% CI: 0.3, 0.8), and mother suffering during pregnancy (gestational diabetes, OR 2.6 95% CI: 1.3, 5.2; pre-eclampsia, OR 1.2, 95% CI: 0.2, 9.7; others, OR 2.0, 95% CI: 0.9, 4.4) (Table 10). These three factors of age, birth type, and mother suffering during pregnancy were associated with the NDD. This study showed that other factors were not associated with NDD, such as vaccination status (vaccinated and not vaccinated), gender (male and female), and birth time (pre-term and full-term).

Table 10. Unadjusted analysis of risk factors for neurodevelopmental disorders.

	Neuro-Developmental Disorders (NDD)					
	Yes (n = 55)	No (n = 921)	Total (n = 976)	Chi-square	P-value	Odds Ratio (95% CI)
Vaccination Status						
Vaccinated	54	882	936	0.771	0.38	2.4 (0.3 - 17.7)
Not vaccinated	1	39	40			Ref
Gender						
Male	28	472	498	0.002	0.961	1.0 (0.6 - 1.7)
Female	27	449	478			Ref
Child Age						
Less than 2	2	174	176	13.601**	<0.01	Ref
2 - 5	14	302	316			0.2 (0.1 - 1.1)
6 - 9	17	174	191			8.5 (1.9 - 7.3)
10 - 13	12	134	146			0.1 (0.03 - 0.6)
13+	10	137	147			0.2 (0.03 - 0.7)
Birth Type						
Cesarian	26	275	301	7.379**	<0.01	0.5 (0.3 - 0.8)
Natural	29	646	675			Ref
Birth time						
Pre-Term	7	101	108	0.164	0.686	1.2 (0.5 - 2.7)
Full Term	48	820	868			Ref
Mother suffering during pregnancy						
Gestational diabetes	12	97	109	9.2*	0.026	2.6 (1.3 - 5.2)
Preeclampsia	1	17	18			1.2 (0.2 - 9.7)
Others	8	86	94			2.0 (0.9 - 4.4)
None of the above	34	721	755			Ref

**Significant at 0.01 level; *Significant at 0.05 level.

Figure 9 shows that some risk factors, such as the child's age, type of birth, and the mother's health problems during pregnancy may be more closely linked to the risk of neurodevelopmental disorders.

3.12. Adjusted Analysis, Logistic Regression

The significant factors that remained associated with NDD after performing adjustment or logistic regression analysis were age of a child (OR 8.6, 95% CI: 1.9, 38 for 2 to 5 years old; OR 7.9, 95% CI: 1.7, 36.1 for 6 to 9 years old; OR 6.1, 95% CI: 1.3, 28.9 for 10 to 13 years old); birth type (OR 1.8, 95% CI: 1, 3.2 for cesarian); and mother suffering during pregnancy (OR 2.6, 95% CI: 1.3, 5.3 for gestational diabetes) (**Table 11**). The possibility of an interaction between the factors of age,

birth type, mother suffering during pregnancy, and NDD was suggested because of the strong association among them.

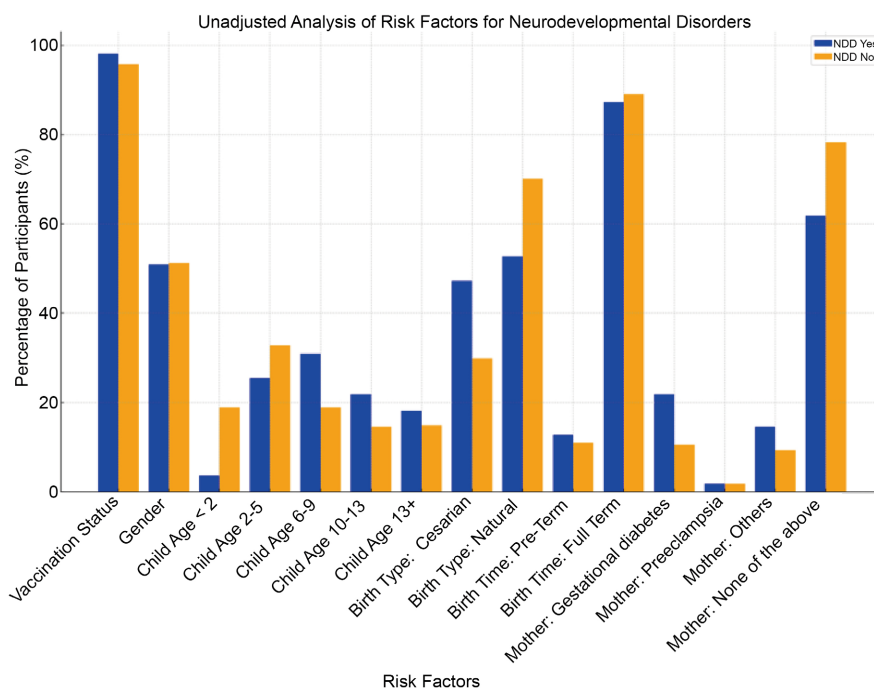


Figure 9. A comparison between the proportion of children with and without neurodevelopmental disorders (NDD) in relation to various risk factors.

