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**PREGNANCY NURSING CARE VIRTUAL NETWORK FOR
THE PREVENTION OF PRE-ECLAMPSIA AND ECLAMPSIA**

Florianópolis, Santa Catarina, Brazil
2016

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THE PREVENTION OF PRE-ECLAMPSIA AND ECLAMPSIA**

Thesis submitted to the Nursing Postgraduate Program at Federal University of Santa Catarina, Brazil in partial fulfillment of the requirements for degree of the Doctor in Nursing.

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Advisor: Dr. Maria de Lourdes de Souza

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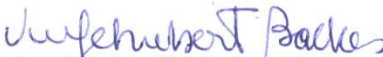
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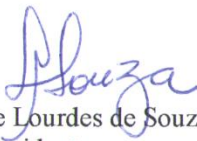
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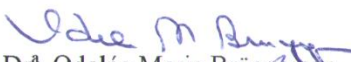
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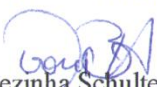

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*Dedicated to my beloved Father and my
dearest Mother for their endless and
unconditional love. They will hold a very
special place in my heart, forever.*

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In the name of Allah, the Most Gracious, the Most Merciful

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*Education is the most powerful weapon
which you can use to change the world.*

(Nelson Mandela)

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Advisor: Dr Maria de Lourdes de Souza

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RESUMO

Antecedentes: A pré-eclâmpsia e eclâmpsia são o transtorno hipertensivo mais comum da gravidez, afeta cerca de 5% de todas as primíparas, sendo uma das três principais causas de mortalidade materna em todo o mundo. É a causa de 10-15% das mortes maternas, e a maioria ocorre nos países em desenvolvimento. **Objetivo:** Desenhar uma rede virtual de cuidados de enfermagem para gestantes visando a prevenção da pré-eclâmpsia e eclâmpsia. **Método:** Os estudos realizados incluíram uma revisão sistemática sem meta-análise, revisões integrativas e uma proposta teórica de uma rede virtual de cuidados de enfermagem para gestantes. **Resultados:** Os resultados são integrados por informações para delinear e justificar a proposta de rede virtual. Os resultados obtidos são apresentados em quatro manuscritos, em observância as Instruções Normativas do Programa de Pós-Graduação em Enfermagem da Universidade Federal de Santa Catarina. O primeiro, denominado "Tecnologias e técnicas para a prevenção e controle da pré-eclâmpsia e eclâmpsia: uma revisão sistemática sem meta análise". Entre os 47 artigos incluídos neste estudo, 18 foram revisões sistemáticas e 29 foram ensaio clínico controlado aleatório. Os estudos incluídos utilizaram diferentes intervenções para a prevenção e tratamento da pré-eclâmpsia, eclâmpsia. O Sulfato de Magnésio, mostrou-se como tratamento de escolha. O segundo manuscrito com o título de "Mortalidade materna associada com pré-eclâmpsia e eclâmpsia em Khyber Pakhtunkhwa, Paquistão. Os 8 artigos incluídos neste estudo foram fundamentados em pesquisa quantitativa e os dados foram coletados em documentos de registros hospitalares, 4 estudos foram transversais, 1 foi descritivo e 3 foram retrospectivos descritivos. Razão de Mortalidade Materna associada à pré-eclâmpsia e eclâmpsia no Khyber Pakhtunkhwa, Paquistão continua elevada, destaca-se que 236 das 1.336 mulheres com pré-eclâmpsia ou eclâmpsia morreram. O terceiro manuscrito sobre "Práticas de cuidados de enfermagem na prevenção e controle da pré-eclâmpsia e eclâmpsia, uma revisão integrativa". Inicialmente foram encontrados 2.895 artigos usando os critérios de busca de todas as bases de dados selecionadas e através de busca manual usando o Google Scholar, nestas 215 foram duplicados. Os títulos dos 2.680

artigos selecionados foram lidos e restaram em 153 estudos para leitura do resumo. Após a leitura dos resumos foram lidos 15 estudos para leitura do texto completo, e destes 14 foram incluídos na revisão. O exame físico de gestantes, a detecção precoce de sinais e sintomas e as técnicas corretas de medição da pressão arterial foram demonstradas como importantes na prevenção da pré-eclâmpsia e eclâmpsia. O quarto manuscrito denominado "Rede virtual de cuidados de enfermagem para gestantes. Um desenho teórico". O modelo de rede foi proposto para melhorar os cuidados a saúde materna. A rede pode impulsionar a comunicação entre prestadores de cuidados a saúde e aumentar a qualidade dos cuidados durante a gravidez e o parto até o período de pós-parto. **Conclusões:** Uma rede virtual de cuidados de enfermagem é um recurso para os enfermeiros prestarem cuidados, de modo que as mulheres tenham uma gestação com o cuidado devido. Uma rede virtual de cuidados de enfermagem visa, também, fortalecer a comunicação entre enfermeiros e outros profissionais de saúde com gestantes.

