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Complete List of Authors:	SUTAN, ROSNAH BINTI; Universiti Kebangsaan Malaysia, community health Batarfi, Suha; Hadhramout University College of Medicine and Health Sciences, Community Medicine department Ismail, Halim; Universiti Kebangsaan Malaysia, community health Bin-Ghouth, Abdulla ; Hadhramout University College of Medicine and Health Sciences, Community Medicine department
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Vaccine hesitancy from parents and healthcare providers perspectives in Hadhramout governorate, Yemen: a mixed-methods study protocol

Rosnah Sutan[1], Suha Ali Batarfi[1,2], Halim Ismail[1], Abdulla Salem Bin-Ghouth[2]

[1]Community Health Department, Medical Faculty, University Kebangsaan Malaysia

[2] Department of Community Medicine, Hadharamout University College of Medicine and health sciences (HUCOM), Yemen

Correspondence author:

Suha Ali Batarfi

Department of Community Medicine, Hadharamout University College of Medicine (HUCOM), Yemen

Email: batarfisuhaali@gmail.com

Phone:+6011-27107155

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ABSTRACT:

Introduction : Although immunisation prevents the death of millions of infants and children each year, vaccination coverage of routine childhood vaccination does not reach its target. Reasons for low vaccination uptake can be related to both the demand and supply-side determinants. The prevalence of vaccine hesitancy is on the rise globally. However, scares data is known about vaccine hesitancy in low-income, Arabic countries. To address this issue in Yemen, as one of the Arabic low-income countries, we decided to address vaccine hesitancy link to child immunisation status among children living in Costal Hadhramout, Yemen, from parents perspectives and healthcare providers.

Methods and analysis: A mixed-methods research design will be used. The study will be conducted in Costal Hadhramout, Yemen. The study will be done through three phases. Phase one will be a situational analysis using secondary data from records of the national expanded program of immunisation in Costal Hadhramout to examine the trend for the last years. Phase two will be a quantitative study aiming to assess the prevalence of vaccination status of under two years of children and the determinants of parental vaccine hesitancy through a validated questionnaire. Finally, phase three will be a qualitative study using in-depth interviews and FGD for parents and health care providers to explore vaccine hesitancy in Yemen.

Ethics and dissemination The study has been approved by the Research Committee of the Faculty of Medicine, Universiti Kebangsaan Malaysia.

STRENGTH AND LIMITATIONS OF THIS STUDY

- The strength of the present study protocol is its ability to determine all aspects of child, parental and healthcare factors of vaccine hesitancy among the Yemeni.
- Using the national data will help in the generalisation of the findings to Yemen.
- Applying the mixed method has an advantage in improving the grey area of socio-perspective, facilitators and barriers.
- The validated questionnaire used will determine better data quality.
- The inability to meet face to face during the current COVID 19 pandemic poses a limitation. Therefore, using telephone video calls or voice calls alone may not visualise the respondent expression and validity of the data captured.

INTRODUCTION:

During the 20th century, there is a significant increase in life expectancy, attributed mainly to improvements in child survival. Universal child immunisation has been effectively used as a preventive measure to protect the vulnerable group. Immunisation has prevented millions of deaths related to vaccine-preventable diseases around the world[1]. From 2007 to 2010, global Diptheria, Tetanus and Pertussis 3rd dose (DTP3) coverage was increased from 79% to 84%, but since 2010, the DTP3 coverage had noted plateauing. The coverage was varied by region, as in the WHO African Region, it is only 72%, while in the Western Pacific Region is 97% [2]

Reasons for low vaccination uptake are often not completely understood and seems to be multifactorial. Inadequate vaccination coverage can be related to both the demand and supply-side determinants. The majority of reasons for the low uptake of childhood vaccination in developing countries are related to lack of access to vaccination and family factors. Low education, literacy, and socio-economic status are well known indirectly contributed to non-achievable coverage. However, in several developing countries, the weakness of the health system is regarded as a significant barrier[3,4]. Persistent challenges seen related to acceptance of the services that affect the uptake, especially in developing countries[5,6].

Vaccine hesitancy is a behavioural phenomenon among both; those who accept all vaccines with no doubt refuse all vaccines[7,8]. It is recognised as a growing problem of global importance that affects both developing and developed countries, and WHO defined it as delay in acceptance or refusal of vaccines despite availability of vaccine services[9]. Recently, vaccine hesitancy prevalence rises as a global problem and can be seen as poor childhood vaccination coverages. The World Health Organization (WHO) identified it as a priority issue and has developed a vaccine hesitancy model framework that emphasises confidence, complacency and convenience[9]. It was further expanded to included confidence, complacency, constraints, risk calculation, and collective responsibility and named these factors as psychological antecedents of vaccination[10]. These models are suggested based on research predominantly conducted in well developed and high-income countries[11]. Studies in neighboured Arab countries have addressed parental vaccine hesitancy as a concerning problem that likely influences the uptake of childhood vaccination[12,13]. However, till present, to the best of our knowledge, no published study address vaccine hesitancy in Yemen.

Yemen's Issues and Challenges on Child Immunisation

Yemen is an Arabic, low-income country with poor socio-economic status and a fragile health system. It has a hard-geographic environment which affects access to essential basic services, and limited financial support cover cost a major challenge[14]. Since March 2015, Yemen

had been engaged in a civil war and has continued to date. Civil war and internal conflict affect Yemen's local development[15,16]. The instability, shortage of services and internal displacement may lead to limited vaccination coverage[17]. The Expanded Program of Immunisation (EPI) in Yemen was initiated in 1979 as a part of the Primary Health Care General Directorate in Public Health and Population. It aimed to prevent morbidity and mortality from preventable diseases through vaccination, and Infants and women of child-bearing age are the target groups[18]. Routine immunisation services in Yemen are given through fixed vaccination posts within the health facilities and outreach vaccinations strategy and based on the proximity of the target populations to the health facility. Table 1 showed the standard schedule of routine immunisation of the child of Yemen.

Table1: Standard schedule of routine immunisation of child of the Republic of Yemen

Vaccine	**Age**					
	At birth	**6weeks**	**10weeks**	**14weeks**	**9months**	**18 months**
BCG*	×					
OPV*	×	×	×	×	×	×
Pentavalent		×	×	×		
Pneumococcal		×	×	×		
ROTA		×	×			
MR*					×	×
IPV*				×		

*BCG: Bacille Calmette Guerin, OPV: Oral Polio Vaccine, MR: Measles, Rubella, IPV: inactivated poliovirus vaccine

According to the last Yemen National Health and Demographic Survey (YNHDS), in 2013, only 42.6% of children aged 12-23 months were fully vaccinated, while 16% did not receive any vaccination. No reported published data available for comparison on-trend. However, vaccines for significant vaccine-preventable diseases (VPDs) are available free for the public[19]. WHO and UNICEF reported vaccination coverage in 2018 for Yemen was 65% based on DTP3, which still below 90% that every country should reach by 2020[20]. From the previous studies done in Yemen, we can conclude that even before the war, the vaccination coverage in Yemen was not achieving

the acceptable target, and the children's percentage that was not vaccinated at all was increased. In addition, various Governorate of Yemen reported unvaccinated or partially vaccinated children mainly due to lack of information and parental motivation[18 21-23].

The rationale for this research

Although vaccine hesitancy is addressed extensively in literature in the past few years, few studies explore this issue in low-income countries. Thus, most finding and model developed was based on studies done in high-income countries[11]. Limited studies addressed the issue of childhood vaccination in Yemen, and most studies focused on coverage and reasons for non-vaccination[17,18,22,23]. Only one study addressed the determinants of complete vaccination[21], although that study did not address the issue of vaccine hesitancy. Furthermore, all published studies addressing childhood vaccination in Yemen used a quantitative method, which cannot give in-depth details about the problem when integrating with available qualitative study findings. In addition, all community-based studies done in Yemen explored the problem from the parents' perspective only and did not consider the healthcare workers who can give a broad picture of the problem.

