**

 MSc. Global Public Health and Policy

**The association between gender inequality and vaccine coverage:**

**An analysis of national level quantitative data**

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**LIST OF ABBREVIATIONS**

DPT3 Diphtheria-tetanus-pertussis vaccine, 3 doses

GDP Gross domestic product

GII Gender inequality index

HDI Human development index

HepB3 Hepatitis B Vaccine, 3 doses

Hib3 Haemophilus influenzae type b, 3 doses

HIC High income countries

LMIC Low-income and middle-income countries

PCV1 Pneumococcal conjugate vaccine, 3 doses

Rota-C Rotavirus vaccine

SCI Service capacity and access index

UHC Universal Health Coverage

UN United Nations

WHO World Health Organization

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**Abstract**

**Introduction and background**

Vaccines are one of the most effective interventions to prevent infectious diseases: they have eradicated or vastly reduced some communicable diseases, such as smallpox and polio and have been reported to save 2-3 million lives a year. However, the implementation of vaccines is still sub-optimal, despite many studies and policymakers continuously urging the necessity of vaccines. Focusing on people’s attitudes towards vaccines, researchers have recently specifically identified the issues of trust in vaccines and vaccine hesitancy as important global health issues. However, various other factors have been identified as driving low vaccine uptake. This study focuses on the relationship between gender inequality and vaccine coverage, since it has been already demonstrated that gender inequality issues strongly influence public health. The aim of this study is to analyse the association between gender inequality and vaccine coverage on a global scale using national-level data.

**Methods**

This study is an ecological study that uses secondary data. The vaccine coverage of DPT3, Hib3, MCV1, PCV3, RotaC, and HepB3 for 195 countries were retrieved from the WHO database. Gender inequality was assessed with the gender inequality index (GII), which can be obtained from the UN database. As independent variables, GDP per capita, service capacity and access index (SCI) of universal health coverage (UHC), and fertility rate were identified and included in this analysis. Univariate and multivariable linear regression models and a polynomial regression model were used to analyse the data.

**Results**

A total of 195 countries were included in this analysis and coverage of DPT3, Hib3, MCV1 and HepB3 were used in the statistical analysis. GII and DPT3 and Hib3 coverage showed significantly strong negative associations (DPT3: coefficient= -12.05(98% CI -21.48 to -2.62), p=0.013, Hib3: coefficient= -11.64(95% CI -21.53 to -1.75), p=0.021) with adjusted models. On the other hand, vaccine coverage for MCV1 and HepB3 did not exhibit any statistically significant association. However, when the models included only low-income countries (LICs) and low and middle-income countries (LMICs), MCV1 and HepB3 coverage also showed a statistically strong negative association, after adjusting for variables.

**Conclusion**

This study revealed that gender inequality negatively influences DPT3 and Hib3 vaccine coverage worldwide, and HepB3 and MCV1 vaccines in LICs or both LICs and LMICs. This is the first study to investigate the association between gender inequality and vaccine coverage for each kind of vaccine. The ecological study possesses some limitations, but this first worldwide scale study might be useful for tackling some parts of unchangeable vaccine coverage. It could be mention that improving gender inequality is an effective strategy to globally increase vaccine coverages. In the future, further investigation, such as qualitative research would be needed to devise effective strategies to improve vaccine coverage around the world.

(450 words)

**Chapter 1: Introduction**

* 1. **Importance of vaccines and current outbreaks of vaccine-preventable diseases**

　The unprecedented COVID-19 pandemic has highlighted the critical importance of vaccines in preventing the outbreak of serious diseases as well as the importance of high vaccine coverage to effectively assure herd immunity. Vaccines have proven themselves to be one of the most cost-effective methods to prevent and eradicate particular communicable diseases, maintain people’s healthy lives, and enhance herd immunity. The World Health Organization (WHO) estimated that vaccines save 2-3 million lives every year and has emphasised that if vaccination coverage were improved, an additional 1.5 million deaths could be avoided. Moreover, the number of children suffering from the complications of communicable diseases could decrease (1, 2). Although health policy-makers have endeavoured to attain herd immunity and prevent a disease from spreading across the entire population, including among people who cannot be vaccinated for medical reasons (1), global vaccination coverage of measles remains at 85%, which is an insufficient number to prevent measles outbreaks, with no significant change being detected over the past few years. Today, many children worldwide still do not receive essential childhood vaccines(3). In addition, insufficient vaccination coverage and a lack of herd immunity has often led to epidemics and outbreaks of preventable communicable diseases; a matter of concern all over the world(4). Measles outbreaks are a good example of this: recently, measles outbreaks have occurred in many countries and the explosive increase of the prevalence of measles from infants to the elderly has threatened people’s lives due to insufficient measles vaccination. Nevertheless, the prevalence of measles has declined greatly since the 1960s when the vaccine was introduced and several countries have declared the eradication of measles (4). But measles is a canary in the coalmine, because it is extremely infectious. For instance, the number of confirmed measles cases in Europe has been increasing, from approximately 5000 cases in 2016 to 24,000 in 2017, 84,000 in 2018 and 90,000 in the first 6 months of 2019. The WHO declared the UK no longer measles free in 2019(5) (6). Moreover, according to the CDC (Centers for Disease Control and Prevention), the USA had the biggest measles outbreak in 2019, with the highest levels seen in more than 25 years(7). As these examples show, insufficient vaccine coverage easily leads to outbreaks of communicable diseases and even pandemics.

* 1. **The trend of current vaccine studies**

One reason increasing the vaccination coverage from the current stable rate is extremely difficult is because countries and populations have different political, cultural, and religious perspectives, socio-economic statuses, and education levels. According to the Wellcome Trust, lack of confidence in the safety or effectiveness of vaccines, shortages of health workers and supplies, overcapacity or destroyed health infrastructure, and poverty and accessibility to the health care facilities, all threaten to disrupt the effectiveness of vaccine programmes(8). Particularly, researchers have identified a lack of public confidence in terms of ‘vaccine hesitancy’, as one of the most important factors hindering the maintenance of a high vaccination rate. The WHO defines ‘vaccine hesitancy’ as ‘the delay in acceptance or refusal of vaccines despite the availability of vaccination services', which is currently one of the top ten health threats to the world(9).

**Table 1:** Perceived safety of vaccines by region: Do you agree, disagree, or neither agree nor disagree about vaccines being safe? Percentage of people who answered ‘strongly agree’, ‘somewhat agree’, ‘neither agree nor disagree’, 'somewhat disagree’, ‘strongly disagree’ or ‘no opinion’ (Source: Welcome Global Monitor, 2018.)