Palavras-chave: Pré-eclâmpsia. Eclâmpsia. Mortalidade Materna. Cuidados de Enfermagem. Rede de Cuidados de Enfermagem.

ABSTRACT

Background: Pre-eclampsia and eclampsia, which are the most common hypertensive disorder of pregnancy, affects about 5% of all first-time mothers and are one of the three causes of maternal mortality worldwide. Pre-eclampsia and eclampsia are the cause for 10-15% of maternal deaths, the major part occurs in developing countries. **Objectives:** To design a nursing care virtual network for prevention the pre-eclampsia and eclampsia. **Method:** Methodological studies including a systematic review without meta-analysis, integrative reviews and theoretical propose of a pregnancy nursing care virtual network, were conducted. **Results:** The results are integrated into studies that add information to justify the virtual network proposal. The result are presented in four manuscripts according to the Nursing Postgraduate Program of the Federal University of Santa Catarina Normative Instructions. The first manuscript is, "*Technologies and techniques for the prevention and control of pre-eclampsia and eclampsia: A systematic review without meta-analysis*". Among the 47 articles included in this study, 18 were systematic reviews and 29 were Random Controlled Trials. The included studies used different intervention for the prevention and treatment of pre-eclampsia, eclampsia and its complications in pregnant women. Magnesium Sulfate, however, has shown a great success in this regards and can be called as treatment of choice. The second manuscript is "*Maternal mortality associated with pre-eclampsia and eclampsia in Khyber Pakhtunkhwa Pakistan. An integrative review*". Among the 8 articles included in this study where data is collected from hospitals records documents, 4 studies were cross-sectional, 1 was descriptive and 3 were retrospective descriptive. Maternal Mortality Ratios associated with pre-eclampsia and eclampsia in *Khyber Pakhtunkhwa* Pakistan continue to remain high (18% - 236 out of 1,336 women with pre-eclampsia or eclampsia died). The third manuscript is "*Nursing care practices in the prevention and control of pre-eclampsia and eclampsia. An integrative review*". A total of 2,895 articles were initially identified using the search criteria from all the selected databases and through manual searching using Google Scholar, where 215 were duplicated. The remaining 2,680 articles were selected for title-wise screening which resulted in 153 studies to be selected for abstract reading. After the abstract screening, 15 studies were selected for full-text reading, of which 14 were included in the review. Physical examination of pregnant women, early detection of signs and symptoms, and correct blood pressure measurement techniques have important role in the prevention of pre-eclampsia and eclampsia. And finally, the fourth manuscript is "Pregnancy Nursing Care Virtual Network: A Theoretical Design". The theoretical model was propose to improve maternal health. It is expected that the network will strengthen communication links between health care providers and pregnant women and to increase awareness, and quality of care during pregnancy and childbirth till the period of post-partum. **Conclusions:** A pregnancy nursing care virtual network

is a technology for nurses in order to play a better role in providing effective nursing care to pregnant women. Nursing care virtual network for pregnant women is therefore designed to strengthen the communication links between nurses and other health care professionals with pregnant women.

Keywords: Pre-eclampsia. Eclampsia. Maternal Mortality. Nursing Care. Nursing Care Network.

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LIST OF ABBREVIATION

ABPM	- Ambulatory Blood Pressure Monitoring
AMTI	- Ayub Medical and Teaching Institution
App	- Application
CI	- Confidence Interval
CHW	- Community Health Worker
CNPq	- Conselho Nacional de Desenvolvimento Científico e Tecnológico
CoP	- Community of Practice
CINAHL	- Cumulated Index to Nursing and Allied Health Literature
DBP	- Diastolic Blood Pressure
DBPC	- Placebo-controlled Double Blinded
FATA	- Federally Administered Tribal Areas
HELLP	- Hemolysis, elevated liver enzymes, low platelets
HMCMTI	- Hayatabad Medical Complex medical and Teaching Institution
ICT	- Information and Communication Technology
ICU	- Intensive Care Unit
KPK	- Khyber Pakhtunkhwa
MAP	- Mean Arterial Pressure
MM	- Maternal mortality
MMR	- Maternal Mortality Rate
Medline	- Medical Literature On Line
MESH	- Medical Subject Heading
MTILRH	- Medical Teaching Institute Lady Reading Hospital
MTIKTH	- Khyber Teaching Hospital Peshawar
NHLBI	- National Heart, Lung and Blood Institute
PhD	- Doctor of Philosophy
PEN	- Programa de Pós-Graduação em Enfermagem
PE	- Pre-eclampsia
PC	- Personnel Computers
PDA _s	- Personal Digital Assistant
PICO	- Population, intervention, Comparison, Outcomes
PIH	- Pregnancy Induced Hypertention
PNCN	- Pregnancy Nursing Care Virtual Network
RCT _s	- Randomized Controlled Trials
SGA	- Small for Gestational Age
SBP	- Systolic Blood Pressure

