Study Profile

The Trend of National and Subnational Burden of Maternal Conditions in Iran from 1990 to 2013: The Study Protocol

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Abstract

Background: It is widely accepted that maternal mortality is a proxy for maternal health status. Maternal deaths only represent the top of the iceberg; morbidity due to maternal causes apart from maternal mortality, poses a huge burden on women's families. There is an excessive need to widen the research on maternal morbidity. Here, we explain the framework of our study on maternal conditions and their burden in Iran as a part of the National and Sub-national Burden of Diseases (NASBOD) study.

Methods: A systematic search will be carried out for both published and unpublished data on maternal mortality and morbidity reported between 1985 and 2013. Data collected through systematic review and those obtained from national and sub-national surveys will be extracted in a data set. Two statistical models will be applied: Bayesian Autoregressive Multi-level models and Spatio-Temporal Regression models. Models will be used to overcome the problem of data gaps across provinces, years and age groups.

Discussion: In order to control and manage maternal conditions and to make more efficient and cost-effective policies, there is an excessive need for data on the burden of such diseases. There are a few sub-national analyses of the burden of disease. In the current study, burden of maternal conditions will be assessed at national and sub-national levels in Iran between 1990 and 2013. The results of this study are undoubtedly required to provide comprehensive information at the national and provincial levels to administer interventions more effectively, since the priority based policies need regional assessments and comparisons.

Keywords: Burden of diseases, Iran, maternal condition, middle east, study profile

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Introduction

It is widely accepted that maternal mortality is a proxy for maternal health status. Reducing maternal mortality to one fourth of its level in 1990 is one of the millennium development goals for 2015, which shows its importance not only as a health indicator but also as a milestone for development.[1] Globally, maternal deaths have declined from 543,000 cases in 1990 to 287,000 in 2010. Nevertheless, the reduction in maternal mortality rate (MMR) lags behind the Millennium Development Goals(MDG's).[2] These initiatives have been the cause of some progresses in developing countries yet Asia and Africa are still suffering from higher MMR.[3]

Hogan, et al. showed a declining trend of MMR in Iran, changing from 101 in 1980, 64 in 1995, and 36 in 2000 to 28 (per 100,000) in 2008.[4] The State of the World's Population 2012 reported Iran's MMR to be 21/100,000 live births.[5] However, in 2000s in Iran, the major causes of pregnancy – related deaths were hemorrhage, eclampsia, and infection.[6]

Maternal deaths only represent the tip of the iceberg. Apart from mortality, the morbidity due to maternal causes additionally poses a huge burden on women's families. There is an excessive need to widen the research efforts to address maternal morbidity. Studies focusing only on maternal mortalities may overlook the most common causes of maternal morbidity and the major issues in obstetric care.[7]

The results of national study burden of diseases in 2003 showed that DALYs of maternal condition in Iran was 81221.[6] In order to control and manage maternal conditions and their burden, more efficient and cost-effective policies are undoubtedly required. To administer interventions more effectively, the priority-based policies need regional assessments and comparisons. Evidence-based resource allocation at the national and provincial levels leads to the provision of a package of services tailored to diverse communities. Consequently, preventive interventions and treatments can be applied based on the regional requirements and conditions.

We will introduce and discuss the general framework for the study of maternal condition and its burden in Iran, which is a part of the National and Sub-national Burden of Diseases[8] study from

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1990 to 2013. The first objective of this study is to estimate national and sub-national trends of incidence and burden of maternal conditions among Iranian population from 1990 to 2013. The second is to estimate national and sub-national inequalities of maternal condition and its burden in Iran from 1990 to 2013.

Materials and Methods

Executive study phases

One of the sub-groups of NASBOD team is the maternal condition group that incorporates domestic and international members and consultants from Tehran University of Medical Sciences, Shahid Beheshti University of Medical Sciences. The group will conduct a systematic review of the prevalence/incidence of maternal mortality and morbidities among Iranian population from 1990 to 2013. Additionally, using the data provided by the maternal mortality surveillance system, mortalities will be calculated by province.