In 2015, the Vaccine Confidence Project introduced a Vaccine Confidence Index (VCI) for measuring changes in confidence in vaccines over time. Based on the index, the Wellcome Global Monitor set up the questions to measure public trust in the safety, effectiveness, and importance of vaccines. One question is whether vaccines are safe(8)(table1). Overall, most people worldwide agreed that vaccines are safe. 79% of people 'strongly' or 'somewhat agree' that they are safe, while 7% of them 'strongly' or 'somewhat disagree'. In several high-income regions, the consensus about vaccine safety was lower than the global average. 72% of people in Northern America and 73% in Northern Europe agreed that vaccines are safe, and only 59% in Western Europe, and 50% in Eastern Europe thought vaccines were safe. On the other hand, 95% of people in South Asia and 92% of people in Eastern Africa thought vaccines were safe. The countries with the highest percentages of people agreeing that vaccines are safe were lower-income countries, and higher-income countries had higher vaccine hesitancy.

* 1. **Complexity of vaccine issues and the orientation of this thesis**

One of the most notable countries where the larger number of people disagreed on vaccine safety was France, where 33% of French respondents ‘disagreed’ that vaccines are safe(8). Some researchers posit that low maternal education levels are associated with low vaccine coverage. This argument might correspond to some low or lower-middle-income countries’ situation, however as shown in the case of France, the reduction of vaccine coverages on low vaccine confidence is likely to be associated with greater knowledge and information about vaccines regardless of whether the information is true or not, rather than education levels. From the Wellcome Trust survey results, they concluded that ‘putting out more scientific information, or trying to educate more people, will not be enough to change minds on this issue’(8).

The notable scepticism on vaccine safety in some countries is considered to be the result of low vaccine confidence, which tends to be brought by biased information about vaccine safety. Examples of this are the purported links between the MMR vaccine and autism, the HPV vaccine and walking disorders, and hepatitis B and multiple sclerosis (2). Some researchers argue that fake news and misinformation on social media often greatly influence people’s attitudes for vaccines’ safety and attribute to the reduction of vaccine coverage (10, 11). Kennedy demonstrated that there is a significant positive association between votes for populist parties and anti-vaccine sentiment in Western Europe(12). He concluded that particularly, in high-income countries, a profound distrust in experts amongst disenfranchised and marginalised people drives vaccine hesitancy and political populism(12). Furthermore, Latour advocated that vaccine hesitancy is associated with conflict and criticism between scientists and sociologists, which empowers distrust of science and establishes skepticism about scientific expertise(13). Reducing vaccine hesitancy could never be accomplished using simple approaches because multiple factors such as political power and distrust of experts are intricately intertwined. However, as lower vaccine confidence results in insufficient vaccine coverage and might lead to outbreaks of vaccine-preventable communicable diseases worldwide, researchers have striven to find the keys for the resolution.

Investigating the issues of vaccine hesitancy is an essential approach to take people’s attitudes into account for the improvement of vaccine coverage, especially, in higher-income countries. This concept often conflicts with actual vaccine coverage because children are sometimes vaccinated regardless of their parents or their own vaccine hesitancy. For example, in the USA almost all states’ childcare facilities require vaccines when children are registered at the childcare facilities, thus children are vaccinated to enter the childcare facilities regardless of their parents’ actual attitudes about vaccines (14). Furthermore, in lower-income countries, it is conflict to connect the high percentages of vaccine trust to the low percentages of vaccination coverage because of a lack of finance and administrative capacity, though they believe vaccines are safe(2).

A large number of vaccine studies has been published, however they are insufficient for addressing gaps in coverage and lack worldwide insight on this issue, as most studies focus on specific countries. A deep analysis of vaccine hesitancy is extremely crucial for recent vaccine related-issues, however this lies beyond the scope of this dissertation. In this dissertation, vaccine issues were analysed from the different perspectives of vaccine hesitancy. Factors related with vaccine coverage were investigated worldwide and focused on one factor, the gender inequality index, which includes multiple dimensions, such as woman’s education levels, women’s participation in the labour force, and the number of parliament seats held by women. Further details of this study including rationale and objectives will be explained in the following section.

**Chapter 2: Background of this research**

1. **The identified characteristics related to the decision-making on vaccinations from recent vaccination studies**

 Researchers have identified several characteristics that impact vaccination coverage. Maternal education levels (15), socio-economic status (16, 17), accessibility of healthcare facilities (18), and health care systems (18) were seen as facilitators or impediments of vaccinations. Remarkable inequalities related to these characteristics remain in vaccination coverage amongst countries and even within countries (19). For example, Forshaw et al. showed in their global meta-analysis that the number of children whose mother a received secondary or higher education were 2.3 times more likely to have had full childhood vaccination than children whose mother had no education (15). Nagaoka et al. argued in their ecological study of Japan’s whole population that developing health policies to decrease of income inequality and the increase of social capital would be effective to achieve uniformly high vaccination coverage among children because high income inequality and low social capital indicate low uptake of the measles contained vaccine (MCV) (17). Furthermore, Arsenault et al. demonstrated in The Vaccine Alliance (Gavi) (of 45 countries) that political stability, gender equity, and health care accessibility are important predictors of higher or more equitable levels of diphtheria-tetanus-pertussis (DPT3) vaccination coverage(20). Additionally, they pointed out that vaccination coverage is influenced not only by country-level policies and attitudes about vaccination, but also by individual attitudes (21). Therefore, addressing the social determinants of health on both country and individual levels is needed to improve vaccine coverage, protect children from preventable communicable diseases and reduce health inequalities.

Some researchers have attempted to understand and visualise people’s attitudes and contexts on vaccine, such as vaccine hesitancy, to develop effective vaccination strategies for the improvement of vaccination coverage. For example, people’s confident and hesitancy about vaccinations are varied even though they possess the same level of socio-economic status or education level, or the same sort of national policy (21). Therefore, in order to identify and assess the cause of unimmunised children on individual levels, the vaccine confident index, which is associated with individual’s attitudes on vaccination, is gradually well-known, and inequalities of vaccination coverage related to vaccine hesitancy are being visualised. However the studies that have already been published do not conduct individual-level study (19, 21, 22). Larson et al. argued that the monitoring of vaccine hesitancy is indispensable to the early engagement of the vaccine decision-making processes, the improvement of vaccination coverage and the reduction of health inequalities (23). Larson concluded that offering a single snapshot of a country’s overall achievements and inequalities from different perspectives would be meaningful. Although country-level studies must be indispensable and meaningful, particularly for the new concept, individual-level studies in terms of people’s attitudes on vaccines would also be necessary because it is obviously impossible to generalise individual thoughts as national-level data. If vaccine hesitancy were investigated much more deeply, narrative studies would be crucial.