- SMS - Short Message Service
- SR - Systematic Review
- TCM - Traditional Chinese Medicine
- TWAS - Academy of Sciences for the Developing World
- UK - United Kingdom
- UFSC - Universidade Federal de Santa Catarina
- WHO - World Health Organization

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THESIS ORGANIZATION

After the chapter one (Introduction), the remaining parts of this thesis are organized as follows. In Chapter 2, the focus is on the literature review. It begins with presenting an overview about the pre-eclampsia and eclampsia, maternal mortality pre-eclampsia and eclampsia, followed by a discussion on the clinical aspects of pre-eclampsia and eclampsia and its etiology and risk factors. Besides, it includes nursing care in the prenatal or antenatal period, the importance of nursing care in the prevention of pre-eclampsia and eclampsia and networking in nursing practices. In Chapter 3, we discuss study methodology which consists of a systematic review without meta-analysis, integrative reviews, and a theoretical design of a virtual network model for pregnant women. In Chapter 4, we present the proposal about the virtual network while Chapter 5 presents the general comments and future research directions.

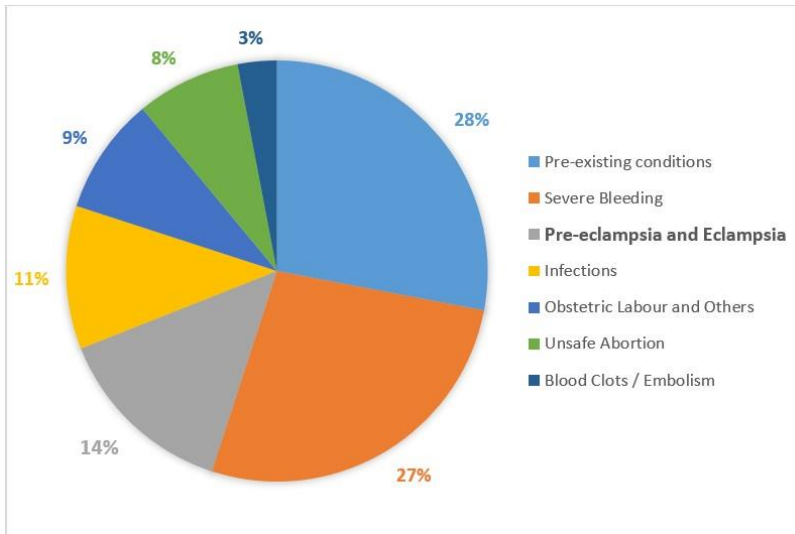
INTRODUCTION

Woman is the source of all human life on this planet. The pleasure and excitement of being a mother cannot be expressed in words, and all the people in the world recognize it an important family process. In all cultures and societies, being pregnant or to give birth to a child is considered as an important, beautiful and divine event (DUTTA, 2001). Pregnancy, the precious period of every woman's life requires continuous, prompt and supportive care throughout pregnancy and also after childbirth for safe motherhood.

Every day in 2015, about 830 women died due to pregnancy complications and childbirth (WHO, 2015a). Almost all of these deaths occurred in low-resource settings, where most could have been prevented. The primary causes of death are hemorrhage, hypertension, infections, and indirect causes, mostly due to the interaction between pre-existing medical conditions and pregnancy. Of these 830 daily maternal deaths, about 550 occurred in sub-Saharan Africa and 180 in Southern Asia, compared to 5 in developed countries. The risk of a woman in a low resource setting dying from a pregnancy-related complication during her lifetime is about 33 times higher compared to a woman living in a developed country (WHO, 2015a).

Pregnant women die as a result of complications which either develop during pregnancy or may exist before pregnancy but are aggravated during pregnancy. The major complications that account for nearly 75% of all maternal deaths consist of pre-eclampsia and eclampsia (together 14%), Severe bleeding (27%) and Infections (11%) (SAY et al., 2014) (See Figure 1).