Table 11. Adjusted logistic regression analyses of risk factors and neuro-developmental disorders (NDD)*.

	Adjusted Model (Model 1)	Adjusted Model with Interaction (Model 2)
Age of the child (in years)		
2 - 5	8.6 (1.9 - 38)	NS
6 - 9	7.9 (1.7 - 36.1)	5.3 (1.1 - 25.3)
10 - 13	6.1 (1.3 - 28.9)	NS
Less than 2	Ref	Ref
Birth type		
Cesarian	1.8 (1.0 - 3.2)	NS
Natural	Ref	
Mother suffering during pregnancy		
Gestational Diabetes	2.6 (1.3 - 5.3)	2.5 (1.2 - 5.2)
None of the above	Ref	Ref
Age of the child and birth type interaction		
Age of the child and Cesarean	Not in the model	NS
No interaction		

*Number of observations used = 976 (NDD = 55 and Not NDD = 921); NS = Not Significant at 0.05 level.

Further, an adjusted model with interaction was validated for the possibility of remaining association of the factors of mother suffering during pregnancy, age, and birth type. The factors like age (OR 5.3, 95% CI: 1.1, 25.3 for 6 to 9 years old) and mother suffering during pregnancy (OR 2.5, 95% CI: 1.2, 5.2 for gestational diabetes). The birth type was not significantly associated with NDD, whereas the interaction of birth type and age was also not associated with NDD (Table 11).

Figure 10 suggests that child age at onset, type of delivery, and maternal gestational diabetes are factors that may be associated with an increased risk of neurodevelopmental disorders.

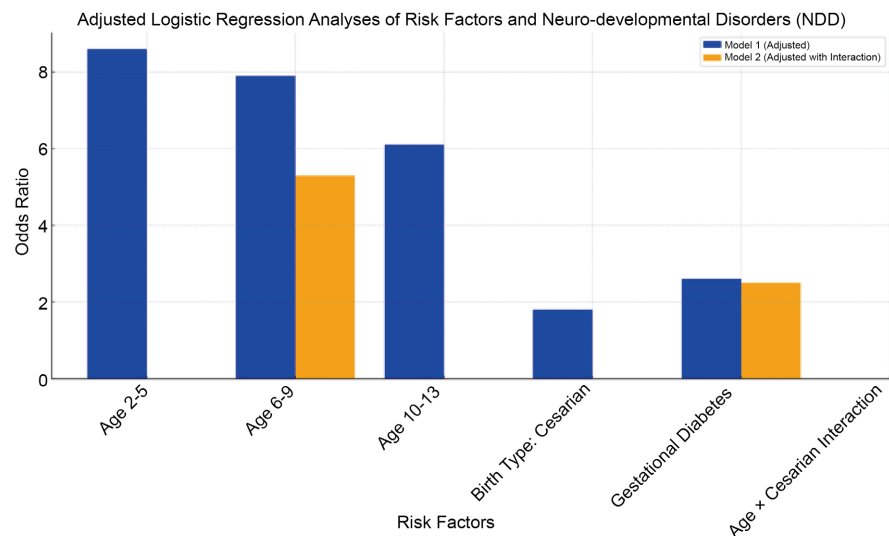


Figure 10. Logistic regression analysis adjusted for risk factors associated with neurodevelopmental disorders (NDD) through two different models.

4. Discussion

This research study presented the discussions on childhood vaccination and its long-term effects on children from birth to thirteen years old based on the comparison of fully vaccinated, unvaccinated, and partially vaccinated status for different health outcomes relevant to acute and chronic conditions. The data findings of this study contributed valuable insights into the effectiveness of childhood vaccination through the analysis of associations with different statuses of vaccination.

4.1. Prevalence of Chronic and Acute Health Conditions in Vaccinated and Unvaccinated Children

This study did not show any significant differences in the prevalence of chronic conditions and some significant differences in acute conditions between unvaccinated and vaccinated children, even though they were more likely to have been diagnosed with vaccination. However, chronic conditions included allergies, allergic rhinitis, NDD, autism spectrum, eczema, learning disability, and any chronic

condition. In alignment with these results, the study by Hooker & Miller [6] reported that chronic conditions like allergies, eczema, and autism spectrum did not result in any significant difference between unvaccinated and vaccinated children. Another study conducted by Straub *et al.* [12] also revealed that there was no potential association between the vaccination status of children and certain chronic health outcomes, such as learning disability and NDD.