1. **The identified gaps in the literature on vaccination studies and the rationale for examining these gaps**

 In this manner, many causal factors related to inequalities on vaccination coverage have already demonstrated and are being monitored; however most studies, which analysed the association between these social determinants of vaccination and vaccination coverage, have focused on a specific country, region or low and middle income countries settings within a country. Nevertheless, this issue should be analysed on a global scale because epidemics or pandemics of communicable diseases, such as measles or COVID-19, easily occur in such a globalised world. In addition, a few high-income countries’ vaccination coverage is not sufficient and have even lower coverage percentages despite having established equity health systems and subsidised healthcare(24). Japan is a good example of this because the Japan Pediatric Society alerted that Japan is more than 10 years behind European and North American countries in vaccination policies though Japan has established a high socioeconomic status and equality health accessibility(25). Hence, from these facts, insufficient vaccination coverage needs to be researched with a worldwide vision. Grasping worldwide trends related to social determinants on vaccination would be a clue for increasing vaccination coverage.

 The association between certain social determinants of health, such as education level and socio-economic status, and vaccination coverage have been studied enough in certain regions; however, the relationship between gender inequality and vaccination coverage have not been examined and or monitored at global level. Gender inequality has been reported as a negative influential sociological power on health issues and the most essential source of social and health inequalities around the world (26-28). This is because it influences access to social power and the utilisation of resources, which is associated with various positive and negative health outcomes. Therefore, gender inequality is also supposed to impact vaccination coverage. Merten et al. argued that gender inequality is an entrenched barrier for vaccination and gender inequality needs to be addressed on structural and community levels because women’s low social status have been seen as a barrier to accessing vaccination since children’s caregivers are woman in most cases (26, 29, 30). Moreover, public health issues related to gender inequality are likely to be passed on to the next generation, which could develop into a complicated situation in terms of the strategies available to improve existing public and global health issues (18). In this light, it is necessary to examine and visualise the association of gender inequality and vaccination coverage on a global scale.

1. **The definition of gender inequality and the method for measuring this index**

Currently many studies focus on gender inequality issues in the public health field using the Gender inequality index (GII) which was introduced in the 2010 Human Development Report by the United Nations Development Programme (UNDP). The GII evaluates gender inequalities from the three dimensions of human development: reproductive health, empowerment, and economic status(31). Reproductive health is measured by the maternal mortality rate and adolescent birth rates; empowerment is assessed by the proportion of parliamentary seats held by women and the proportion of males and females of 25 years old and above who received at least some secondary education; and economic status is evaluated by labour market participation and the labour force participation rate of female and male populations aged 15 years old and above. The concept of the GII is combination of different social inequalities’ measurements. Therefore, unveiling and measuring the association of vaccination coverage and gender inequality leads to a comprehensive understanding of the relationship between societal backgrounds and vaccination coverage with country levels.

1. **The research question, aim and objective, and dissertation outline**

 The research question is guided by the literature review and this section will describe the aim and objectives of this dissertation as well as its outline. In previous studies, maternal education levels and vaccination coverage or vaccine hesitancy are positively correlated (15, 23). Income inequality and vaccine coverage also showed the significant relation on certain vaccines (16, 17, 32). Furthermore, it is pointed out that the increase of gender inequality was negatively correlated to the vaccination coverage in only Gavi-supported countries(20). The research question therefore seeks to ask how gender inequality and vaccine coverage are associated on country levels, following a global level framework

To examine this question, the aim of this project is to examine the association between vaccination coverage and gender inequality using national statistics.

The objectives will be reached by the following six steps:

1. Reviewing the literature to identify possible explanations for national level variations in vaccine coverage.
2. Determining what kinds of vaccines are included in the analysis for maximizing statistics power.
3. Identifying with dependent and independent variables.

Building a dataset using publicly available data that includes: vaccine coverage (the dependent variable); GII (the independent variable); and other possible explanatory variables.

Analysing the dataset using descriptive analysis, scatterplots, univariate linear regression, and multivariate linear regression.

1. Considering the policy implications of my findings.

**Chapter 3: Methodology**

1. **Study design**

This chapter describes the ecological study method, which was carried out for the aim and objectives mentioned in the previous chapter. An ecological study is defined as an observational study at the population or group level, rather than on the individual level (33). According to Sedgwick, ecological studies are one of the means for generating hypotheses rather than deriving definitive information about associations between risk factors and health outcomes (34). When focused on the relationship between gender inequality and vaccination coverage, the target population was considered at group levels or some population levels because there have not been any population-based studies on this topic until now, and it is too complex or impossible to focus on the individual levels as quantitative studies in this topic because there are no measurements. In this context, an ecological study is suitable study design for this topic although generally the ecological study’s evidence level is not high, compared to other observational studies, such as cohort studies. According to Levin, the purpose of an ecological study is to monitor population health so that public health strategies may be developed and to analyse the association between population-level exposure to risk factors and disease (22). This study might be somewhat meaningful for the intervention of the increase of vaccination coverage as the first study that focuses on the association between gender inequality and vaccination coverage.

1. **Data collection**
2. **The vaccines included in this study**

 All secondary data related to vaccine coverage and gender inequality at country level, 195 countries, at a specific time point were collected for the ecological study. The data of vaccine coverage of a third dose of diphtheria toxoid, tetanus toxoid and pertussis vaccine (DPT3), Measles-containing vaccine (MCV1), third dose of haemophilus influenzae type B vaccine (Hib3), third dose of pneumococcal conjugate vaccine (PCV3), Rotavirus last dose that 2nd or 3rd administration was depending on schedule (RotaC), and third dose of hepatitis B vaccine (HepB3) in 2017 and 2018 were retrieved from the WHO database as dependent variables (35). However, the data on vaccine coverage of PCV3 only covered 141 countries and that of RotaC only covered 94 countries, hence these two vaccines were excluded from the statistical analysis in order to maximize the number of analysed countries on worldwide analysis. The vaccine coverage of DPT3, MCV1, Hib3, and HepB3 were included as dependent variables and the average vaccine coverage of these vaccines in each country in 2017 and 2018 were calculated using excel and were used for the statistical analysis (Table 1

A).

A)

|  |  |
| --- | --- |
| **The kinds of vaccines** | **The number of observed countries**  |
| DPT3 | 190 |
| MCV1 | 191 |
| Hib3 | 188 |
| HepB3 | 185 |
| PCV3 | 141 |
| Rota-C | 94 |

B)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Predicted variables**  | **The number of observations** | **High value** | **Low value**  | **Mean** | **SD** |
| Gender inequality | 162 | 0.834(Rwanda) | 0.039(Argentina) | 0.350 | 0.190 |
| GDP per capita (US dollars) | 195 | 185741.35 | 271.8 | 16883.1 | 131146.7 |
| Fertility rate | 192 | 7 | 1.1 | 2.729 | 4.17 |
| SCI of UHC for children | 184 | 96 | 15 | 73.59 | 16.24 |

Table 1. The kinds of vaccines, the number of observed countries of vaccine coverage, and predicted variables on the associated with vaccine coverage.