Most maternal deaths are preventable, as the health-care solutions to prevent or manage these complications are well-known (WHO, 2015a). WHO recommends that all pregnant women should have access to antenatal care in pregnancy, skilled care during childbirth, and care and support in the weeks after childbirth. It is particularly important that all births are attended by skilled health professionals, as timely management and treatment can make the difference between life and death for both the mother and the baby (WHO, 2015a). Nurses need to study and develop technologies to prevent and control the major complications associated with toxemia or without toxemia, highlighted below:

Figure 1 - World Wide Maternal Death Causes.

Source: Say et al., (2014).

Severe bleeding after birth can kill a healthy woman within hours if she is unattended. She needs injecting oxytocin immediately after the labor.

Infection after childbirth can be eliminated if good hygiene is practiced and if early signs of infection are recognized and treated in a timely manner.

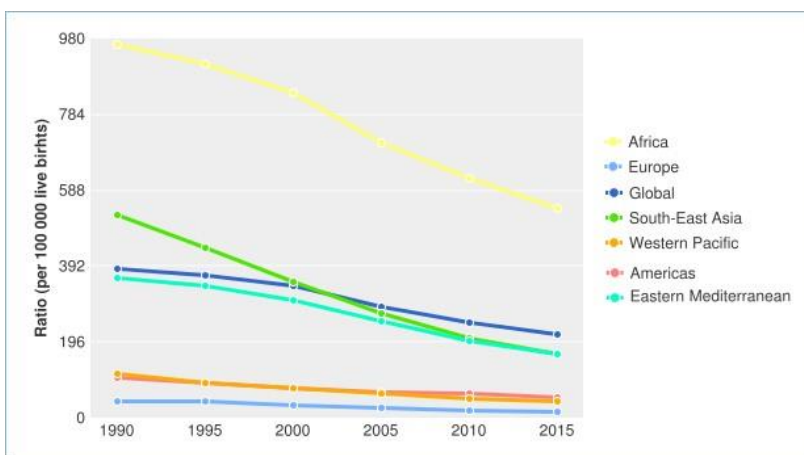
Pre-eclampsia should be detected and appropriately managed before the onset of convulsions (eclampsia). Administering drugs such as Magnesium Sulfate for pre-eclampsia can lower a woman's risk of developing eclampsia.

On the other hand, to avoid maternal deaths, it is also vital to prevent unwanted and too-early pregnancies. All women, including adolescent girls, need access to contraception, safe abortion services to the full extent of the law, and quality post-abortion care (WHO, 2015a).

In 2015, Maternal Mortality Ratio in developing countries was 239 per 100,000 live births and in developed countries was 12 per 100,000 live births. In south-east Asia 166 maternal deaths per 100,000 live births occurred, in western pacific 41 maternal deaths per 100,000 live births occurred, in Africa 542 maternal deaths per 100,000 live births occurred, in Europe 16 maternal deaths per 100,000 live births

occurred, in America 52 maternal deaths per 100,000 live births occurred and in Eastern Mediterranean 166 maternal deaths per 100,000 live births occurred. Figure 2 shows the graph of Maternal Mortality Ratio (maternal deaths per 100,000 live births) globally by WHO region, 1990-2015. It is important to understand the disparities between countries included within countries, and between women with high and low income and those women living in rural versus urban areas. The number of women dying due to complications during pregnancy and childbirth has decreased by 43% from an estimated 532,000 in 1990 to 303,000 in 2015 (WHO, 2015a).

Figure 2 - Maternal deaths per 100,000 live births, globally and by WHO region (1990-2015).



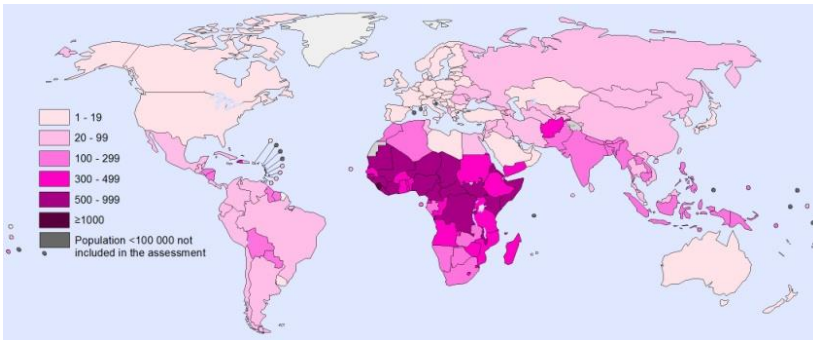
Source: WHO, (2015b).