Studying the perspective of parents and healthcare workers on vaccine hesitancy toward childhood vaccination is vital in improving service delivery and vaccine uptake. In addition, it helps to reduce the high morbidity and mortality rate among children from vaccine-preventable diseases, which is known to be the leading cause of under-five mortality. Therefore, it is crucial to understand their perceptions as they play a vital role in vaccination programs. Also, explore their perspectives are informative in understanding the barriers faced by them. So, to add knowledge in literature gaps about vaccine hesitancy and childhood vaccination in Yemen, the present study protocol is designed as a mixed-method study to assess the vaccine hesitancy determinants from the perspective of parents and healthcare workers. A conceptual framework (Figure 1) illustrated the concept of the present study to overcome the gap of evidence in the literature, which must be explored.

Aims and objectives:

This research aims to address the vaccine hesitancy issue and the child immunisation status among children living in Costal Hadhramout, Yemen, from the perspectives of parents and healthcare providers. The specific objectives of our research are:

1. To conduct a situational analysis of the routine childhood immunisation EPI data in Costal Hadhramout, Hadhramout Governorate, Yemen.

2. To measure the prevalence of vaccine hesitancy and child immunisation status among children and their mothers living in Costal Hadhramout, Hadhramout Governorate, Yemen.

3. To identify the factors associated with and predict vaccine hesitancy and immunisation status of children living in Costal Hadhramout, Yemen.

4. To explore mothers' reasons for hesitancy towards childhood vaccination.

5. To explore barriers in achieving immunisation coverage among the healthcare providers in Costal Hadhramout, Yemen.

METHODS

The present study used a complementary explanatory sequential mixed-method study design. The study will take place at the Hadhramout in Yemen, consisting of 30 districts and occupying vast areas of the Arabian Sea coast. Hadhramout has divided administratively into two parts: the valley\ desert (Wadi Hadhramout) and the Coastal Hadhramout. Coastal Hadhramout overlooking the south to the Arabian Sea, possesses a coastline length of about 120 kilometres. It is estimated that the total population of coastal Hadhramout in 2018 was 893502 people, and the population grows at a rate of 3.08% annually. The research targets the twelve districts of coastal Hadhramout[24]. This study consisted of three phases: Phase1: Situation analysis, Phase 2: Quantitative study and Phase 3: Qualitative study. An overview of the study phases and their flow is illustrated in figure 2.

Phase 1: situation analysis

This part of our study will be a retrospective descriptive study. Records from the national immunisation program for all 12 districts in coastal Hadhramout for the past ten years (from January 2011 to December 2020) will be reviewed and analysed (secondary data analysis). After taking permission from the general manager of the Health and Population Affairs Office - Coastal Hadhramout, data will be extracted from data collected in the Department of EPI in Health and Population Affairs Office – Costal Hadhramout. First, we will assess the immunisation coverage rate (which estimated for each vaccine and, for multi-dose vaccines, for each dose received (e.g., diphtheria-tetanus-pertussis-containing vaccine (DTPCV1, DTPCV2, DTPCV3) in each year (trend analysis which is the first outcome of this phase). Also, the districts will be classified into good or low coverage districts. The classification will be dependent on the Global Immunisation

Vision and Strategy goal, which is at least 90% national vaccination coverage and at least 80% vaccination coverage in every district or equivalent administrative unit. So each district that has coverage of 80% or above will be good, and any district that has below 80% will be considered a low coverage district (WHO, 2015). This classification is considered the second outcome of this phase and will be used to select districts in phase 2.

Phase 2: a quantitative study

In this phase, a community based, cross-sectional study design will be used. The study population in this study will be mothers or caretakers of children living in coastal Hadhramout, Hadhramout Governorate, Yemen 2021, and aged less than two years. The stratified cluster sampling method incorporated a combination of stratified and cluster sampling methods will be used in this study. First, the 12 districts in Coastal- Hadhramout will be stratified by immunisation coverage level as good or low coverage districts depended on Phase 1. Two districts will be selected randomly from each stratum. Second, a 30 cluster (approximately estimated by the researcher and maybe more according to the absolute number of houses in each cluster) will be chosen from the selected districts proportionally to the size. Then all households in those clusters will be surveyed for an eligible child.

The researcher will prepare the sampling frame used in this study after consultation with the director-general of the expanded immunisation program in Coastal Hadhramout. Moreover, The preparation of this sampling frame will be based on the list of household distribution used in the last National Immunisation Days (NIDs). Based on this list, the clusters in each district will be identified (approximately every cluster contains 20 to 30 households). Then, the researcher will select the number of clusters that need to cover the sample size in this study from each district proportionally. In this study, an eligible mother or caretaker will be a mother who has a child aged less than two years. The youngest child will be taken for mothers with more than one child aged less than two years. We will exclude the Non-Yemeni family.

The sample size for this phase is calculated based on the formula of estimating proportion (prevalence) using the Kish formula[25] and comparing two proportions using Fleiss formula[26] with a confidence interval of 95% and power of study 0.80. The largest sample size from using both formulae is 767, so this will be our sample size for this phase. Data will be collected from households in selected clusters by the researcher and researcher assistants (health workers). Four health workers will be trained to collect data from mothers, and during fieldwork, each health worker will be a team. Each team will be supervised in the field by the researcher or fieldwork supervisor. Respondents will be interviewed

using a structured pretested designed questionnaire after being informed about the purpose of the study and after giving their agreement to take part in the study.

The questionnaire will be adopted and adapted to the Yemeni population, and validation will be conducted. The questionnaire will cover the following domain: domain1: child-related characteristics, e.g. age, sex, birth order, place and type of delivery, gestational age at delivery and health status of the child. Domain 2: family-related characteristics, e.g. age, education, work, monthly income, residency and number of people living in the family. Domain 3: immunisation related knowledge. Domain 4: hesitancy. Domain 5: psychological antecedents of vaccination (confidence, complacency, constraints, calculation and collective responsibility). Domain 6: vaccination status of the child (fully, partial or unvaccinated): based on the child's immunisation card, the history of immunisation provided by the mothers. Domain 7: availability and accessibility to vaccination service. Domain 8: Reasons for the incomplete or unvaccinated child. The operational definition of the study variables is listed in Table2.

In this study, the primary dependent variable is the mother's hesitancy level which will be assessed using an Arabic version of the Parent Attitudes about Childhood Vaccines questionnaire (PACV) after permission from the author granted (Alsuwaidi et al. 2020; Opel et al. 2011). This questionnaire is divided into three domains: the first about behaviour, the second about safety and efficacy, and the third about general attitude and trust. Furthermore, under these domains, fifteen items are grouped. A numeric score is used in this PACV, as items answered with a hesitant response are given a score of 2, items answered with a response of do not know or not sure given a score of 1, and items answered with a non-hesitant response are scored as 0. The raw score is then converted to a score range from 0 to 100. Accordingly, parents are assigned as 1 to indicate a hesitant score value ≥ of 50 or 0 as a non-hesitant parent with a score <50.

The second dependent variable in this study is the immunisation (vaccination) status of children aged 12-23 months. The immunisation status can be completed (Fully) immunised, and incomplete immunised or unimmunised. The definition of those classifications is according to the Yemini EPI schedule: Complete (Fully) immunised: A child aged 12-23 months who received one BCG, at least three doses of pentavalent, at least three pneumococcal, at least three doses of OPV, two doses Rotavirus vaccine and one dose MR (Measles Rubella) vaccine. Incomplete immunised: A child who did not receive all the routine EPI vaccines before his/her first birthday. Unimmunized (unvaccinated): A child did not receive any thirteen doses of recommended vaccines (Al-Tarbi& Bin Ghout 2020).

The Independent Variables in our study will include child and family characteristics:age, sex, birth order, place and type of delivery, gestational age at delivery and health status of the child, parents age, education, work, monthly income, residency and number of people living in the family.

Immunisation-related knowledge: this variable will be assessed using a scale adapted from a previous study done in Yemen[21]. Psychological antecedents of vaccination**:** confidence, complacency, constraints, calculation and collective responsibility. Those variables will be measured using the 5C scale [10]. To the best of our knowledge, there is no Arabic version of the 5C scale, so, according to the sample study protocol, the translation and validation of the 5C scale proposed by Betsch et al.[27] will be done. Availability and accessibility to vaccination service: this will be assessed using four questions adapted from previous literature. Permission from the authors of all mentioned scales will be adapted to suit the local population.