Notes: SCI: Service capacity and access index, UHC: Universal Health Coverage

1. **Gender inequality index for looking at the association between gender inequality and vaccine coverage**

Regarding gender inequality, quantitative data is also available as Gender Inequality Index from the United Nations database. Gender inequality measured GII at the country level. The latest data covered 2018 and 162 countries (31). GII ranges from 0 to 1 and a higher GII represents greater gender inequality and a lower GII represents a gender-unequal society. In this study, analysing these two association, vaccine coverages and the gender inequality which is an independent variable, is the main purpose and this analysis is able to take maternal education level into account, which was also one of independent variables and identified with one of the mediators related to vaccine coverage from Chapter 2, Section 2-1. This is because GII includes the percentage of people who received secondary education by gender. GII is a comprehensive index for gender-related issues, hence, the analysis of the association between DPT3, MCV1, Hib3, and HepB3 coverage, as explained in the previous paragraph and gender inequality index would be sufficient to explain gender-related variables on vaccine issues. When focusing on gender inequality-related issues, the human development index is also somewhat related to the gender inequality index since the gender inequality issue is integral to human development. Nevertheless, these two indices are different from each other(36). Therefore the association between gender inequality and vaccine coverage were analysed in each classification of human development, namely very high human development, high human development, medium human development, and low human development. In addition, this main subject was analysed in each division of GDP per capita, namely high income, upper middle income, low and middle income, and low-income countries, as will be explained in the next paragraph.

1. **Other possible variables that may influence vaccine coverage**

In order to analyse potential confounders related to vaccine coverage and gender inequality, it is necessary to take the socioeconomic dimension into account as was mentioned in Chapter 2, Section 2-1. As a socioeconomic mediator, GDP per capita, fertility rate and service capacity and access index (SCI) of Universal Health Coverage (UHC) were extracted from the data repository of the World Bank and the WHO. The definition of GDP per capita is a country’s economic yearly output divided by its total population. GDP per capita measures the sum of marketed goods and services produced within the country, which is averaged across all people who live within its territory (37). The relationship between better health and better economic performance had already been well established and has been explained in the previous paragraph. Economic status greatly impacts on health status and it also influences vaccination coverage because the public expenditure of health declines along with the decrease of GDP and health structure tends to be fragile in lower GDP countries(38, 39). In addition, Masia argued that considering the relation between economic status and vaccine coverage for better health is essential, since vaccines had been shown to generate significant Return on Investment (ROI) in a cost-benefit framework(39). In this context, analysing the association between vaccine coverage and GDP per capita is inevitable as it is one of the related factors of the main subject. Therefore the relationship between GDP per capita and vaccine coverage was investigated; and in addition, as mentioned above, the association between gender inequality index and vaccine coverage in each division of GDP per capita groups was also analysed.

Another variable is fertility rate. The definition of total fertility rate is that the total number of children that would be born to each woman during their reproductive years and it is obtained by summing the single-year age-specific rates at a given time(40). Danis demonstrated that for increasing vaccine coverage, socioeconomic factors are more important determinants than parental perspectives. This is because incomplete vaccination for age-appropriate immunization status is statistically higher in children who have siblings in the household, who belonged to a minority group, and whose parents are concerned by the long distance they must travel to the vaccination provider. (41).From these factors that related to vaccine coverages of Danis’s research, total number of siblings was taken into one of the potential associated factors on vaccine coverages. However, the worldwide data of the average number of siblings were not obtained; therefore, the fertility rate is substituted for the variable of the average number of siblings although this rate is not exactly the same index as the average number of siblings in each country.

Finally, the variable of SCI of UHC will be explained. The definition of SCI of UHC is based on four components of service coverage among the general and the most vulnerable population: 1) Reproductive, maternal, new-born and child health, 2) Infectious diseases, 3) Non-communicable diseases, and 4) Service capacity and access. The indicator is an index that is reported on a unitless scale of 0 to 100, which accumulates the geometric mean of 14 tracer indicators of health service coverage that are composed of the four service coverage components (42). Figueiredo argued that government health spending, basic sanitation, and the proportion of births attended by skilled health staff significantly is correlated with immunisation coverage across many regions(16). In this context, the variable of SCI of UHC is meaningful for considering Figueiredo’s argument, and it is necessary to take this variable into account as a confounding factor for looking at gender inequality and vaccine coverage.

1. **Statistical analysis**

A quantitative study, in particular an ecological study, was selected as the strategy for the analysis of the association between gender inequality and vaccine coverage. For the data analysis, the mean vaccine coverage for 2017 and 2018 were applied because the vaccine coverage for 2017 and 2018 had some variability in each country. The distribution of all variables were verified and a univariate linear regression analysis between gander inequality index and other mediating factors (GDP per capita, fertility rate, and SCI UHC, and DPT3, MCV1, Hib3, and Hep3 vaccine coverage) was conducted in order to predict what socioeconomic factors influence vaccine coverage on a global scale. Next, multivariable linear regression models were conducted to explore the association between gender inequality and vaccine coverage taking into account all potentially confounding socioeconomic variables. Third, the association between vaccine coverage and gender inequality index for each four groups of human development was analysed using a linear regression model. Lastly, the four divided income status group with country levels based on the World Bank definition were used with polynomial regression to explore the variations of gender inequality and vaccine coverage. The statistical analyses were carried out using Stata Version 14.1 software (StataCorp, Texas, USA). A two-tailed p-value of <0.05 was considered statistically significant.

1. **Limitations of an ecological study**

There are three main limitations to an ecological study. First, it is common knowledge to assume the existence of ecological fallacy (Robinson 1950) (43). The purpose of an ecological study is not to analyse the factors of individual levels, but to investigate large scale comparisons between certain groups of people: for example its usage would be in assessing the health status of countries, hence results cannot be inferred at the individual level (34). Second, it is well known that the ecological study data does not show causality even if a significant correlation between two analysed factors was observed: for instance, it cannot be inferred that the decrease in child wellbeing for a country would have been caused by a rise in income inequality (34). Therefore, it is better to interpret that the *P* value as estimating the probability is only valid under limitations and assumptions. Furthermore, the estimated small *P* value does not stand for any potential impact of bias and confounding factors, which are major threats to the validity of this type of study (43, 44). Third, a problem can arise in observing time trends because it is possible that the value of many factors varies with a certain measured time, which results in the spurious correlations (43). It means the results of the association between two factors can be statistically changed during a certain time period. Ecological studies possess a large number of limitations in this manner, however, ecological study is helpful for generating hypotheses for a short timeframe because existing data sets can be used. Additionally, the strong points of this type of quantitative study include the large number of groups of people and the large number of the predicting association factors that can be analysed(45). In order to finalise the thesis, only quantitative research was conducted due to time span, though qualitative research is crucial to address entangled issues. Therefore, further investigation, such as qualitative research, is needed to strengthen this study.