WHO is supporting countries to deliver integrated, evidence-based and cost-effective nursing care for all mothers during pregnancy, childbirth and the postpartum period. Improvement in health systems, particularly in training midwives and in making emergency obstetric care available 24/7, is very important to reduce maternal mortality. Globally, the reduction in maternal deaths between 1990 and 2015 was 43% (WHO, 2015a). Maternal Mortality Ratio (maternal deaths per 100,000 live births) globally and by WHO region from 1990 to 2015, is shown in Figure 3.

Pre-eclampsia is a hypertensive disorder of pregnancy that usually occurs after 20 weeks of pregnancy, determined by many

factors, most of which are preventable, particularly in prenatal care. Preeclampsia is a combination of hypertension (high blood pressure) and proteinuria (protein in the urine) (DULEY; HENDERSON-SMART; WALKER, 2009).

Figure 3 - Maternal Mortality Ratio (maternal deaths per 100,000 live births) globally by country, 2015.



Source: Alkema et al., (2016).

But this condition is also associated with abnormalities of the coagulation system, liver failure, renal and cerebral ischemia. Most women with pre-eclampsia give birth without problems. However, severe pre-eclampsia can cause problems such as stroke, kidney failure, liver failure and blood clotting (DULEY; HENDERSON-SMART; WALKER, 2009).

Similarly, eclampsia, which is usually rare, but potentially fatal characterized by the presence of a seizure associated with pre-eclampsia, weight gain, headaches and dizziness (DULEY et al., 2010a). Research has shown that about 1 in 200 women who had pre-eclampsia, possibly progress to a more dangerous condition of eclampsia, which is responsible for about 50,000 maternal deaths each year (KHAN et al., 2006).

Pre-eclampsia and eclampsia together are one of the three leading causes of maternal mortality in the world (GHULMIYYAH; SIBAI, 2012). Pre-eclampsia and eclampsia are associated with substantial maternal complications, both acute and long-term. (GHULMIYYAH; SIBAI, 2012). Over the past 50 years, there has been a significant reduction in rates of eclampsia and maternal mortality in developed

countries. In contrast, most maternal deaths and complications are due to lack of prenatal care, lack of access to services of hospitals, lack of resources and inadequate diagnosis and treatment of patients with pre-eclampsia. Similarly, the lack of protocols for disease management or failure to follow clinical protocols of care contributes toward high maternal mortality. Clear protocols for management of hypertension in pregnancy at all levels of health care is required for better maternal as well as perinatal outcome (MIKO et al., 2013).

The term eclampsia was first coined by a French physician Francois Boissier de Sauvages de Lacroix in 1739, as an acute form of convulsion, and contrasted with the chronic condition now known as epilepsy (CHESLEY, 1974). Similarly, proteinuria in the context of eclamptic seizures was first described in 1840, and high blood pressure shortly after that. By 1894, it was reported that high blood pressure and proteinuria could occur in pregnant women, without eclamptic seizures, and the term pre-eclampsia was thus born (CHESLEY, 1984).

Approximately 10% of pregnant women have blood pressure recorded above normal at some point during pregnancy. Pre-eclampsia, which is now known to be a multisystem disorder of pregnancy, complicates 2-8% of pregnancies in the western world and 5% of first-time mothers (NORTH et al., 2011). The effect of pre-eclampsia and eclampsia in the developing world is staggering and about 10-15% of maternal deaths are attributed to pre-eclampsia, of which 99% occur in the developing world (DULEY, 2009).

Table 1 - Complications of pre-eclampsia.

System	Complications
Central nervous system	Eclampsia, Cerebral haemorrhage, Cerebral edema, Retinal edema, Cortical blindness
Renal system	Renal tubular necrosis, Renal cortical necrosis
Respiratory system	Pulmonary edema, Laryngeal edema
Hepatic system	Disseminated intravascular coagulation, Haemolysis
Liver	Haemolysis, elevated liver enzymes, low platelets, (HELLP) syndrome, Jaundice
Placenta	Placental abruption, Placental infarction
Baby	Growth restriction, Preterm delivery, Death

Source: Adapted from Duley (2009, p.132).

Hypertension is not always associated with pre-eclampsia. The difficult and often delayed diagnosis is due to the fact that most women with pre-eclampsia are symptom-free. Women with more severe forms of pre-eclampsia often complain of a headache, abdominal pain and visual disturbance, and can suffer complications to virtually all the body's systems, as summarized in Table 1. The disease does not just affect the mother and about one-third of babies born to women with pre-eclampsia are born premature, and one-quarter is growth restricted.

1.1 MOTIVATION AND PROBLEM STATEMENT

Nursing knowledge represents the science of nursing, and nursing care represents the art of nursing. The knowledge of nursing and nursing care practice, both must be present, and both are important for quality nursing care (FINKELMAN; KENNER, 2013). According to WHO, the majority of deaths due to pre-eclampsia and eclampsia are avoidable through the provision of timely and effective care to the women, especially in the prenatal period (WHO, 2011a).