Diseases selection and definitions

In this study, similar to the project carried out by World Health Organization, the technical committee decided to include only three direct obstetric causes of morbidity and mortality: post-partum hemorrhage, post- partum infection, and preeclampsia and eclampsia. Definitions of maternal conditions and sequelae were adopted from GBD 2010 (Table 1). Various heterogeneous data sources will be used in the present study that could be categorized in two main groups:

A. In general, published, unpublished, and grey literature will be used as sources of data in the present study.

B. Data from National surveys will be utilized accordingly.

A) Published, Unpublished and Grey literature

A systematic search will be carried out for both published and unpublished data on maternal mortality and morbidity reported between 1985 and 2013. The sources of search will include three electronic international (ISI Web of Science, Scopus, Pubmed) and three Iranian databases (IranMedex, SID Iran.doc). Hand searching, screening reference lists of the retrieved articles, conference abstracts, books, and conference proceedings will be searched as well. Experts in respective fields will be contacted and invited to collaborate in enriching the available datasets.

Appendix-1 shows search activities in the selected search engines. It presents all MeSH terms, Entry terms and Emtree used for searching in PubMed, ISI and Scopus, and all Persian equivalents used for searching in IranMedex, SID and Iran.doc. Population-based studies at national, provincial, district and community levels, reporting the prevalence and/or incidence of maternal conditions, will be included in our study. All included papers from January 1990 to December 2013 will be reviewed. Both English and Persian language papers will be included. Studies that have not reported sampling methods, have used non-representative sampling frame, and have selected their participants through non-probability sampling methods will be excluded. Research papers will be retrieved and will be reviewed by two independent reviewers.

B) National data

National maternal mortality Surveillance system and death registration system

The maternal deaths reported by national maternal mortality surveillance system will be compared with the maternal deaths reported by the death registration system (Mohammadi, et al.) and if there would be any difference between the two sources, the incompleteness of each registration system will be estimated using capture recapture methods.

Other National Data

We will utilize National and Sub-national data of Zij Hayati, IMES (Integrated Monitoring and Evaluation Survey 2006), and DHS (Demographic and Health Survey 2000).

Hospital data

We will utilize hospital discharge data as an important source of data about pregnancy complications. While using this data source, we should take into account the problems associated with the selection bias and the variations of patients in terms of access to hospital care. More details on hospital registry data are described elsewhere.[9]

Data extraction

Included studies will be reviewed and all needed information will be extracted and inserted in data extraction sheet. The data collected from registration systems and other national studies, which provide the individual level data, will be aggregated and inserted in the data extraction sheet. All studies included in our review will be cited in the final report and in the publications of NASBOD results. If we need more detailed information, we will contact the corresponding authors of each study and ask them to re-analyze the data. In such a case, we will add the name of authors as our collaborating coauthors. Finally, data extraction sheet will be used to summarize the study data by age, sample size, prevalence, incidence, mean, standard deviation, standard error and confidence interval, (Table2).

Statistical methods and analysis plans

To overcome the gap caused by the lack of representative data at provincial level, in some age groups,, two distinct statistical models (includes Spatio-temporal regression model and Bayesian multilevel autoregressive model) will be used to estimate mean and uncertainty intervals. The data will be entered into the models by age, year, and province. The problem of misalignment due to changes in provincial map is going to be addressed by both models. Using two different models will reduce model dependency of the results.