The questionnaire's validity and reliability will be assessed. The univariate analysis describes frequencies and percentages. Bivariate analyses will assess the associations between dependent and independent variables. A p-value of less than 0.05 was set up as a determinant for the significant variable. Multiple logistic regression will be used to assess the effect of different variables on hesitancy and children's immunisation status. The study results will be presented as tables and graphs.

Phase 3: a qualitative study

The case study design will be conducted in coastal Hadhramout, Yemen. The study population of this phase will be mothers\ caretakers who participate in phase 2 and are identified as hesitant mothers, and health care providers and health leaders who involve in the immunisation program in coastal Hadhramout, Hadhramout Governorate, Yemen. The purposive sampling method will be used in this phase. Mothers/caretakers will be selected from those who participated in phase 2 and showed good cooperation. Health care providers and leaders will be selected from the health facilities that provide immunisation in the selected cluster area in phase 2.

For this part of the study, data will be collected through In-depth interviews for mothers/ caretakers. In contrast, Focus Group Discussions (FGD) will collect data from health care providers and health leaders. First, in-depth interviews for mothers/ caretakers and FGD for health care providers and health leaders will be done until saturation is reached after triangulation. Then, the thematic analysis will be done to analyse the contents of In-depth interviews and FGD. The key questions are listed in Table 3.

Patient and public involvement

Participants in the study, parents and healthcare providers, can be involved in the study's design mainly in phase 2. In this phase, Study tools will be piloted and tested by a research team that needs contribution from the parents and health providers. Also, in phase 3, participants will give the chance to state any additional comments during the interview and FGD; therefore, their priorities, experiences and perception can be considered.

ETHICS AND DISSEMINATION:

The study proposal was reviewed and approved by the Research Ethics Committee of Faculty of Medicine, Universiti Kebangsaan Malaysia, project code: FF-2021-051. Permission was obtained from the health affairs office – Costal Hadhramout, Hadhraumout governorate to conduct the research. A simple and clear explanation of the study's aim and procedure will be provided to participants involved in the study. Consents will be obtained from all participants taking part in this study. Risks to participants or researchers involved in this study are unexpected. The privacy and confidentiality of participants will be assured. Study findings will be communicated through publication in peer-reviewed academic journals and disseminated to healthcare professionals, stakeholders, researchers and the public through academic conferences and public presentations.

Table 2 List of Independent Variables and their definition in this study

Independent variables	**Definition and analysis**
I. Child-related variables	
Age	Age of child in months, at time of data collection, obtained from the child's birth certificate, child's immunisation card or by asking mother /caretaker. Mean with Sd will be calculated.
Gender	boy or girl
Birth order	Position of the child among his or her siblings. categorised to: 1st born, 2–3, 4–5 and ≥6 [28]
Place of delivery	The place of delivery of the child is either delivered at a health facility or home [28 29]
Type of delivery	The type of delivery, either vaginal or cesarean delivery [21]
Gestational age at delivery	Referred to either the child full-term or premature
Health status of the child	Referred to either the child well or has a medical problem.

ii. Family-related variables	
Mother's age (years)	age of the mother in years at the time of data collection. Mean with Sd will be calculated.
Age at first birth (years)	Mother's age when she births her first child. Mean with Sd will be calculated.
Mother's Marital status	The mother's current marital status is either married or currently unmarried (divorced or widowed) [21]
Mother's educational level	The mother gained the highest formal education. categorised as either illiterate, able to read and write, Essential education, Secondary education or university and above [30]
Occupation of mother	The mother's working status categorised as either employed or housewife [31]
Father's educational level	My father's highest formal educations were categorised as either illiterate, read and write, Essential education, Secondary education, or university and above.
Father's occupation	Father's type of work categorised as either government employee, daily labourer, merchant unemployed or others.
Family size	The total number of persons in the household. this variable then will be categorised to: 0= ≤4, 1= 5–9 , 2= ≥10 [32]
Family residency	Permanent place of residence of the child's family categorised as urban or rural [21 33]
Monthly family income	Average total income per month in Yemeni Riyals YR (1 US $ = 600 YR). Mean with Standard deviation will be calculated.
III. Mother's / caretaker's immunisation related knowledge	
Source of information	The source that the participant hears from is about vaccination and vaccine-preventable disease. It categorised to: 0= Radio, 1= TV, 2= internet, 3= friends, 4= schools, 5= Health personnel, 6= others.
immunisation related knowledge	Mother's knowledge regarding preventable diseases by immunisation, the best way of protection from vaccine-preventable diseases, causes and number of vaccine doses, and the time of vaccine administration was assessed through five groups of questions containing 38 items. Each item was scored as I: correct, 0: wrong, or know the answer. the scale was adopted from the previous study done in Yemen after taken permission from the author [21] Analysis: Calculation of the total knowledge score was made by summation of the participant's responses, which ranged between 0 - 38 and was classified into 0 and 1 as follows: 0= For poor knowledge, range from 0 – 19, representing ≤ 50% of the maximum point in the score range. 1= For good knowledge, which ranges from 20 – 38, representing >50% of the maximum point in the score range [21]
V. physiological antecedents of vaccination: those variables will be measured by using the 5C scale [10]	
Confidence	This factor will be assessed through 3 items from The 5C scale: "1- I am completely confident that vaccines are safe. 2- Vaccinations are effective. 3- Regarding vaccines, I am confident that public authorities decide in the best interest of the community". Each item was scored on seven points Likert scale ((1=strongly disagree, 2=moderately disagree, 3=slightly disagree, 4=neutral (or: neither disagree nor agree), 5=slightly agree, 6=moderately agree, 7=strongly agree). Analysis: The mean score will be calculated by summing the respondent's responses for the three items and divided by 3 [10]
Complacency	This factor will be assessed through 3 items from The 5C scale: "1- Vaccination is unnecessary because vaccine-preventable diseases are not common anymore. 2- My immune system is strong, and it also protects me against diseases. 3- Vaccine-preventable diseases are not so severe that I should be vaccinated". Each item was scored on seven points Likert scale same as described in the confidence variable. Analysis: The mean score will be calculated by summing the respondent's responses to the three items and divided by 3 [10]

Constraints	This factor assessed through 3 items from The 5C scale: "1- Everyday stress prevents me from being vaccinated. 2- For me, it is inconvenient to be vaccinated. 3- Visiting the doctor makes me feel uncomfortable; this keeps me from being vaccinated". Each item was scored on seven points Likert scale same as described in the confidence variable. Analysis: The mean score will be calculated by summing the respondent's responses to the three items and divided by 3 [10]
Calculation	This factor assessed through 3 items from The 5C scale: "1- When I think about being vaccinated, I weigh its benefits and risks to make the best decision possible. 2- For every vaccination, I closely consider whether it is useful for me. 3- I need to understand the topic of vaccination before I get vaccinated fully". Each item was scored on seven points Likert scale same as described in the confidence variable. Analysis: The mean score will be calculated by summing the respondent's responses to the three items and divided by 3 [10].
Collective responsibility	This factor assessed through 3 items from The 5C scale: "1- When everyone else is vaccinated, I do not have to be vaccinated, too. 2- I get vaccinated because I can also protect people with a weaker immune system. 3- Vaccination is a collective action to prevent the spread of diseases". Each item was scored on seven points Likert scale same as described in the confidence variable. Analysis: The mean score will be calculated by summing the respondent's responses to the three items and divided by 3 [10].
VI. Access to vaccination service	
Distance	Referred to time take to reach the nearest health facility. this variable categorised to: 0 = ≤ 30 min, 1= > 30 min.
ways to reach the health facility	They referred to how parents can reach to health facility either by walk or use transport.
Availability of vaccine or vaccinator	Referred to was the vaccines and vaccinator are available in the health facility or not.
Time waiting	Referred to was the parents wait for a long time to get the vaccination for their child.

Table3: critical questions for the qualitative phase

A- The key question for an in-depth interview with mothers:	B- The critical question for FGD with healthcare providers and leaders:
Why parents refuse or incomplete vaccination for their children? - socio-economic reason - culture and religious reasons - parental vaccination knowledge reasons - services access reasons - staff-related reasons	What are the barriers to achieving immunisation coverage? - staff knowledge barriers - staff communication skills barriers - staff training and competency barriers - staff numbers barriers - supply and infrastructure barriers. `

Figure legend/caption:

Figure 1: Conceptual Framework

Figure2: An overview of the study phases

Author Contributions

RS and SB designed the study protocol and wrote the manuscript. All authors proofread the final manuscript before submission.