In contradictory to the previous research by Di Pietrantonj *et al.* [13], this study found that no prevalence rates of acute infections were exhibited between vaccinated and unvaccinated children included whooping cough (pertussis), pneumonia, rubella, otitis media, hepatitis A or B, measles, mumps, meningitis, influenza, rotavirus, chronic fatigue, cancer, inflammatory bowel disease, Crohn's disease, diabetes type 1 or 2, conduct disorder, obesity, seizures, polio, depression, hearing loss, tetanus, and diphtheria, while the influenza increased with vaccination, chickenpox and encephalopathy increased in unvaccinated, and rheumatoid arthritis increased in partially vaccinated all with significant differences. This is inconsistent with the findings of a study by Yoon & Shin [14], which disclosed that vaccinated children exhibited reduced prevalence rates than unvaccinated children for acute conditions, such as whooping cough, mumps, and measles. Another study by Chung *et al.* [15] also depicted that vaccines could reduce the incidence of acute conditions like influenza among children compared to unvaccinated status.

4.2. Impact of Partial Vaccination on the Incidence of Chronic and Acute Health Outcomes

This study disclosed that partially vaccinated children occupied an intermediate position between unvaccinated and fully vaccinated children for certain chronic health conditions, including allergic rhinitis, autism spectrum, learning disability, neuro-developmental disorders, and any chronic condition. However, the study did not show any significance for partially, fully, and not vaccinated statuses. These findings are not in agreement with the studies that highlighted children with partial vaccination showed a reduced prevalence of chronic conditions than unvaccinated children [16]. This study did not show any importance for partial vaccination as a crucial factor in reducing the incidence of chronic conditions.

The outcomes of this research revealed that partial vaccination played an intermediate role between unvaccinated and fully vaccinated for certain acute illnesses without any significance, such as conduct disorder, depression, obesity, diabetes type 1 or 2, inflammatory bowel disease, rotavirus, and influenza. Similar to these findings, the study by Mawson & Croft [16] discussed that acute illnesses like inflammatory bowel disease and depression could be diagnosed with partial vaccination than the unvaccinated, not as low as full vaccination. On the other hand, the incidence of rheumatoid arthritis was increased with partial vaccination than with fully vaccinated and unvaccinated children. Consistent with these

results, the research by Safary *et al.* [17] is evident that acute conditions like rheumatoid arthritis could be diagnosed with partial vaccination rather than unvaccinated status. Fully vaccinated children showed an increased prevalence of acute conditions of influenza than the partially and not vaccinated children in this study.

4.3. Gender Differences for Effectiveness of Vaccination

This study proved that males showed a significantly higher prevalence of chronic conditions than females in terms of allergies among vaccinated children. Similarly, Liu & Liu [18] resulted in an increased rate of diagnosis for males compared to females regarding chronic conditions of allergies and allergic rhinitis for vaccinated children. On the other hand, males with vaccination were likely to be diagnosed with acute conditions like pneumonia compared to females with vaccination in this study. In addition, females showed a significant increase in acute illnesses with vaccination than males, including inflammatory bowel disease, hepatitis A or B, and whooping cough. Similarly, the study by Ford *et al.* [19], showed a reduced incidence of inflammatory bowel disease for males than females with vaccination status.

4.4. Effects of Childhood Vaccination on Use of Medications, Health Service Applications, and Living Conditions

This study demonstrated that children who had been vaccinated were much more interested in using medications for allergies, fever, and antibiotics than unvaccinated children. They were also likely to have had sick visits and emergency visits in the past year while interested in having the COVID-19 vaccine. In support of this, Chapman *et al.* [20] indicated that the children with vaccination were more likely to use the medications for antibiotics and allergies in addition to the sick visits. Moreover, this study did not show any impact of vaccination because of the living conditions of children, such as living nearer to industrial areas, electrical substations, waste dump areas, and communication and electric towers.

4.5. Association between Vaccination and Neurodevelopmental Disorders (NDD)

One of the aims of this study was to determine the potential association between the vaccination of children and the development of NDD, including autism spectrum, even after using the controlled measurement factors. The factors of age with 2 to 5, 6 to 9, and 10 to 13 years old, cesarian birth type, and mother suffering from gestational diabetes during pregnancy remained associated with NDD significantly after adjustment. In the final adjusted model with interaction (birth type and age), the age of 6 to 9 years old and mothers suffering from gestational diabetes during pregnancy remained associated with NDD.

This study highlighted a possible link between gestational diabetes and an increased risk of neurodevelopmental disorders in children. This is a significant

finding, as it mirrors the results of several key studies in the field. Xiang *et al.* [21] found that children born to mothers with gestational diabetes had a significantly higher risk of developing autism spectrum disorder (ASD). Similarly, Krakowiak *et al.* [22] observed a higher incidence of autism and other NDDs among children whose mothers had metabolic conditions such as gestational diabetes. Also, Perea *et al.* [23] investigated the effects of gestational diabetes and found that prenatal exposure to GDM increases the risk of ADHD in offspring, regardless of treatment complexity.