Spatio-temporal regression model

One of the commonly used frameworks to overcome the above-mentioned limitations is Spatio-temporal regression modeling with Conditional Auto Regression (CAR) prior to spatial and temporal random effects.[10] In spatial framework, observations that are closer in space are assumed to be more correlated than observations farther away. The structure enables model to "borrow information" from neighboring areal units and time periods to improve estimates for areas and times with missing values and/or small number of observations. In addition, we will employ Spatio-temporal misalignment modeling to combine incompatible areal units between data sources and/or over the years. The model covers covariates effects, non-linear age trend, and variations in the study quality and source of data.[11]

Table 1. Case and sequelae definitions for Maternal Conditions

Cause / sub-cause	Compatibility with clinical sequela	Sequela name	Description	ICD-10 Cods for maternal morbidity conditions O00-O99
Maternal hemorrhage		Anemia, mild	This person feels slightly tired and weak at times, but this does not interfere with normal daily activities	O20, O44–O46, O67, O72
Maternal sepsis		Abdomino-pelvic problem, mild	This person has some pain in the belly that causes nausea but does not interfere with daily activities.	O85–O86
Hypertensive disorders of pregnancy	Compatible with temporary renal complications	Chronic kidney disease (stage IV)	This person feels tired easily, has nausea, reduced appetite and difficulty sleeping.	O10–O16
Abortion	Acute short duration disability	Abdominopelvic problem, mild	This person has some pain in the belly that causes nausea but does not interfere with daily activities.	

[a]Each piece of this table may be updated during the study.

Table 2.

General information	Study name, citation, city (where the study was conducted), publication year, study year, journal, characteristics and contact address of corresponding author. Population characteristics: Age (age groups as, 10–14,15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49)
Methodological information	Study design, data source, scope of study (urban, rural or Urban-rural), coverage of the study (national, provincial, district, and community level), measurement tools, sample size, sampling method, sample weight, response rate.
Study outcomes	Proportion of cases to the total number of population included in the study (prevalence), incidence, mortality; all presented with 95 % uncertainty interval and stratified by age groups.

Bayesian Multilevel Autoregressive model

Another advanced method to handle the challenges is Bayesian autoregressive multi-level model.[12] In this framework, observations are hierarchically nested at districts, provinces, sub-regions, regions, and national levels, respectively. In this hierarchical model, lower levels borrow information from the higher levels and units of each level borrow information from each other depending on the degree of data availability. The model considers several different components including linear time trends, nonlinear change over time, covariate effects, non-linearity associated with age, heterogeneity of data sources, and age-by-study variability. Time-varying covariates at district-level or province-level covariates inform the estimates, if practical.[13]

It is difficult to estimate abortion-caused morbidity because it usually happens in places where abortion is illegal and there is no precise information about such cases.[11] Therefore, it is necessary to use adjustment methods to correct the problem of under reporting.[14] In this study adjustment methods will be used to correct under reporting.

All programs will be written in R-statistical packages (version 3.0.1).

Since the present work is a secondary study, there are no specific ethical considerations. However, the publication of the results will depend on the permission of the study funders. Likewise, Tehran University of Medical Sciences' Institutional Review Board has approved this study in terms of ethical considerations.

Discussion

The study of the burden of maternal conditions as a sub-component of a comprehensive project named NASBOD[8] has been designed to understanding geographic distributions of the selected Maternal conditions and health gaps in this population and their inequality between provinces.

Some research studies in the world have estimated the burden of maternal condition at Regional or National level.[15–17]

In 2003, the burden of diseases was estimated in Iran based on nationally representative data.[6] Drawing from the experiences learned through the GBD 2010 and the previous national study in 2003, the National and Sub-national Burden of Diseases (NASBOD) study was designed as the first effort to provide national and sub-national estimates for burden of diseases in Iran over the past two decades.

While studying to estimate the burden of pregnancy morbidity, the World Health Organization faced a significant shortage of data and therefore, it determined the rates of just five direct obstetric causes of morbidity and mortality, including: post-partum hemorrhage, post- partum infection, preeclampsia and eclampsia, obstructed labor, and abortion. On the other hand, all types of morbidity do not lead in maternal mortality.[14] In the present study, only three direct obstetric causes of morbidity and mortality are included.