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ORCID iDs:

Rosnah Sutan: https://orcid.org/0000-0001-9956-4727

Suha Ali Batarfi: https://orcid.org/0000-0003-0060-5694

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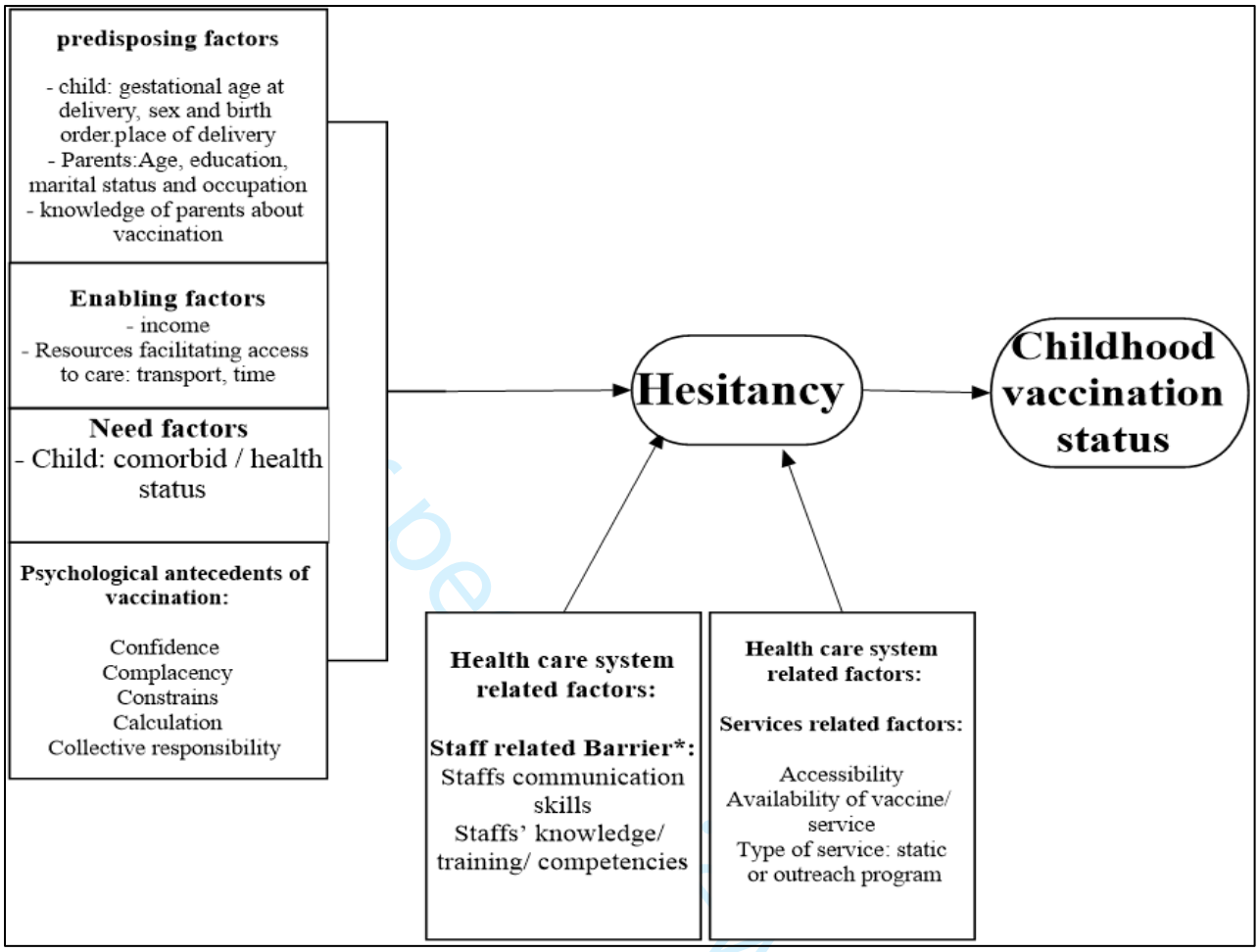

Figure 1: Conceptual Framework

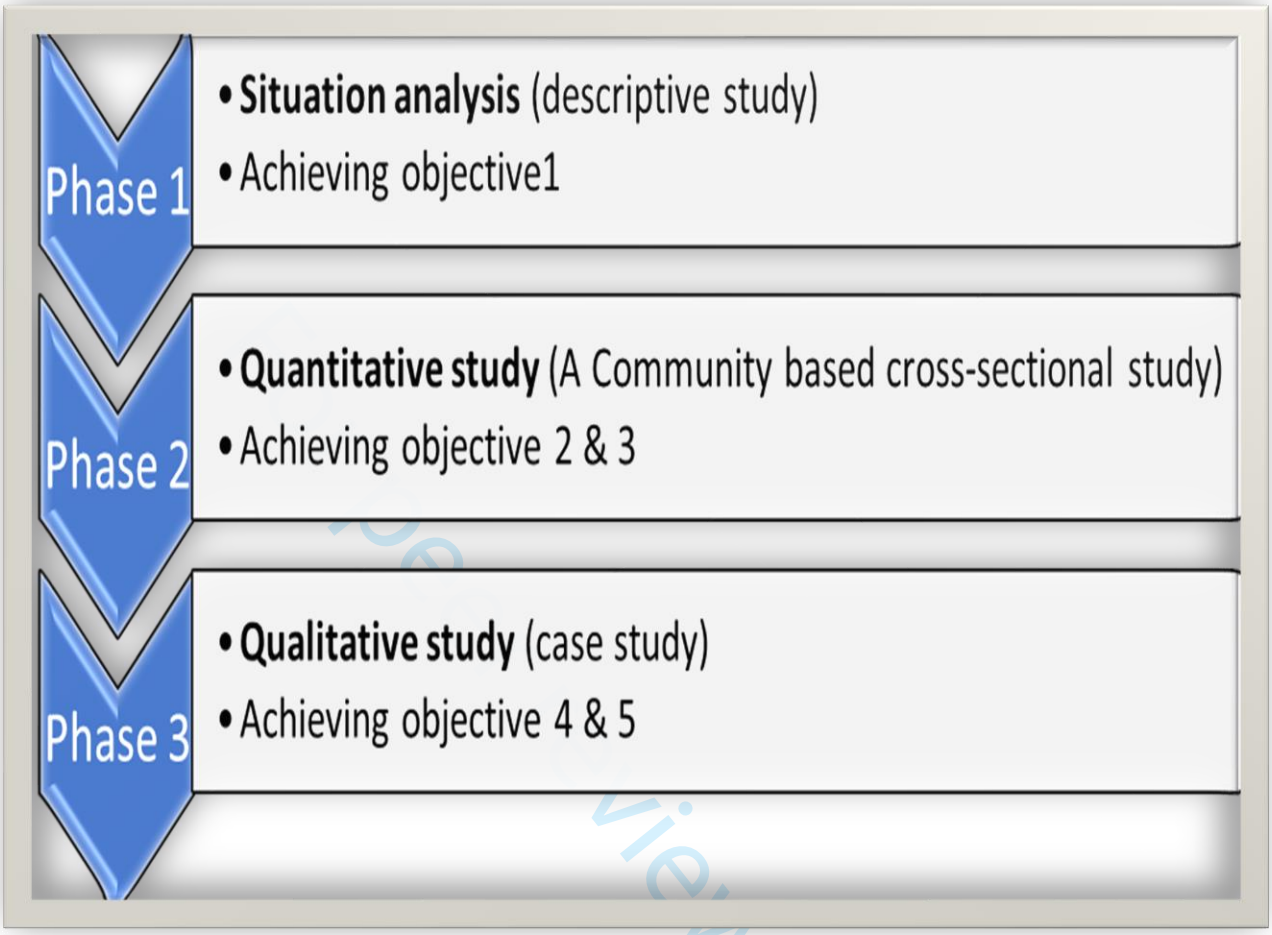

Figure2: An Overview of the Study Phases

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Vaccine hesitancy from parents and healthcare providers perspectives in Hadhramout governorate, Yemen: a mixed-methods study protocol