Maternal mortality associated with eclampsia is high in Brazil, especially in low-resource settings and lower income regions. Promoting quality maternal health care and improving the availability of obstetric emergency care are essential actions to relieve the burden of eclampsia in Brazil (GIORDANO et al., 2014; PACHECO et al., 2014). All women should have access to antenatal care in pregnancy, skilled nursing care during childbirth, and care and support in the weeks after childbirth (WHO, 2015a).

Among the developing countries in Pakistan eclampsia is a common cause of maternal deaths (MICHEAL, 2000). In Pakistan each year, an estimated 25,000 to 30,000 women die of pregnancy-related complications. It shows that the maternal health figure is poor. The main factors are access to the health care services, low socioeconomic conditions. The poor emergency obstetrical condition is also a reason for high maternal mortality (GILLANI; HASSAN, 2011).

Poor access to health care facilities, poverty, lack of trained primary health care providers and local tradition/preference of home deliveries are contributing towards higher mortalities in Pakistan (BUTT, 2004).

In Pakistan, maternal mortality is a public health concern which needs to be highlighted. There are many factors contributing to maternal mortality. Poverty is the most significant determinant that prevents

females from receiving education, having nutritious foods and accessing reproductive healthcare services. Reducing inequity and promoting female education are among the key strategies to empower women and balance their status.

Maternal mortality due to obstetric emergencies can be prevented by strengthening the available healthcare facilities and increasing the skills of female birth attendants. Moreover, governmental and non-governmental organizations should implement a focused program for female education, which would consequently reduce the rate of early marriage. In fact, empowering educated women will consequently improve their socio-economic status and will reduce the gender inequality, as well.

Underprivileged women should be encouraged to use antenatal care services in order to eliminate financial issues. Food supplements and medicines for the correction of anemia should be also provided for pregnant women. In addition, reproductive healthcare services including post-abortion care and family planning services should be made available, accessible and affordable within community settings.

Civil society organizations, educationists, and healthcare professionals should raise awareness regarding Child Marriage Restraint Act 1929 and its reinforcement, as child marriage is widely practiced in some parts of the country. More skilled birth attendants should be trained and employed in order to provide 24-hour healthcare services and facilitate timely referral in case of obstetric emergencies (ABBASI; YOUNAS, 2015).

For prevention of pre-eclampsia and other causes of the maternal mortality, the prenatal nursing care support is very important. In face the rapid improvement in information and communication technologies and the growing acceptability of mobile devices, we, therefore, proposed a theme of the study that meets both the demands of nursing care and women health. So we opt to develop a Pregnancy Nursing Care Virtual Network to strengthen links between nurses and pregnant women and prevent pre-eclampsia and eclampsia to reduce the maternal mortality. I also presented this proposal when I applied for TWAS-CNPq (The World Academy of Sciences and National Council for Scientific and Technological Development Brazil) Postgraduate fellowship in 2012.

1.2 RESEARCH QUESTION

What components should be integrated into a network model of nursing care for prevention of pre-eclampsia and eclampsia?

1.3 OBJECTIVES

To design a nursing care virtual network for prevention pre-eclampsia and eclampsia.

1.3.1 Specific Objectives

- To assess the technologies and techniques for prevention of pre-eclampsia and eclampsia;
- To show the maternal mortality associated with pre-eclampsia and eclampsia in Khyber Pakhtunkhwa province of Pakistan, from the scientific literature published between 2000 to 2015;
- To assess the nursing care practices for prevention and control of pre-eclampsia and eclampsia;
- To define the requirement for designing a nursing care virtual network for pregnant women.

2 BACKGROUND AND LITERATURE REVIEW

A number of different definitions related to eclampsia are used in literature. Some of them are more detailed than others, some are more inclusive than others, and in some cases, the same term has been used to describe different disorders by different authors. This chapter starts the discussion by defining the main terms and definitions used in this thesis.

2.1 DEFINITIONS

Maternal death is defined as the death of a woman during pregnancy or within 42 days of termination of pregnancy, caused or aggravated by the pregnancy or its management, irrespective of the location or duration (WHO, 2016).

Live Birth occurs when a fetus, irrespective of the duration of the pregnancy, exits the maternal body and subsequently shows any sign of life, such as voluntary movement, heartbeat, or pulsation of the umbilical cord, for however brief time (WHO, 2016).

Hypertension is defined as elevation of systolic blood pressure by 30mmHg above the normal and/or 15mmHg of diastolic blood

pressure above the normal (ACOG, 2002).