It is difficult to estimate the burden of morbidity; a major problem in estimating pregnancy complications is the disparity of data sources that are not comparable. Hence, the World Health Organization computes MMR based on systematic reviews and expert consensus.[14] Unfortunately, in Iran due to the lack of community-based studies with soundness methodology, we do not have reliable estimates of total morbidity caused by acute and long-term conditions related to pregnancy and childbirth. Under this scenario, national estimate of maternal morbidities is practically incomplete and relying only on national Maternal Mortality and Morbidity statistics hides the differences between regions and population subgroups (age, region geography, and race). In this study, the data collected from different sources are used to estimate the incidence and prevalence of Maternal morbidity via the

systematic review methodology.

The variety of sources and methods used to calculate maternal mortality rate and the absence of national data in many countries are the main problems identified by the global surveillance system of maternal mortality rate.[8] Consequently, in 2000, the World Health Organization used a regression model to estimate MMR in 62 countries without national maternal mortality data.[18] The underestimation of MMR is not only due to sampling errors, but it is also caused by differences in the precision of reporting and classification systems within different regions and populations.[13] In order to control consistency, it seems important to compare estimates from various sources with the estimates produced by the multiple regression model.[9,19]

To measure health inequalities, it is essential to find out how these differences are distributed among the populations and also to determine whether the distributions are socially plausible or not. Studies on health inequalities are mainly focused on inequalities in non-biological factors such as gender, nationality, race and income.[16] Currently, novel methodologies and different data sources allow more precise estimates of maternal mortality and morbidity,[4] and their inequality between provinces.

The key differences of this study with the previous study in Iran are including scope and coverage of the study, data sources, and methods and analyses.[8] Given the availability of high quality sub-national data and updated analytic methods, the NASBOD study will provide a chance to assess both in-depth sub-national estimates and trends in epidemiological metrics of diseases over the period 1990 – 2013 in Iran. It provides a clearer picture for disease management and efficient interventions and can help the health system to allocate services effectively and cover the related ethical issues.

The limitations of this study are as follows: First, we will use various sources of data, and there may be heterogeneity between data sources, which will be managed by methodological strategies. Second, there may be limited access to the full texts of certain published or unpublished epidemiological studies, as one of the main data sources. Third, due to absence of community-based studies, there are not sufficient data on maternal conditions. Finally, for estimating abortion-caused morbidity, it usually happens in places where abortion is illegal and there is no precise information about such cases, in this study adjustment methods will be used to correct under reporting.

This study is the first comprehensive systematic study assessing the prevalence and burden of maternal conditions in Iran at national and sub-national levels. Since the findings will be used to identify distributions and inequalities of maternal conditions in our country, they can play an important role in directing future policies and planning cost-effective strategies .

Abbreviations

DALY: Disability-Adjusted Life Years; GBD: Global Burden of Disease; NASBOD: National and Sub-national Burden of Disease; YLL: Years of Life Lost due to premature mortality; YLD: Years of Life Lost due to Disability; MDGs: Millennium Development Goals.

Competing interests

The authors declare that they have no competing interests.

Author's Contributions

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Designing of models: *Mahboubeh Parsaeian, Amir Kasaeian, Farshad Farzadfar.*

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Appendix 1. Search activity in selected search engines, Burden of Maternal Conditions Study

Search engine	Search activity
PubMed	all MeSH terms will be searched in "All fields"
ISI (Web of Science)	all MeSH terms and Entry terms will be searched in "Topic"
Scopus	all MeSH terms, Entry terms and Emtrees will be searched in "Title, Abstract, Keyword"
IranMedex and SID (English)	all MeSH terms and Entry terms will be searched in "Title, Abstract, Keyword"
IranMedex and SID (Persian)	all Persian equivalents will be searched in "Title, Abstract, Keyword"
Irandoc (Persian)	all Persian equivalents will be searched in "All fields"

All the key words will be combined by "OR" operator in the search engines; Limitations of search: Geographical Limitation is defined by the following phrase: [Iran* OR Persia* OR "I.R.Iran" OR "IR.Iran"] in all databases and will be added to the search by "AND" operator; Time Limitation is from 1985 to 2012 in PubMed and Scopus and from 1990 to 2012 in ISI. Only the human studies are included in the study.