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Vaccine hesitancy from parents and healthcare providers perspectives in Hadhramout governorate, Yemen: a mixed-methods study protocol

Rosnah Sutan[1], Suha Ali Batarfi[1,2], Halim Ismail[1], Abdulla Salem Bin-Ghouth[2]

[1]Community Health Department, Medical Faculty, University Kebangsaan Malaysia

[2] Department of Community Medicine, Hadhramout University College of Medicine and Health Sciences (HUCOM), Yemen

Correspondence author:

Suha Ali Batarfi

Department of Community Medicine, Hadhramout University College of Medicine (HUCOM), Yemen

Email: batarfisuhaali@gmail.com

Phone:+6011-27107155

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ABSTRACT

Introduction: Although immunisation prevents the death of millions of infants and children each year, the vaccination coverage of routine childhood vaccination does not reach its target. The reasons for low vaccination uptake can be related to both demand and supply side determinants. The prevalence of vaccine hesitancy is increasing globally. However, data on vaccine hesitancy in low-income Arabic countries are scarce. To investigate this issue in Yemen, an Arabic low-income country, we aim to examine the link between vaccine hesitancy and the immunisation status of children living in Costal Hadhramout, Yemen, from the perspective of their parents and healthcare providers.

Methods and analysis: We will use a mixed-method research design. The study will be conducted in Costal Hadhramout in three phases. Phase 1 will involve a situational analysis using secondary data from records of the national expanded immunisation program in Costal Hadhramout to examine the trend for previous years. Phase 2 will be a quantitative study aimed at assessing the prevalence of vaccination status of children aged <2 years and the determinants of parental vaccine hesitancy perception through a validated questionnaire. Lastly, Phase 3 will be a qualitative study that explores vaccine hesitancy in Yemen using in-depth interviews and focus group discussions with parents and healthcare providers, respectively.

Ethics and dissemination: The study has been approved by the Research Committee of the Faculty of Medicine, University Kebangsaan Malaysia. The findings will be disseminated via publication in peer-reviewed academic journals, academic conferences and public presentations.

STRENGTH AND LIMITATIONS OF THIS STUDY

- The strength of the present study protocol is its ability to determine all aspects of child, parental and healthcare factors of vaccine hesitancy among the Yemeni.
- Using national data will aid generalisation of the findings to Yemen.
- Using mixed methods has the advantage of improving the grey area of socio-perspective, facilitators, and barriers.
- The validated questionnaire used will ensure better data quality.
- The inability to meet face to face during the current coronavirus disease 2019 (COVID-19) pandemic poses a limitation. Video or voice calls alone may not fully depict the respondent's expression and validity of the data captured.

INTRODUCTION

During the 20th century, there was a significant increase in life expectancy, attributed mainly to improvements in child survival. Universal child immunisation has been an effective preventive measure for protecting the vulnerable group. Immunisation has prevented millions of deaths related to vaccine-preventable diseases (VPDs) around the world[1]. From 2007 to 2010, global third dose diphtheria, tetanus and pertussis (DTP3) coverage increased from 79% to 84% but has been plateauing since 2010. DTP3 coverage varies by region, being only 72% in the World Health Organization (WHO) African Region while it is 97% in the WHO Western Pacific Region[2].

The reasons for low vaccination uptake are often not completely understood and appear to be multifactorial. Inadequate vaccination coverage can be related to both demand and supply side determinants. Most of the reasons for the low uptake of childhood vaccination in developing countries are related to lack of access to vaccination and family factors. Low education, literacy and socioeconomic status are well-known indirect contributors to coverage not being achieved. However, in several developing countries, the weakness of the health system is considered a significant barrier[3 4]. Persistent challenges seen related to acceptance of the services that affect vaccine uptake, especially in developing countries[5,6].

Vaccine hesitancy is a behavioural phenomenon among both those who accept all vaccines without hesitation and those refuse all vaccines[7,8]. Vaccine hesitancy has been recognised as a growing problem of global importance that affects both developing and developed countries. The WHO has defined it as a delay in acceptance or refusal of vaccines despite the availability of vaccine services[9]. Recently, vaccine hesitancy prevalence has emerged as a global problem and is evident in poor childhood vaccination coverage. The WHO has identified it as a priority issue and has developed a vaccine hesitancy model framework that emphasises confidence, complacency and convenience[9]. The framework was expanded to included confidence, complacency, constraints, risk calculation and collective responsibility. These factors were identified as the psychological antecedents of vaccination[10]. These models have been suggested based on research predominantly conducted in well-developed and high-income countries[11]. Studies in neighbouring Arab countries have addressed parental vaccine hesitancy as a concerning problem that likely influences the uptake of childhood vaccination[12,13]. However, to the best of our knowledge, no published study to date has addressed vaccine hesitancy in Yemen.

Yemen's Issues and Challenges Regarding Child Immunisation

Yemen is a low-income Arabic country with poor socioeconomic status and a fragile health system. It has a hard geographic environment, which affects access to essential basic services, and limited financial support for covering costs presents a major challenge[14]. Since March 2015, Yemen had been engaged in civil war, which has continued to date. Civil war and internal conflict affect local development in Yemen[15,16]. The instability, shortage of services and internal displacement may lead to limited vaccination coverage[17]. The Expanded Program of Immunisation (EPI) in Yemen was initiated in 1979 as a part of the Primary Health Care General Directorate in Public Health and Population. It is aimed at preventing morbidity and mortality from Vaccine Preventable Diseases (VPDs). The target groups are infants, and women of child-bearing age[18]. Routine immunisation services in Yemen are provided through fixed vaccination posts within health facilities and outreach vaccination strategies and are based on the proximity of the target populations to the health facility. Table 1 shows the standard schedule of routine immunisation of children in Yemen.

Table 1: Standard schedule of routine immunisation of children in the Republic of Yemen

Vaccine	Age					
	At birth	6 weeks	10 weeks	14 weeks	9 months	18 months
BCG*	×					
OPV*	×	×	×	×	×	×
Pentavalent (DPT,Hep B,Hib)		×	×	×		
Pneumococcal		×	×	×		
Rotavirus		×	×			
MR*					×	×
IPV*				×		

*BCG: Bacillus Calmette-Guerin, OPV: oral polio vaccine, DPT: Diphtheria, Tetanus and Pertussis, Hep B: Hepatitis B, Hib: Hemophilus influenzae type b, MR: measles and rubella, IPV: inactivated poliovirus vaccine

According to the last Yemen National Health and Demographic Survey, in 2013, only 42.6% of children aged 12–23 months were fully vaccinated, while 16% did not receive any vaccination. No reported published data are available for comparison on trend. However, vaccines for significant VPDs are publicly available for free[19]. The WHO and the United Nations

International Children's Emergency Fund (UNICEF) reported that the 2018 vaccination coverage for Yemen was 65% based on DTP3, which remains below the 90% every country has achieved by 2020[20]. From previous studies performed in Yemen, we may conclude that even before the war, vaccination coverage in Yemen had not been meeting an acceptable target, and the percentage of children who are completely unvaccinated has increased. In addition, various Governorates of Yemen have reported that children are unvaccinated or partially vaccinated mainly due to a lack of information and parental motivation[18, 21-23].

The Rationale for This Research

Although vaccine hesitancy has been addressed extensively in the literature in the past few years, few studies have explored this issue in low-income countries. Thus, most findings and models developed are based on studies performed in high-income countries[11]. Limited studies have addressed the issue of childhood vaccination in Yemen, and most studies have focused on coverage and the reasons for non-vaccination[17 18 22 23]. Only one study has addressed the determinants of complete vaccination[21], although it did not address the issue of vaccine hesitancy. Furthermore, all published studies addressing childhood vaccination in Yemen used a quantitative method, which cannot yield in-depth details on the problem when integrated with available qualitative study findings. In addition, all community-based studies performed in Yemen explored the problem from the parents' perspective only and did not consider that of the healthcare workers, who can provide a bigger picture of the problem.