Gestational Hypertension is defined as arterial hypertension (systolic BP \geq 140 mmHg and / or diastolic BP \geq 90 mmHg on 2 occasions $>$ 6 hours apart) occurring after gestational week 20, which returns to normal post-partum (PILLITTERI, 2010).

Chronic Hypertension is hypertension diagnosed before the 20th gestational week or hypertension which fails to settle post-partum (PILLITTERI, 2010).

Pre-eclampsia is defined as a blood pressure of at least 140mmHg systolic pressure and 90mmHg diastolic pressure measured on two occasions 6 hours apart, accompanied by proteinuria of at least 300 mg per 24 hours, or dipstick analysis of \geq + 1, after 20 weeks of pregnancy (ACOG, 2002; SIBAI, 2008).

Pre-eclampsia superimposed on chronic hypertension is defined as the appearance of proteinuria starting after gestational week 20. A sudden increase in blood pressure or proteinuria or the appearance of thrombocytopenia or deranged transaminases is said to be suggestive but not diagnostic of superimposed pre-eclampsia (PILLITTERI, 2010).

Eclampsia refers to the development of grand mal seizures in a woman with gestational hypertension or pre-eclampsia (SIBAI, 2005).

Despite this general agreement, many questions remain about how the disease should be classified. Some classifications define preeclampsia as pregnancy-induced hypertension in association with proteinuria, or other complications such as renal insufficiency, liver disease, neurological problems, haematological disturbance, or intrauterine growth restriction (NORTH et al., 2011). Further definitions separate proteinuric from non-proteinuric pre-eclampsia. Proteinuric preeclampsia is reported to carry a worse prognosis than non-proteinuric pre-eclampsia, which is in turn reported to carry a worse prognosis than gestational hypertension alone (HOMER et al., 2008).

It is also still unknown, whether the early onset which is usually defined as that occurring before 34 weeks' gestation and late-onset variants of pre-eclampsia are the same disease, or whether they have completely different pathological mechanisms. Similarly, what is the difference or how to define severe and mild pre-eclampsia is another matter for debate. A further complicating factor is that the association of pre-eclampsia with preterm delivery, small for gestational age (SGA) babies, or both, appear to have different consequences, particularly for the mother's future cardiovascular health (SMITH; PELL; WALSH, 2001).

Although the cause of pre-eclampsia remains largely unknown, the pathogenesis is thought to occur in two main phases. The first phase begins in the placenta while the second stage is characterized by an abnormal maternal endothelial response, resulting in hypertension, proteinuria, and edema that characterize the condition.

2.1 MATERNAL MORTALITY DUE TO PRE-ECLAMPSIA AND ECLAMPSIA

Each year worldwide about 300,000 women die due to pregnancy-related complications. In these deaths about 50,000 women die due to pre-eclampsia and eclampsia, of which 99% occur in developing countries (WHO, 2015a). In Brazil, maternal mortality ratio was 44 while in Pakistan it was 178 per 100,000 live births in the year 2015 (WHO et al., 2015).

Hypertensive disorders of pregnancy are responsible for one out of ten maternal deaths in Africa and Asia, and nearly one-quarter in Latin America (CAMPBELL et al., 2006). Among the hypertensive disorders of pregnancy, pre-eclampsia and eclampsia are the important causes of maternal mortality (DULEY, 2009).

Globally, pre-eclampsia is a leading cause of maternal mortality (GHULMIYYAH; SIBAI, 2012). Worldwide an estimated 300,000 or more women die each year from complications of pregnancy and 95% of these women are in Africa and Asia (WHO, 2015a). Pre-eclampsia and eclampsia together affect about 10% of all pregnant women around the world (GHULMIYYAH; SIBAI, 2012). In Afghanistan, pre-eclampsia and eclampsia are the second leading cause of maternal deaths (AHADI et al., 2015). Another study conducted in September 2014 in Tanzania found that in 2011 there were 155 maternal deaths and hence MMR of 1,541 per 100,000 live births. In these maternal deaths, 69.5% were analyzed for direct causes. Of the direct causes, pre-eclampsia and eclampsia were the major cause (19.9% of all deaths) (PEMBE et al., 2014).

Eclampsia, which is usually rare but potentially life-threatening, is characterized by the occurrence of a seizure in association with pre-eclampsia, headaches, swelling feet, sudden weight gain and changes in vision (DULEY et al., 2010a). About 1 in 200 women who had preeclampsia, eventually also progress to a dangerous condition known as eclampsia which is responsible for about 50,000 maternal deaths each year worldwide (KHAN et al., 2006b).