Maternal Mortality
"Maternal Mortality"OR"Mortality, Maternal" OR "Maternal Mortalities" OR "Mortalities, Maternal"

Pregnancy Complications
"Pregnancy Complications"OR"Complications, Pregnancy"OR "Complication, Pregnancy" OR"Pregnancy Complication"

Pre Eclampsia
"Pre Eclampsia"OR"EPH Complex" OR "EPH Gestosis" OR "EPH Toxemias" OR "EPH Toxemia" OR "Toxemia, EPH"OR "Toxemias, EPH" OR "Toxemias, Pregnancy" OR "Hypertension-Edema-Proteinuria Gestosis" OR "Gestosis, Hypertension-Edema-Proteinuria" OR"Hypertension Edema Proteinuria Gestosis" OR "Preeclampsia" OR "Pregnancy Toxemias" OR "Pregnancy Toxemia" OR "Toxemia, Pregnancy" OR "Proteinuria-Edema-Hypertension Gestosis" OR "Gestosis, Proteinuria-Edema-Hypertension" OR "Proteinuria Edema Hypertension Gestosis" OR "Edema-Proteinuria-Hypertension Gestosis" OR "Edema Proteinuria Hypertension Gestosis" OR "Gestosis, Edema-Proteinuria-Hypertension" OR "Gestosis, EPH"

Eclampsia
"Eclampsia" OR "Eclampsias"

Hypertension, Pregnancy-Induced
"Hypertension, Pregnancy-Induced"OR"Pregnancy-Induced Hypertension" OR"Pregnancy Induced Hypertension" OR"Hypertensions, Pregnancy Induced" OR"Induced Hypertension, Pregnancy" OR"Induced Hypertensions, Pregnancy" OR"Gestational Hypertension" OR"Hypertension, Gestational" OR "Transient Hypertension, Pregnancy" OR"Hypertension, Pregnancy Transient" OR"Pregnancy Transient Hypertension"

HELLP Syndrome
"HELLP Syndrome"OR"Syndrome, HELLP" OR"Hemolysis, Elevated Liver Enzymes, Lowered Platelets"

Placenta Accreta
"Placenta Accreta"OR"Accreta, Placenta"OR "Placenta Increta"OR "Increta, Placenta"OR "Placenta Percreta" OR"Percreta, Placenta"

Postpartum Hemorrhage
"Postpartum Hemorrhage"OR"Hemorrhage, Postpartum"OR "Immediate Postpartum Hemorrhage"OR "Hemorrhage, Immediate Postpartum"OR"Postpartum Hemorrhage, Immediate"OR "Delayed Postpartum Hemorrhage"OR "Hemorrhage, Delayed Postpartum"OR "Postpartum Hemorrhage, Delayed"

Uterine Inversion
»Uterine Inversion«OR"Inversion, Uterine" OR"Inversion of Uterus" OR "Uterus Inversion"

Uterine Rupture
"Uterine Rupture"OR"Rupture, Uterine" OR"Ruptures, Uterine" OR"Uterine Ruptures"

Vasa Previa
"Previa, Vasa"OR "Previas, Vasa"OR "Vasa Previas"OR "Vasa Praevia"OR "Praevia, Vasa"OR"Praevias, Vasa"OR "Vasa Praevias"

Puerperal Infection
"Puerperal Infection"OR"Infection, Puerperal"OR "Infections, Puerperal"OR "Puerperal Infections"