Studying the perspective of parents and healthcare workers on vaccine hesitancy regarding childhood vaccination is vital for improving service delivery and vaccine uptake. In addition, it aids the reduction of the high morbidity and mortality rate among children from VPDs, which are the leading cause of under-five mortality. Therefore, understanding their perceptions is crucial, as they play a vital role in vaccination programs. Furthermore, exploring their perspectives would be informative for understanding the barriers they face. Accordingly, to bridge the knowledge gap in the literature on vaccine hesitancy and childhood vaccination in Yemen, the present study is a mixed-method study for assessing the determinants of vaccine hesitancy from the perspective of parents and healthcare workers. A conceptual framework (Figure 1) illustrates the concept of the present study to bridge the evidence gap in the literature, which must be explored.

Aims and Objectives

This research aims to address the issue of vaccine hesitancy and child immunisation status among children living in Costal Hadhramout, Hadhramout Governorate, Yemen, from the perspective of parents and healthcare providers. The specific research objectives are:

1. To conduct a situational analysis of routine childhood immunisation EPI data in Costal Hadhramout.
2. To measure the prevalence of vaccine hesitancy and child immunisation status among children and their mothers living in Costal Hadhramout.
3. To identify the associated factors and predict the vaccine hesitancy and immunisation status of children living in Costal Hadhramout.
4. To explore mothers' reasons for hesitancy regarding childhood vaccination.
5. To explore the barriers healthcare providers face in achieving immunisation coverage in Costal Hadhramout.

METHODS

A complementary explanatory sequential mixed-method study design is used. The study will take place in Hadhramout in Yemen, consisting of 30 districts and occupying vast areas of the Arabian Sea coast. Hadhramout is divided administratively into two parts: the valley/desert (Wadi Hadhramout) and the coast (Coastal Hadhramout). Coastal Hadhramout overlooks south to the Arabian Sea and has a coastline of approximately 120 km. The estimated total population of Coastal Hadhramout in 2018 was 893,502 people. The population grows at a rate of 3.08% annually. This research targets the 12 districts of Coastal Hadhramout: Al-Mukalla, rural Al-Mukulla, Gail Bawazeer, Al-Shahr, Al-Dees, Ridh and Gosaiar, Ghail bin Yumin, Doan, Al-dulaia, Yeabeth, Hajer and Broome-Mayfa'a[24]. This study will consist of three phases: (1) situation analysis, (2) quantitative study and (3) qualitative study. Figure 2 illustrates the overview of the study phases and their flow.

Phase 1: Situation analysis

Phase 1 is a retrospective descriptive study. The records from the national immunisation program for the past 10 years (from January 2011 to December 2020) for the 12 Coastal Hadhramout districts will be reviewed and analysed (secondary data analysis). After permission has been obtained from the general manager of the Coastal Hadhramout Health and Population Affairs Office, data will be extracted from Coastal Hadhramout Health and Population Affairs Office Department of EPI data. First, we will assess the immunisation coverage rate (estimated for each vaccine, and for multi-dose vaccines, for each dose received (e.g., diphtheria-tetanus-pertussis-containing vaccine (DTPCV1, DTPCV2, DTPCV3) in each year (trend analysis, the first outcome of this phase). The districts will be classified into good or low coverage. The classification will be dependent on the Global Immunisation Vision and Strategy goal: at least 90% national vaccination coverage and at least 80% vaccination coverage in every district or equivalent administrative unit. Therefore, each district with ≥80% coverage will be classified as good coverage while any district with <80% coverage will be considered a low-coverage district. This classification is the second outcome of this phase and will be used for selecting districts in Phase 2. Phase1 data collection and analysis began in August 2021 and ended in December 2021.

Phase 2: Quantitative study

Phase 2 uses a community-based, cross-sectional study design. The study population is the mothers or caretakers of children aged <2 years in 2021 and living in Coastal Hadhramout. The study will use stratified cluster sampling, combining stratified and cluster sampling methods. First, the 12 Coastal Hadhramout districts will be stratified by immunisation coverage level, i.e. good or low as per Phase 1. Two districts will be selected randomly from each stratum. Second, a 30-household cluster (estimated by the researcher and may be more based on the absolute number of houses in each cluster) will be chosen from the selected districts proportionally to size. Then, all households in those clusters will be surveyed for an eligible child.

The researcher will prepare the sampling frame used in this study after consultation with the Coastal Hadhramout EPI director-general. Moreover, this sampling frame will be prepared based on the list of household distribution used in the last National Immunisation Days (NIDs). The clusters in each district will be identified based on this list (every cluster contains approximately 20–30 households). Then, the researcher will select the number of clusters required to cover the sample size in this study from each district proportionally. In this study, an eligible mother or caretaker refers to a mother with a child aged <2 years. The youngest child will

be taken for mothers with more than one child aged <2 years. We will exclude non-Yemeni families.

The sample size for this phase is calculated based on estimating proportion (prevalence) using the Kish formula[25] and comparing two proportions using the Fleiss formula[26] with a confidence interval of 95% and study power of 0.80. The largest sample size derived using both formulae was 767, so this will be the sample size for this phase. The researcher and research assistants (health workers) will collect data from the households in the selected clusters. Four health workers will be trained to collect data from the mothers. During fieldwork, each health worker will work in a team. Each team will be supervised in the field by the researcher or fieldwork supervisor. Respondents will be interviewed using a structured, pretested designed questionnaire related to vaccine hesitancy perception (VHP) after being informed of the purpose of the study and after agreeing to participate in the study.

The VHP questionnaire will be adopted from varies validated questionnaire and adapted to the Yemeni population. The VHP questionnaire will cover the following domains: Domain 1: Child-related characteristics, e.g. age, sex, birth order, place and type of delivery, gestational age at delivery and health status. Domain 2: Family-related characteristics, e.g. age, education, work, monthly income, residency and number of people living in the family. Domain 3: Immunisation-related knowledge. Domain 4: vaccine hesitancy. Domain 5: Psychological antecedents of vaccination (confidence, complacency, constraints, calculation, collective responsibility). Domain 6: Vaccination status of the child (full, partial or unvaccinated) based on the child's immunisation card and history of immunisation provided by the mother. Domain 7: Availability and accessibility to vaccination service. Domain 8: Reasons for the child's incomplete vaccination or non-vaccination. Table 2 lists the operational definitions of the study variables.

In this study, the primary dependent variable is the mother's hesitancy level, which will be assessed using an Arabic version of the Parent Attitudes about Childhood Vaccines questionnaire (PACV) after granted permission from the author[12 27]. The PACV questionnaire is divided into three domains: behaviour, safety and efficacy, and general attitude and trust. Fifteen items are grouped under these domains. The PACV uses a numeric score, where items answered with a hesitant response are scored 2 points, items answered with a response of do not know or not sure are scored 1 point and items answered with a non-hesitant response are scored 0 points. The raw score is then converted to a score of 0–100. Accordingly, parents are assigned 1 to indicate a hesitant score ≥ 50 or 0 as a non-hesitant parent with a score < 50.

The second dependent variable in this study is the immunisation (vaccination) status of children aged 12–23 months. The immunisation status is classified as complete (Full), incomplete or unimmunised. These classifications are defined according to the Yemini EPI schedule: Complete (Full) immunisation: A child aged 12–23 months who has received one bacillus Calmette-Guerin (BCG) dose, at least three doses of pentavalent vaccine, at least three doses of pneumococcal vaccine, at least three doses of oral polio vaccine (OPV), two doses of rotavirus vaccine and one dose of MR (measles and rubella) vaccine. Incomplete immunisation: A child who has not received all routine EPI vaccines before their first birthday. Unimmunised (unvaccinated): A child who did not receive any of the 13 doses of the recommended vaccines[22].

The independent variables in our study are the child and family characteristics: Age, sex, birth order, place and type of delivery, gestational age at delivery and health status of the child; parents' age, education, work, monthly income, residence and number of people living in the family. Immunisation-related knowledge: This variable will be assessed using a scale adapted from a previous study performed in Yemen[21]. Psychological antecedents of vaccination: Confidence, complacency, constraints, calculation and collective responsibility (5C scale). These variables will be measured using the 5C scale[10]. To the best of our knowledge, there is no Arabic version of the 5C scale. Therefore, according to the sample study protocol, the translation and validation of the 5C scale proposed by Betsch, et al. [28] will be used. Availability and accessibility of vaccination service will be assessed using four questions adapted from the literature[21]. After permission has been obtained from the author, all mentioned scales will be adapted to suit the local population.