This study found a potential association between caesarean section (C-section) birth and an increased risk of neurodevelopmental disorders (NDD), including autism and ADHD. While this relationship was not statistically significant in some cases, it is consistent with emerging evidence suggesting that mode of delivery can influence a child's long-term neurodevelopmental health. Several studies support these findings.

Tianyang and others [24], in their systematic review and meta-analysis of 61 studies comprising more than 20 million deliveries, found that birth by cesarean delivery was significantly associated with autism spectrum disorder and attention-deficit/hyperactivity disorder.

Curran *et al.* [25] conducted a systematic review and meta-analysis, concluding that children born by C-section were at an elevated risk of both autism and ADHD.

However, cesarian birth type was no longer associated with NDD, while cesarian birth type combined with age was also not associated with NDD in contrast to the study findings of Zhang *et al.* [26].

In summary, age (2 to 5, 6 to 9, 10 to 13, and 13+), cesarian birth type, and mother suffering from gestational diabetes, pre-eclampsia, and others during pregnancy were significantly associated with NDD. Although cesarian birth was significantly associated with ND for unadjusted analysis, it was not strongly associated with NDD in the final adjusted model. In the interaction model, the ages of 6 to 9 years old and the mother suffering from gestational diabetes during pregnancy were strongly associated with NDD. This evidence-based study suggests that the age of 6 to 9 years old and the suffering of the mother from gestational diabetes would play contributing roles in the reduced prevalence of NDD (ADHD, ASD, and learning disability).

The simultaneous examination of these two risk factors—type of birth and maternal health conditions—provides valuable insight in this study. Few studies have explored how these factors interact or compound, but these results suggest that both factors could independently or jointly influence the risk of neurodevelopmental disorders in children. This complexity points to the need for more nuanced research, particularly studies that consider the cumulative effects of birth method and maternal health conditions.

4.6. Potential Limitations

One of the major limitations of the study is the sample size and socio-demographics.

The small sample size may not represent the whole Kuwaiti population. To improve the generalizability of data findings for Kuwait, it would be essential to increase the sample size and consider the diverse population, including children from different socio-economic backgrounds and regions across Kuwait. Another limitation is the self-reported data from mothers that would be prone to the possibility of recall bias because the participants may not report correct details about their children's health issues and vaccination history. This study may affect the accuracy of data due to the misrepresentation of health effects and vaccination status by participants.

This study demonstrated the association between factors like socio-demographics and health conditions but did not fully account for other measured variables. These include genetic factors or healthcare access, which influence the associations between health outcomes and vaccination status. In the future, this study should consider the potential measurement factors with a comprehensive set to improve the data validity and accuracy of study findings.

This study lacks detailed information about the type of vaccines, vaccination times, and deviations from vaccination schedules. However, it included the categorization of vaccination into unvaccinated, fully, and partially vaccinated groups. Future research will assist in overcoming this limitation and provide an analysis of the effects of vaccination schedules and specific vaccines on health outcomes, including chronic and acute illnesses.

5. Conclusion

The study aimed to provide long-term effects of vaccination among children from birth to 13 years old. However, it determined the associations between vaccination status and health outcomes, including chronic and acute conditions, by comparing unvaccinated, partially vaccinated, and fully vaccinated children. The results revealed that reduced odds of acute conditions like influenza and rheumatoid arthritis were found among fully vaccinated children and partially vaccinated children, respectively. Moreover, males exhibited reduced prevalence rates of allergies and pneumonia. In contrast, females were more likely to be diagnosed with inflammatory bowel disease, hepatitis A or B, and whooping cough among vaccinated children. On the other hand, this study showed that children with age between 6 to 9 years old and mothers suffering from gestational diabetes during pregnancy remained strongly and significantly associated with NDD, whereas the cesarian birth type was not associated with NDD after the interaction of age and birth type. Additional research is required to determine the data findings with causal interpretation and larger samples while understanding the association of potential factors with the vaccination schedule. Such types of studies should be considered in the future to optimize the long-term effects of vaccination on health outcomes of children from birth to 13 years old in Kuwait.

There is a need for a potential measure to spread the knowledge of vaccination. The evidence-based knowledge of vaccination needs to be transparency, using

Open Data Access to make vaccine research and safety data publicly available, ensuring that people can verify claims about vaccine efficacy and side effects; also organize Public Discussions, Q&A sessions and open forums where individuals can ask experts about their concerns regarding vaccines; and provide seminars and workshops that give parents and educators accurate information about the benefits and risks of vaccination.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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