Abortion, Spontaneous
»Abortion, Spontaneous"OR"Abortions, Spontaneous" OR"Spontaneous Abortions" OR"Miscarriage" OR"Miscarriages" OR"Spontaneous Abortion" OR"Abortion, Tubal" OR"Abortions, Tubal" OR"Tubal Abortion" OR"Tubal Abortions«

Abortion, Habitual
»Abortion, Habitual"OR"Abortions, Habitual" OR"Habitual Abortion" OR "Habitual Abortions" OR"Miscarriage, Recurrent" OR"Miscarriages, Recurrent" OR"Recurrent Miscarriage" OR"Recurrent Miscarriages" OR"Abortion, Recurrent" OR"Abortions, Recurrent" OR"Recurrent Abortion" OR"Recurrent Abortions«

Abortion, Incomplete
»Abortion, Incomplete"OR"Abortions, Incomplete" OR"Incomplete Abortion" OR"Incomplete Abortions«

Abortion, Missed
»Abortion, Missed"OR"Abortions, Missed" OR"Missed Abortion" OR"Missed Abortions«

Abortion, Septic
»Abortion, Septic"OR"Abortions, Septic" OR"Septic Abortions" OR"Septic Abortion«

Abortion, Threatened
»Abortion, Threatened"OR"Abortions, Threatened" OR"Threatened Abortion" OR"Threatened Abortions«

Embryo Loss
»Embryo Loss"OR"Embryo Disintegration" OR"Disintegration of Embryo" OR"Blastocyst Disintegration" OR"Disintegration, Blastocyst" OR"Disintegration of Blastocyst" OR"Embryo Resorption" OR"Resorption, Embryo" OR"Embryo Death" OR"Death, Embryo" OR"Embryo Deaths«

Abruptio Placentae Abortion, Missed
»Abruptio Placentae Abortion, Missed"OR"Abortions, Missed"OR"Missed Abortion"OR"Missed Abortions«

Abortion, Induced
»Abortion, Induced" OR"Induced Abortion" OR"Abortions, Induced" OR"Induced Abortions" OR"Abortion (Induced)" OR"Abortions (Induced)" OR"Abortion Rate" OR "Abortion Rates" OR"Rate, Abortion" OR"Rates, Abortion" OR "Abortion Techniques" OR"Abortion Technique" OR"Technique, Abortion" OR "Techniques, Abortion" OR"Abortion Technics" OR"Abortion Technic" OR"Technic, Abortion" OR"Technics, Abortion" OR"Abortion, Drug-Induced" OR"Abortion, Drug Induced" OR"Abortions, Drug-Induced" OR"Drug-Induced Abortion" OR"Drug-Induced Abortions" OR"Previous Abortion" OR "Abortion, Previous" OR"Abortions, Previous" OR"Previous Abortions" OR"Abortion History" OR"Abortion Histories" OR"Histories, Abortion" OR"History, Abortion" OR"Abortion, Saline-Solution" OR"Abortion, Saline Solution" OR"Abortions, Saline-Solution" OR"Saline-Solution Abortion" OR"Saline-Solution Abortions" OR"Abortion, Soap-Solution" OR"Abortion, Soap Solution" OR"Abortions, Soap-Solution" OR "Soap-Solution Abortion" OR"Soap-Solution Abortions" OR"Anti-Abortion Groups" OR"Anti Abortion Groups" OR"Anti-Abortion Group" OR"Group, Anti-Abortion" OR"Groups, Anti-Abortion" OR "Embryotomy" OR"Embryotomies" OR"Fertility Control, Postconception" OR "Postconception Fertility Control"OR "Abortion Failure" OR "Abortion Failures" OR "Failure, Abortion" OR "Failures, Abortion" OR "Abortion, Rivanol" OR "Abortions, Rivanol" OR "Rivanol Abortion" OR "Rivanol Abortions«

Abruptio Placentae
»Abruptio Placentae"OR"Placental Abruption"OR "Abruption, Placental"OR "Abruptions, Placental"OR "Placental Abruptions«

Placenta Previa
"Placenta Praevia"