**Chapter 4: Results and findings**

1. **Worldwide vaccine coverage**

 A total of 195 countries were included in this analysis. Overall, more than 90 vaccine coverage percentages were observed in most of high and middle-income countries, although some variations were identified. On the other hand, low and lower middle-income countries tended to have lower vaccine coverage than high and middle-income countries and the variations of vaccine coverage were large (Table 2). The highest means for vaccine coverage were observed in high-income countries, the percentages were 95.33% for DPT3, 94.85% for MCV1, 94.84% for Hib3, and 92.0% for HepB3. On the contrary, the lowest means for vaccine coverage were seen in low and lower-middle-income countries, the percentage were 88.18% for DPT3 and 88.04% for MCV1 in lower-middle-income countries, and 88.29% for Hib3 and 87.45% for HepB3 in low-income countries. Regarding DPT3 and Hib3 vaccine coverage, the lowest coverages were observed in lower-middle-income countries and those coverages in low-income countries were slightly higher than in lower-middle-income countries (Table 2). Regarding HepB3 vaccine coverage, it was lower than the other three vaccine coverages in high-income countries (Table 2).

The ranges of the mean vaccine coverages in 2017 and 2018 across the 195 countries were 47% to 99% for the DPT3 vaccine, 46% to 99% for the MCV1 vaccine, 47% to 99% for the Hib3 vaccine, and 47% to 99% for the Hepbe3 vaccine respectively (Table 3). The mean vaccine coverages and the standard deviation in 195 countries was 91.78% and 7.344 for the DPT3 vaccine, 90.7% and 8.17 for the MCV1 vaccine, 91.55% and 35.70 for the Hib3 vaccine, and 88.73% and 5.26 for the HepB3 vaccine (Table 3). In high-income countries, most of vaccine coverage reached more than 90%, but for the HepB3 vaccine, a low vaccine coverage, 69%, in Switzerland and 71.5% in Canada was identified, which is the lowest and second lowest value in high-income countries’ vaccine coverage.

When focusing on the lowest and second lowest vaccine coverage worldwide, those percentages are 47% and 54% for the DPT3 in Equatorial Guinea and South Sudan respectively, 46% and 60% for the MCV1 in Equatorial Guinea and The former Yugoslav Republic of Macedonia respectively, 47% and 48.5% for the Hib3 in Equatorial Guinea and Ukraine, and 47% and 54% for the HepB3 in Equatorial Guinea and Dominica respectively. These countries are not Gavi-supported countries and Gavi-supported countries were not included in the lowest vaccine coverages. Equatorial Guinea was identified the lowest vaccine coverage countries for these four vaccines.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  coveragevaccines | High income  | Upper middle income | Lower middle income | Low income  |
| DPT3 | 95.33 | 93.25 | 88.18 | 88.46 |
| MCV1 | 94.85 | 92.26 | 88.04 | 84.55 |
| Hib3 | 94.84 | 93.05 | 87.88 | 88.29 |
| HepB3 | 92.00 | 91.88 | 88.38 | 87.45 |

Table2. The mean vaccine coverage (%) divided by income groups.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Vaccines | High value (%) | Low value (%) | Mean (%) | SD |
| DPT3 | 99 | 47 | 91.78 | 7.344 |
| MCV1 | 99 | 46 | 90.70 | 8.17 |
| Hib3 | 99 | 47 | 91.55 | 35.70 |
| HepB3 | 99 | 47 | 88.73 | 5.26 |

Table3. High and low vaccine coverages worldwide at country levels.

Table4: The results of a univariate linear regression of the variables and vaccine coverage

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Gender Inequality | GDP per capita | Fertility rate |  SCI of UHC |
| DPT3 | N=157 | N=187 | N=185 | N=177 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -14.25(-19.78 to -8.727) | <0.001\* | 0.79^10\*-4(0.39^10\*-4 to 1.19^10\*-4) | <0.001\* | -2.00(-2.77 to -1.23) | <0.001\* | 0.199(0.137 to 0.261) | <0.001\* |
| MCV1 | N=159 | N=189 | N=187 | N=179 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -16.25(-22.0 to -10.49) | <0.001\* | 0.756^10\*-4(0.312^10\*-4 to 1.2^10\*-4) | 0.001\* | -2.92(-3.72 to -2.11) | <0.001\* | 0.254(0.189 to 0.320) | <0.001\* |
| Hib3 | N=158 | N=187 | N=186 | N=178 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -13.529(-19.33 to -7.72) | <0.001\* | 0.87^10\*-4(0.39^10\*-4 to 1.35 ^10\*-4) | <0.001\* | -1.824(-2.65 to -0.99) | <0.001\* | 0.192(0.126to 0.258) | <0.001\* |
| HepB3 | N=153 | N=182 | N=181 | N=174 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -8.58(-15.89 to -1.27 | 0.022\* | 0.44^10\*-4(-0.105^10\*-4 to 0.98^10\*-4) | 0.113 | -1.43(-2.38to -4.79) | 0.003\* | 0.134(0.057 to 0.212) | 0.001\* |

\*p<0.05:statistically significant, ( ):95% confidence interval

1. **The association between vaccine coverage and potential variables**

**a. Univariate linear regression**

 The results of univariate linear regressions of all variables (GII, GDP per capita, fertility rate, and index of service coverage (SCI)) showed a statistically significant association with the vaccine coverage for DPT3, MCV1, Hib3, and HepB3 (Table 4). Vaccine coverage of PCV3 and RotaC were not analysed in this study as the number of obtained counties’ data were not sufficient in order to maximise the denominator of vaccine coverage and increase statistical accuracy. First, the result of GII will be explained. The range of gender inequality index (GII) was from 0.039 of Argentine to 0.834 of Rwanda. GII showed Argentine is the most gender-equal society in the world and Rwanda is the most unequal one. The mean GII was 0.35(SD 0.19) and the median was 0.356 (IQR 0.187-0.495). Overall, GII declined along with the increase of income level of countries and many European counties were registered as low levels of GII. Next, regarding the association between GII and 4 vaccines coverage in univariate linear regression, it showed a statistically negative association (DPT3 coefficient -14.25(95% CI -19.78 to -8.727), p<0.001, MCV1 coefficient -16.25(95% CI -22.0 to -10.49), p<0.001, Hib3 coefficient-13.529(95% CI-19.22 to -7.72), p<0.001, HepB3 coefficient-8.58(95% CI-15.89 to -1.27), p<0.001) (Table 4). Take the DPT3 vaccine as an example, it means if gender inequality index increased to 1.0, DPT3 vaccine coverage would decline by 14.25%. It could be interpreted that a more gender-equal society would mean an increase in vaccine coverage.