The validity and reliability of the VHP questionnaire will be assessed. The univariate analysis describes frequencies and percentages. The associations between dependent and independent variables will be assessed with bivariate analysis. A p-value of <0.05 will determine the significant variables. The effect of different variables on hesitancy and children's immunisation status will be assessed with multiple logistic regression. The results will be presented as tables and graphs. Data collection and analysis for this phase will begin in January 2022 and should end in May 2022.

Phase 3: Qualitative study

The case study will be conducted in Coastal Hadhramout. The study population is the mothers/caretakers who participated in Phase 2 and who were identified as hesitant mothers, and

the healthcare providers and health leaders involved in the immunisation program in Coastal Hadhramout. This phase will involve purposive sampling. Mothers/caretakers will be selected from among those who participated in Phase 2 and showed good cooperation. Healthcare providers and leaders will be selected from the health facilities that provide immunisation in the selected cluster areas in Phase 2.

Data will be collected through in-depth interviews with the mothers/caretakers and from healthcare providers and health leaders via focus group discussions (FGD) (Table 3). The in-depth interviews and FGD will be performed until saturation is reached after triangulation. Then, thematic analysis will be performed to analyse the contents of in-depth interviews and FGD. Table 3 lists the key questions. Data collection and analysis for this phase will begin in June 2022 and should end in October 2022.

Patient and Public Involvement

The participants, i.e. the parents and healthcare providers, will be involved in the study design mainly in Phase 2. In this phase, a research team will pilot and test the study tools, which would require contributions from the participants. Furthermore, in Phase 3, participants will have the opportunity to present any additional comments during the interview and FGD. Therefore, their priorities, experiences and perception can be taken into consideration.

ETHICS AND DISSEMINATION

The study proposal has been reviewed and approved by the Research Ethics Committee of the Faculty of Medicine, University Kebangsaan Malaysia (project code: FF-2021-051). Permission for conducting the research has been obtained from the Costal Hadhramout health affairs office. The participants will receive a simple and clear explanation of the study's aim and procedure. Consent will be obtained from all participants. Personal safety risks to the participants or researchers involved in this study are not expected. The participants' privacy and confidentiality will be assured. The findings will be communicated through publication in peer-reviewed academic journals and disseminated to healthcare professionals, stakeholders, researchers and the public through academic conferences and public presentations.

Table 2 List of independent variables and their definitions in this study

Independent variable	Definition and analysis
I. Child-related variables	
Age	Age in months at data collection obtained from the child's birth certificate, immunisation card or by asking the mother/caretaker. The mean and SD will be calculated.
Sex	Male or female.
Birth order	The child's position among their siblings. Categorised as firstborn, 2–3, 4–5 and ≥6[29].
Place of delivery	At a health facility or at home[29 30].
Type of delivery	Vaginal or caesarean[21].
Gestational age at delivery	Full-term or premature.
Health status	Well or has a medical problem.
ii. Family-related variables	
Mother's age (years)	Age in years at data collection. The mean and SD will be calculated.
Age at first birth (years)	Mother's age when she birthed her first child. The mean and SD will be calculated.
Mother's marital status	Married or unmarried (divorced or widowed)[21].
Mother's education level	The highest formal education gained. Categorised as illiterate, able to read and write, essential education, secondary education or university and above[31].
Mother's occupation	Employed or homemaker[32].
Father's education level	The highest formal education gained. Categorised as illiterate, able to read and write, essential education, secondary education or university and above.
Father's occupation	Government employee, daily labourer, merchant, unemployed or other.
Family size	The total number of persons living in the household[33].
Family residency	Permanent place of residence of the child's family. Categorised as urban or rural[21 34].
Monthly family income	Average total income per month in Yemeni riyals (YR). The mean and SD will be calculated.
III. Mother/caretaker's immunisation-related knowledge	
Source of information	The source from which the participant learns about vaccination and VPD. Categorised as 0 = Radio, 1 = TV, 2 = internet, 3 = friends, 4 = schools, 5 = health personnel, 6 = other.
Immunisation-related knowledge	The mother's knowledge on VPDs, the best means of protection against VPDs, the causes of VPDs, number of vaccine doses, and the time of vaccine administration was assessed through five groups of questions containing 38 items. Each item was scored as I = correct, 0 = wrong, or 0=Don't' know the answer. The scale is adapted from a previous study performed in Yemen after permission has been obtained from the author[21]. Analysis: The total knowledge score is calculated by summing the participant's responses. The median of the summative calculation score will be used. We classify it as 0 = poor knowledge (less than the median score) or 1 = good knowledge (equal and more than the median score).
V. Physiological antecedents of vaccination. These variables will be measured by using the 5C scale[10]	
Confidence	Assessed via three items from the 5C scale: 1) I am completely confident that vaccines are safe. 2) Vaccinations are effective. 3) Regarding vaccines, I am confident that public authorities decide in the best interest of the community. Each item is scored on a 7-point Likert scale (1 = strongly disagree, 2 = moderately disagree, 3 = slightly disagree, 4 = neutral (neither disagree nor agree), 5 = slightly agree, 6 = moderately agree, 7 = strongly agree). Analysis: The mean score will be calculated by summing the participant's responses for the three items and dividing it by 3[10].

Complacency	Assessed via three items from the 5C scale: 1) Vaccination is unnecessary because VPDs are not common anymore. 2) My immune system is strong, and it also protects me against diseases. 3) VPDs are not so severe that I should be vaccinated. Each item is scored on a 7-point Likert scale as described for the confidence variable. Analysis: The mean score will be calculated by summing the participant's responses to the three items and dividing it by 3[10].
Constraints	Assessed via three items from the 5C scale: 1) Everyday stress prevents me from being vaccinated. 2) For me, it is inconvenient to be vaccinated. 3) Visiting the doctor makes me feel uncomfortable; this keeps me is being vaccinated. Each item is scored on a 7-point Likert scale as described for the confidence variable. Analysis: The mean score will be calculated by summing the participant's responses to the three items and dividing it by 3[10].
Calculation	Assessed via three items from the 5C scale: 1) When I think about being vaccinated, I weigh its benefits and risks to make the best decision possible. 2) For every vaccination, I closely consider whether it is useful for me. 3) I need to understand the topic of vaccination before I get vaccinated fully. Each item is scored on a 7-point Likert scale same as described for the confidence variable. Analysis: The mean score will be calculated by summing the participant's responses to the three items and dividing it by 3[10].
Collective responsibility	Assessed via three items from the 5C scale: 1) When everyone else is vaccinated, I do not have to be vaccinated too. 2) I get vaccinated because I can also protect people with a weaker immune system. 3) Vaccination is a collective action to prevent the spread of diseases. Each item is scored on a 7-point Likert scale as described for the confidence variable. Analysis: The mean score will be calculated by summing the participant's responses to the three items and dividing it by 3[10].
VI. Access to vaccination service	
Distance	The time taken to reach the nearest health facility. Categorised as 0 = ≤30 min, 1 = >30 min.
Means of accessing the health facility	Refers to how parents can arrive at the health facility, i.e. either by walking or using transport.
Availability of vaccine or vaccinator	Refers to whether the vaccines and vaccinator are available at the health facility.
Waiting time	Refers to the parents waiting for a long time before their child can be vaccinated.