　　The association between vaccine coverage and fertility rate also showed a statistically negative association in this analysis (DPT3 coefficient -2.0(95% CI -2.77 to -1.23), p<0.001, MCV1 coefficient -2.92 (95%CI-3.72 to -2.11), p<0.001, Hib3 coefficient -1.824 (95%CI -2.65 to -0.99), p<0.01, HepB3 coefficient-1.43(95%CI-2.38 to -4.79), p=0.003). This means that a high fertility rate decreases the vaccine coverage and 4 kinds of vaccine coverage decreased by approximately 2.6 to 3.5% if fertility rate increased by 1.0. In this analysis, fertility rate was examined for looking at the association between vaccine coverage and the number of siblings, because national data of the number of siblings was not obtained. If the usage of this variable is reasonable, it could be interpreted that the more siblings a child has, the lower the probability it will be vaccinated. According to Danis, number of siblings is one of the most influential socioeconomic factors for the decrease in the vaccine coverage and this analysis supports his result (41).

　Contrary to the association between vaccine coverage and GII and fertility rate, the relationship between GDP and UHC SCI, and 4 kinds of vaccines coverage showed a statistically-positive association (Table 4). Regarding GDP per capita, the results of the linear regression of 4 kinds of vaccine coverage and GDP per capita was coefficient 0.79^10\*-4 (95% CI 0.39^10\*-4 to 1.19^10\*-4, p<0.001) in DPT, coefficient 0.756^10\*-4 (95% CI 0.312^10\*-4 to 1.2^10\*-4, p=0.001) in MCV1, coefficient 0.87^10\*-4 (95% CI 0.39^10\*-4 to 1.35^10\*-4, p<0.001) in Hib3, and coefficient 0.44^10\*-4 (95% CI -0.105^10\*-4 to 0.98^10\*-4, p=0.113) in HepB3(Table 4). 4 kinds of vaccine coverages increased the range by almost 0.4 to 0.87 % if GDP per capita increase by 10,000 US dollars, but the association between HepB3 vaccine coverage and GDP per capita was not shown to be a statistical association because the p value was more than 0.05. When analysing this association by polynomial regression lines, variation was identified with the association between HepB3 and GDP per capita, compared to the associations of GDP per capita and other vaccines (Figure 1). The dots in Figure 1 show each country and the dots far from the line in the figure of HepB3 and GDP per capita were Switzerland, Canada, and San Marino. There is a possibility that these countries’ data influenced the p value to render the association between HepB3 vaccine coverage and GDP per capita statistically insignificant.





Figure1: Scatterplot showing the association between GDP per capita on X-axis and DPT3, MCV1, Hib3, and HepB3 vaccine coverages on Y-axis at country level, worldwide. The lines show polynomial regression for vaccine coverages.

 As well as the association between vaccine coverage and GDP per capita, UHC SCI showed positive relations between vaccine coverage and 4 kinds of vaccine coverage, whereby the range increased by 0.195 to 0.289 if UHC SCI increased by 1.0 (DPT3 coefficient 0.199(95%CI0.137 to 0.261), p value <0.001, MCV1 coefficient 0.254(95%CI 0.189 to 0.32), p value<0.001, Hib3 coefficient 0.l92 (95%CI 0.126 to 0.258), p value<0.001, HepB3 coefficient 0.134(95%CI 0.057 to 0.212), p value=0.001) (Table 1). It means that countries with more successful health care services and stronger capacities for health care for all children had higher vaccine coverage rates. From the perspective of this univariate linear regression, a robust health care system also has a great impact on vaccine coverage.

Table 5: The results of a multivariable linear regression of the variables and vaccine coverages.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | GII | GDP per capita | Fertility rate | UHC SCI |
| DPT3 | N=149 | N=149 | N=149 | N=149 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -12.05(-21.48 to -2.62) | 0.013\* | 0.102^10\*-4(-0.59^10\*-4 to 0.79^10\*-4) | 0.772 | 0.733(-0.733to 2.199) | 0.325 | 0.0812(-0.044to 0.206) | 0.20 |
| MCV1 | N=151 | N=151 | N=151 | N=151 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -7.315(-16.90to 2.28) | 0.134 | -0.158^10\*-4(-0.88^10\*-4 to 0.56^10\*-4) | 0.666 | -0.97 (-2.46 to 0.519) | 0.200 | 0.096(-0.032 to 0.224) | 0.139 |
| Hib3 | N=150 | N=150 | N=150 | N=150 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -11.64(-21.53to -1.75) | 0.021\* | 2.71^10\*-7(-0.735^10\*-4 to 0.74^10\*-4) | 0.994 | 0.88(-0.66 to 2.42) | 0.261 | 0.097(-0.036to 0.23) | 0.150 |
| HepB3 | N=146 | N=146 | N=146 | N=147 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -9.62(-21.98 to 2.73) | 0.126 | -0.23^10\*-4(-0.113^10\*-4 to 0.68^10\*-4) | 0.621 | 0.226(-1.62to 2.075) | 0.809 | 0.207(-0.139 to 0.181) | 0.798 |

\*p<0.05:statistically significant, ( ):95% confidence interval

**b. Multivariable linear regression**

The results of the multivariable linear regression are shown in Table 5. Regarding the association between GII and 4 kinds of vaccine coverage, the coefficient and the p-value were -12.05(95% CI -21.48 to -2.62) and 0.013 for DPT3, -7.315(95%CI -16.90 to 2.28) and 0.134 for MCV1, -11.64(95% CI -21.53 to -1.75) and 0.021 for Hib3, and -9.62(95%CI -21.98 to 2.73) and 0.126 for HepB3 (Table 5). This means that the coverage of DPT3 and Hib3 vaccines decreases the range by approximately 11% to 12% if GII increases by 1.0. The association between DPT3 and Hib3 vaccine coverage and GII were identified as statistically significant, however, for MCV1 and HepB3 there were no statistically-significant associations on this adjusted variable model (Table 5).



HIC

LIC

MIC

LMIC





Figure 2: The association between DPT3, Hib3, MCV1 and HepB3 vaccine coverage and GII with the division of income categories.

The p-values of GDP per capita, fertility rate, and UHC SCI for 4 kinds of vaccine coverage were more than 0.05 in this adjusted regression model: p-values for GDP per capita were above 0.6, for fertility rate were above 0.2, and for UHC SCI were above 0.139 for 4 kinds of vaccine coverage (Table 5). When all analysed variables in this study were adjusted, GII was the only independent variable that was identified as a statistically-significant association for DPT3 and Hib3 vaccine coverage (Table 5). In order to research the cause of the statistically insignificant association between GII and MCV1 and HepB3 vaccines, polynomial regression lines were divided into income categories which were analysed (Figure2). The X-axis represents GII and the Y-axis represents vaccine coverage and four lines stand for the predicted vaccine coverage of the four different income categories (high-income, middle-income, low and middle-income, and low income countries). The dots represent countries’ actual vaccine coverage. Overall, there were very few variations in the high-income group in the coverage for four different kinds of vaccines. On the other hand, the variations were most noticeable among the low and middle-income countries. Compared to the figures for DPT3 and Hib3 vaccine coverage, large variations were seen on MCV1 and HepB3 vaccine coverage figures, as many dots were far from the lines of predicted vaccine coverage. The countries that showed vaccine coverage different from the predicted vaccine coverage would influence the result of the p-values, which are the statistically insignificant association between GII and MCV1 vaccine coverage and HepB3 vaccine coverage. The association between GII and four types of vaccine coverage with the division of human development groups was also analysed using polynomial lines (Figure3). The X-axis represents GII and the Y-axis represents vaccine coverage and the four lines stand for predicted vaccine coverage with the different four human development groups: very high human development:1, high human development: 2, medium human development: 3, and low human development: 4. The dots represent each country’s actual vaccine coverage. There were few variations in human development group 2 in terms of DPT3 and Hib3 vaccine coverage and the distribution of dots of DPT3 and Hib3 is almost the same. On the other hand, the figures for MCV1 and HepB3 exhibited large variations, especially in human development group 2 in HepB3 and the group 2, 3, and 4 in MCV1. There were very few variations in human development group 1 in the coverage for four different kinds of vaccines. Focusing on the shape of the line, only group 4 was close to the straight line and the other 3 groups’ lines were far away from the straight one. These variation patterns for each kind of vaccine coverage were the same the patterns for the relationship between GII and vaccine coverage with the division of income groups. These findings would reflect the results of a multivariate regression model, in which the p-value of the analysis between GII and MCV1 and HepB3 vaccine coverage did not show a statistically significant association.

To examine these results further, a linear regression analysis was performed for the group divided income status and HDI (table 6, 7). Regarding the result of MCV1 in the group divided income status, statistical significance between gender inequality and vaccine coverage was only shown in LMICs and LICs. On the other hand, HICs and MICs did not show statistical significance. Regarding HepB3 in the same group, only LICs showed an association between the gender inequality index and HepB3 coverage and other income groups did not show statistical significance (Table 6). In regards to the result of the group divided HDI, only LICs were shown to be statistically significant in both MCV1 and HepB3. From these results, the association between gender inequality and MCV1 and HepB3 coverage was shown in only LICs or both LICs and LMICs. It would be considered that the impact of gender inequality for all 4 vaccines was a more active factor in LICs or in both LICs and LMICs, while no relationship was observed for MCV1 and HepB3 in HICs and MICs.

 

 

Figure 3: The association between DPT3, Hib3, HepB3 and MCV1 vaccine coverage and GII with the division of human development groups.

Table 6: The results of a multivariable linear regression of the variables and MCV1 and HepB3 coverages with the group divided income group.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | HIC | MIC | LMIC | LIC |
| MCV1 | N=54 | N=48 | N=34 | N=21 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| -3.240(-19.48 to 13.003) | 0.795 | 4.506(-17.207to 26.22) | 0.678 | -32.63(-56.48 to -8.78) | 0.009\* | -49.83(-86.83 to -12.84) | 0.011\* |
| HepB3 | N=50 | N=47 | N=34 | N=20 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| 1(-6.95 to 9.038) | 0.69 | 6.95 (-21.53to 35.45) | 0.625 | -24.39(-54.38 to 5.60) | 0.107 | -31.72(-54.90 to -8.54) | 0.01\* |

\*p<0.05:statistically significant, ( ):95%conffident interval

Table 7: The results of a multivariable linear regression of the variables and MCV1 and HepB3 coverages with the group divided HDI.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | HDI1 | HDI2 | HDI3 | HDI4 |
| MCV1 | N=55 | N=44 | N=31 | N=29 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| 1.877(-7.9to 11.70) | 0.703 | 12.29(-15.20to 39.80) | 0.372 | -23.38(-65.59 to 18.81) | 0.261 | -55.13(-87.31to -22.94) | 0.002\* |
| HepB3 | N=50 | N=44 | N=31 | N=28 |
| Coefficient | p value | Coefficient | p value | Coefficient | P value | Coefficient | P value |
| 6.92(-13.086 to 26.93) | 0.49 | -9.91 (-47.55to 27.73) | 0.598 | -2.33(-37.73o 33.08) | 0.89 | -40.78(-75.38 to -6.17) | 0.023\* |

\*p<0.05:statistically significant, ( ):95%conffident interval

**Chapter 5: Discussion**

1. **. Summary of findings**

 The finding from these results is that gender inequality is associated with the decrease of DPT3 and Hib3 vaccine coverages, regardless of countries’ income status. The research question that this dissertation focused on is “the association between gender inequality and vaccine coverages at worldwide level”. The answer to this question is there is a negative association between two variables, although the strength and significance of this association depends on the kind of vaccines, with a significant relationship between GII and DPT3 and Hib3 vaccines. The countries that have lower vaccine coverages than average possessed higher gender inequality measured by GII. This trend was confirmed even after adjusting for potential socioeconomic confounders, namely GDP, fertility rate, and SCI of UHC in even high-income countries. Nevertheless, the previous studies just demonstrated this association in only low and lower and middle-income countries. This finding reinforces the notion that gender inequality issues affect diverse health-related issues not only in low, lower and middle-income countries but also in high-income countries and in addition it has important worldwide implications for public health strategies.

My analysis suggests that low vaccine coverage will not be improved unless gender inequality is mitigated, since gender-related issues perpetuate themselves (26). The main purpose of this study was to focus on sociocultural public health issues, which is the association between gender inequality and vaccine coverage. Thus, children’s immunizations were focused on rather than adults’ because children whose behaviour is dependent upon societal norms and family practices are likely to be influenced much more by sociocultural structures (46). Moreover, vulnerable populations, such as children, directly influence the capacity of the health system, hence a consideration of the influence of UHC for children was also inevitable (47). In the univariate linear regression analysis, SCI of UHC was positively associated with vaccine coverage, however, after adjusting for all independent variables, there was no statistically significant association. At first glance, SCI of UHC, which is likely to be significantly related to vaccination rates, did not show a significant association for vaccine coverage, while gender inequality showed a significant association. This is also a notable finding in the study.