Table 3: Critical questions for the qualitative phase

A. The key question for the in-depth interview with the mothers	B. The critical question for the FGD with the healthcare providers and leaders
Why do parents refuse or not complete vaccination for their children? - Socioeconomic reasons - Cultural and religious reasons - Parental vaccination knowledge reasons - Service access reasons - Staff-related reasons	What are the barriers to achieving immunisation coverage? - Staff knowledge barriers - Staff communication skill barriers - Staff training and competency barriers - Staff numbers barriers - Supply and infrastructure barriers

Figure legend/caption:

Figure 1: Conceptual Framework

Figure2: An overview of the study phases

Author Contributions

Batarfi, Suha Ali: write the research protocol, conduct, and report of the work described in the article. Sutan, Rosnah: provide idea in research protocol planning, review critically information reporting of the work described in the article. Ismail, Halim: review critically information reporting of the work described in the article. Bin-Ghouth, Abdulla Salem: review critically information reporting of the work described in the article. Batarfi, Suha Ali and Sutan, Rosnah: responsible for the overall content as guarantor(s)

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ORCID iDs:

Rosnah Sutan: https://orcid.org/0000-0001-9956-4727

Suha Ali Batarfi: https://orcid.org/0000-0003-0060-5694

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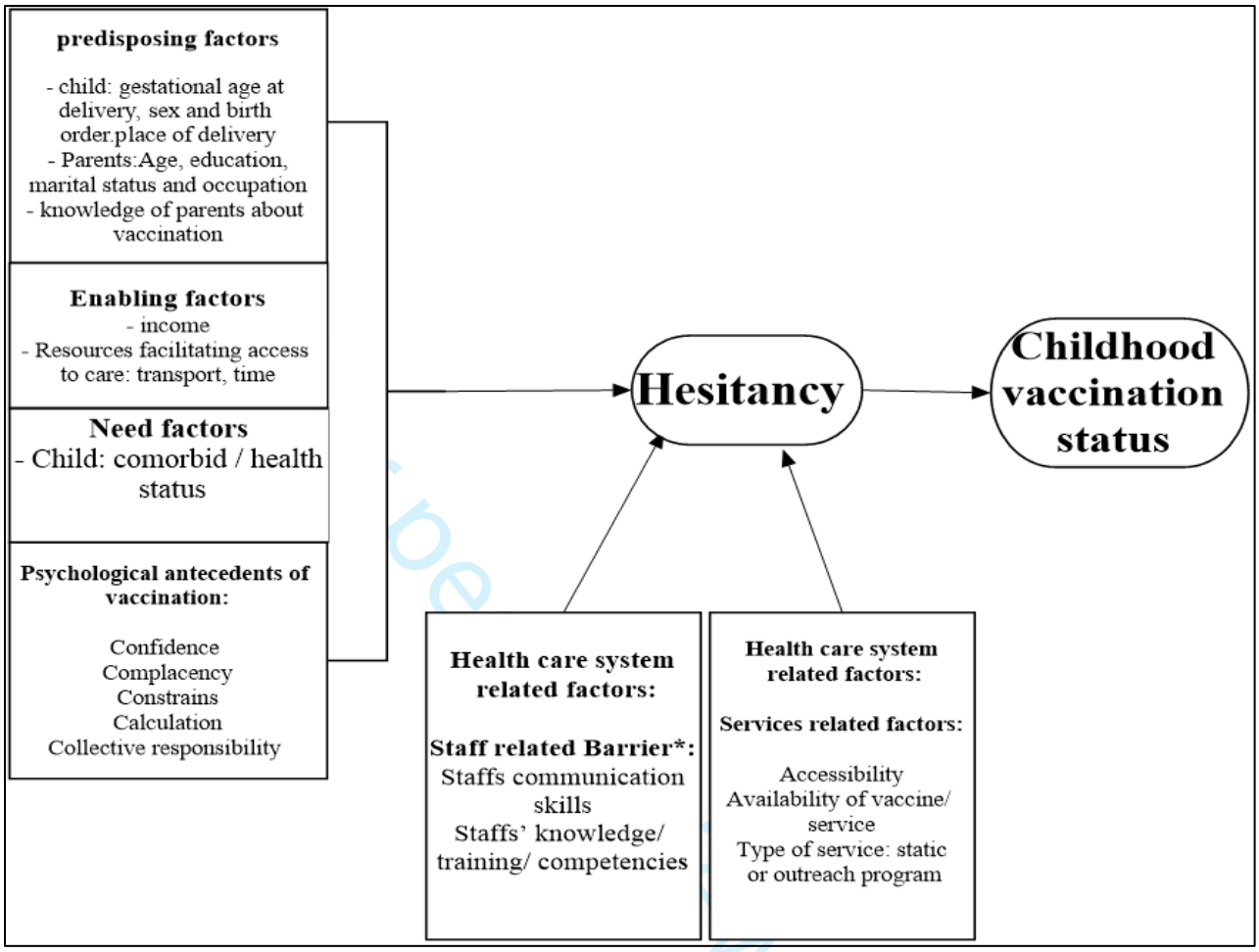

Figure 1: Conceptual Framework

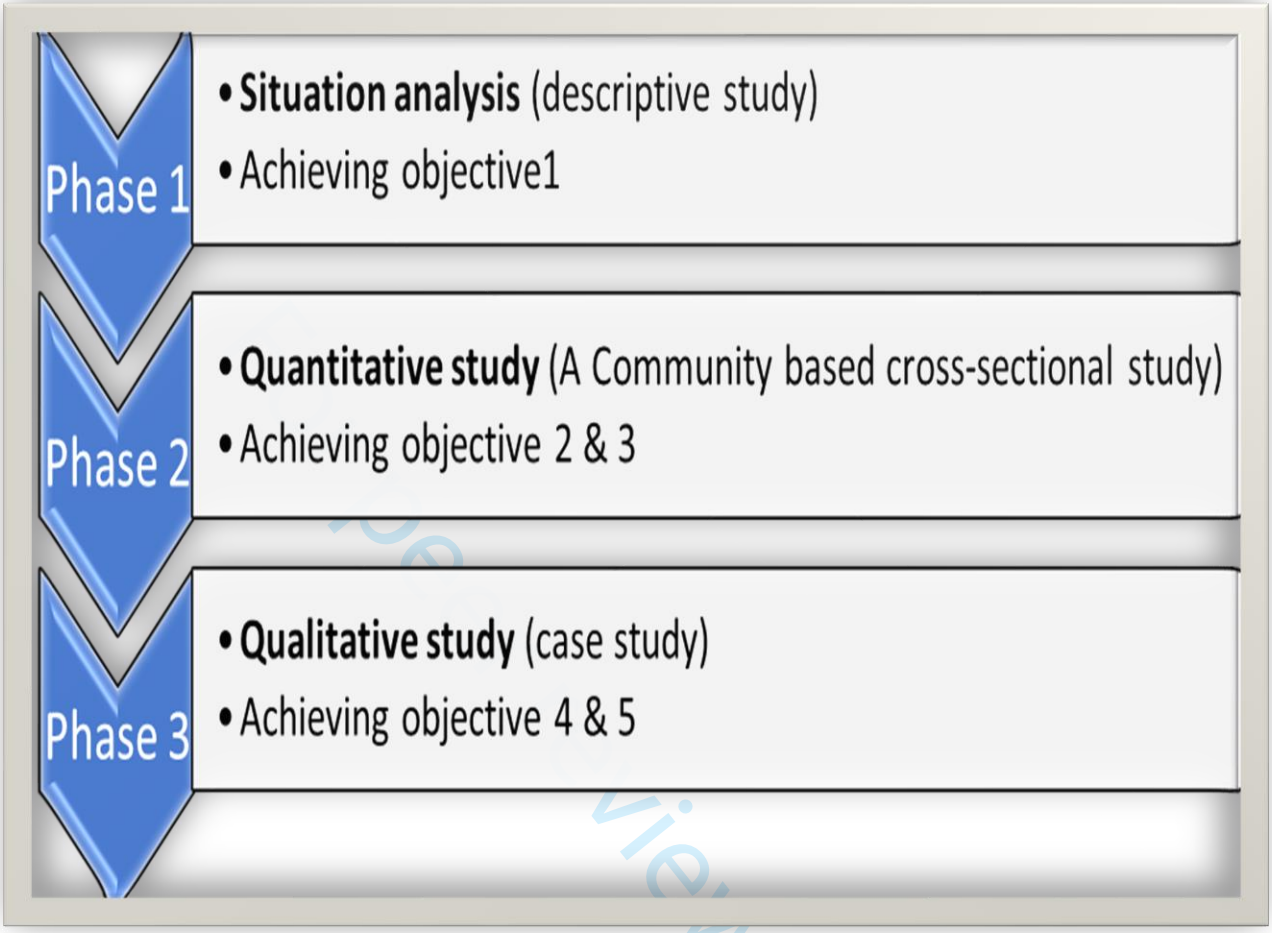

Figure2: An Overview of the Study Phases