Several previous studies have also demonstrated the association between gender inequality and vaccine coverages in one country or some countries, however, these studies focused on one country’s survey or only on Gavi-supported countries and just one study focused on this issue globally. Moreover, these studies also showed a strong association on DPT3 vaccines, compared to MCV1, however, in these studies, the reason of this different result on DPT3 and MCV1 were not examined. For example, Corsi showed that girls were less vaccinated than boys and girls tended to be vaccinated later than boys in age-appropriate vaccinations in India for the DPT3 vaccine and BCG. However for the MCV there was no significant difference between genders but the author did not mention the details (48). Arsenault’s Gavi-supported countries study involved the gender inequality index and vaccination coverages, and it also brought important findings, however this association was also shown on only the DPT3 vaccine and there was no strong association between gender inequality and the MCV1 vaccine, however, they also did not refer to this reason or details in their studies (20). This study examined the details of the subject for different vaccine coverages in each income status group and HDI. The direct reason for differences in results for each vaccine was not found by examining worldwide data, however some new findings were obtained. When polynomial regression lines were analysed by 4 income categories for every 4 vaccines, conspicuous variations were seen on MCV1 and HepB3 vaccines, compared to DPT3 and Hib3 vaccines which were shown to have statistically-significant associations between gender inequality index and vaccine coverages in multivariable regression analysis (Figures 2 and 3, Tables 6 and 7). This means that the predicted vaccine coverages which were statistically estimated values by STATA (trajectories) for GII and actual vaccine coverages, and which were plotted from countries’ data by STATA for GII for each country (dots), obviously do not correspond on MCV1 and HepB3 vaccines. The predicted lines were far away from straight shape, particularly in HICs and MICs (Figure 2). The same trends were seen in Figure 3 shown by the 4 groups divided by HDI (Figure 3). After this result, the coefficient and the p-value were examined; it was found that gender inequality was also associated with MCV1 and HepB3 coverage in only LICs or both LICs and LMICs despite there being no association in HICs and MICs.

It might be interpreted that MCV1 and HepB3 vaccine coverages are more likely to be influenced by other factors in HICs and MICs, such as the strong hesitation about vaccines or some groups’ political rhetoric against vaccines rather than gender inequality. In contrast, in regard for Hib3 and HepB3 vaccine coverage, gender inequality might possess an important role for increasing vaccine coverage. Gender inequality issues are well known to be among some of the most influential factors on health issues, however, the association between gender inequality and vaccine coverage have not been examined globally until now. Nevertheless, the gender inequality issue manifests itself worldwide and has to be examined and discussed at the global level. Therefore, this global scale study’s findings would be meaningful and helpful for vaccination policies, although further investigation is needed to establish strategies to increase vaccine coverage.

1. **. Impact of gender inequality on health and the importance of resolving gender inequality issues**

 Gender inequality issues include the wide range of women’s long-standing issues and it perpetuates itself, this issue therefore influences a considerable number of public health issues. Mothers who do not have financial power and autonomy to make decisions would be unable to seek immunization services on their own (49). Moreover, younger, poorly educated and illiterate mothers tend to lack practical knowledge about vaccination services and are less likely to understand vaccination schedule cards, return dates and the fact that multiple visits are required for complete immunization (50). Thus, enhancing the quality of maternal health care is also essential in order to provide an important entry point for information and services, and empower mothers to protect children’s health, as well as their own (51). Improving gender equality by improving female literacy rates, labour market participation, and the reduction of teenage pregnancies and domestic violence have repeatedly been shown to improve child survival and well-being (20). Guaranteeing woman’s rights and providing them opportunities to utilise their potential is critical not only for obtaining gender equality but also for accomplishing a wide range of sustainable development goals. Empowered women and girls would contribute to the health and productivity of their families, communities, and countries, which creates benefits for everyone and breaks the vicious cycle of gender inequality.

Past studies that researched the relationship between health issues and gender inequality showed the statistically positive or negative relationships even after having been adjusted for socio-economic status, namely GDP, these inequalities existed not only at country-level but also at individual levels (15, 16, 32, 52). Focusing on the individual level, inhibition factors for vaccination coverage are much more complicated, because an individual’s attitude greatly influences vaccine coverage and this does not represent the statistical method. Thus deeper research, such as narrative studies, would be crucial to obtaining further details on this issue. When looking at the issue of vaccine coverage, the concept of vaccine hesitancy has recently been focused on, because it is one of the major impediments to improving vaccination coverage. Furthermore, the individual factor is considered key to improving vaccine coverage and it is attracting the attention of many policymakers(53). However, sufficient qualitative studies have not been conducted for even the issue of vaccine hesitancy. Effective interventions through qualitative research after establishing and demonstrating a hypothesis are needed to resolve this tangled issue and further elucidate the relationship between individual-level attitudes and improving vaccine coverage around the world, including in HICs.

1. **. Limitation of this study.**

The key limitation of this study is ecological fallacy, which cannot apply to individuals and demonstrate the causal dependence. Thus, this study can be interpreted as demonstrating that there is an association between gender inequality and vaccine coverage worldwide, however it cannot demonstrate this within each country. Additionally, the gender inequality index is a new and relative indicator, so it is not necessarily a representative measure for gender inequality. Furthermore, there is a possibility all independent variables were not included in this research though all variables took as much into account as possible through the literature review. Finally, only quantitative research was conducted in this study, thus the establishment of effective interventions cannot be indicated, although it can be mentioned that gender inequality influences vaccine coverage and resolving gender inequality issues is essential to improving vaccine coverage. In the future, qualitative research, such as a narrative research focusing on individuals in a certain country, should be explored to shed light on the contexts behind the gender inequality issues and also vaccine hesitancy, particularly in HIC and MIC. Integrating this study and future study including individual-level research would be a clue to addressing the issues of vaccine coverage and might be useful for devising effective policy-making strategies.

**Conclusion**

This study set out to examine the link between gender inequality and vaccine coverage on a global scale. An ecological study was conducted for this analysis. The ecological study has several limitations and the rank of evidence level is not high. However, this is the first global-scale analysis of the association between gender inequality and vaccine coverage. It was revealed that gender inequality was the only variable that decreased DPT3 and Hib3 vaccine coverage worldwide even after controlling for other possible explanatory variables. Additionally, in LIC or both LIC and LMIC, gender inequality is also associated with MCV1 and HepB3 coverage; in contrast, MCV1 and HepB3 did not show a statistically significant association in HIC and MIC. Past research associated with gender inequality and vaccine coverage in one country or low-income countries had shown that gender inequality was related to DPT3 coverage, however, it did not find and mention the different results for each vaccine or discuss worldwide trends. This worldwide scale ecological analysis for different vaccines would be crucial for one of the strategies to increase vaccine coverage; nevertheless, this result cannot be applied to individuals and within countries, due to the limitations of the study design. Further investigation such as qualitative studies would be needed in the future for determining the effective interventions for vaccine coverage, since people’s attitudes and cultural and political contexts are also essential determinants for vaccinations.

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