Maternal mortality rate and health care quality vary among low and middle-income countries (KIDANTO et al., 2012). In developed countries due to the provision of effective antenatal care services and extensive research now pre-eclampsia and eclampsia have controlled and has become rare complication of pregnancy (KEELING et al., 1991).

Although the rate of pre-eclampsia and eclampsia and the number of maternal deaths associated with it have fallen over recent years but in places where maternal mortality is high, most of these deaths are still associated with pre-eclampsia and eclampsia. Even in countries with low maternal mortality, a substantial proportion is due to preeclampsia and eclampsia (GOLDENBERG et al., 2011; DANSO; OPARE-ADDO, 2010). For example, in the United Kingdom, pre-eclampsia and eclampsia together account for 15% of direct maternal deaths and two thirds are related to pre-eclampsia (ALTMAN et al., 2002; WALKER, 2000).

The rate of pre-eclampsia and eclampsia is higher in the developing countries due to the lack of prenatal care and access to proper hospital care (GOLDENBERG et al., 2011). For example, hospital-based studies in Nigeria have reported that eclampsia accounted for up to 32% of all maternal deaths (MAIRIGA; SALEH, 2009). Similarly, the lowest rate for eclampsia was reported in the United Kingdom as 2.7/10,000 deliveries (KNIGHT, 2007).

A survey realized in 2003 with approximately 300,000 deliveries reported that severe maternal morbidity was associated with hypertensive disorders of pregnancy in the United States. The data were obtained from the National Hospital Discharge Survey from 1988 to 1997. The overall incidence of hypertensive disorders in pregnancy was 5.9%. Eclampsia was reported at 1.0 per 1000 deliveries. The incidence of eclampsia, severe pre-eclampsia, and superimposed pre-eclampsia remained unchanged during the 10-year period (ZHANG; MEIKLE; TRUMBLE, 2003).

Women with preeclampsia and eclampsia had an increased risk of 3-25 times of serious complications such as placental abruption, thrombocytopenia, disseminated intravascular coagulation, pulmonary edema and aspiration pneumonia. African-American women not only had a higher incidence of hypertensive disorders in pregnancy but also tend to have a higher risk of serious complications (ZHANG; MEIKLE; TRUMBLE, 2003).

These findings suggest that pre-eclampsia and eclampsia constitute a worldwide public health problem to be dealt with, especially

in developing countries (GOLDENBERG et al., 2011; DANSO; OPARE-ADDO, 2010).

It is well known that pre-eclampsia and eclampsia carry a high risk for severe maternal morbidity. Compared to Caucasians, African-American women have a higher incidence of hypertensive disorders in pregnancy and suffer from more severe complications. The dangers of a high systolic blood pressure, especially in combination with a low platelet count, seem to be much underestimated in relation to intracerebral hemorrhage (MARTIN JR et al., 2005).

As for hospitalizations without hypertensive disorders, the risk of serious obstetric complications was 3.3 to 34.8 times for hospitalizations with eclampsia or severe preeclampsia and 1.4-2.2 times for gestational hypertension (KUKLINA; AYALA; CALLAGHAN, 2009).

In reviewing all maternal deaths in the United States, among almost 1.5 million deliveries within 124 Hospitals, 95 maternal deaths occurred in 1,461,270 pregnancies (6.5 per 100,000 pregnancies). The leading causes of death were complications of pre-eclampsia, pulmonary thromboembolism, amniotic fluid embolism, obstetric hemorrhage, and cardiac disease (CLARK et al., 2008).

Maternal mortality associated with eclampsia is high in Brazil, especially in low-resource settings and lower income regions (PACHECO et al., 2014).

A multicenter, cross-sectional study based in 27 centers in all regions of Brazil, conducted in 2014, showed that eclampsia is the leading cause of maternal death in Brazil, especially in low-income areas. The study indicates that obstetric care for women with eclampsia has the worst performance in low-income areas in Brazil. Improving the quality of maternal care and increasing access to emergency obstetric care are essential actions to minimize the mortality associated with eclampsia (GIORDANO et al., 2014).

According to the latest national estimate, pre-eclampsia and eclampsia are major contributors to the Maternal Mortality Rate in Brazil, which account for about 20% of all maternal deaths in the country (BRASIL, 2012a). Hypertensive disorders are also a major cause of premature elective deliveries, morbidity and perinatal mortality (LANGENVELD et al., 2011; YÜCESOY et al., 2005). Every year, the public health system of Brazil spends more than 14 million US dollars for the treatment of pre-eclampsia and eclampsia, a considerable expense for a developing country (BRASIL, 2011).

A population-based retrospective descriptive study was conducted in the state of Santa Catarina Brazil in 2014. Total 256

maternal deaths occurred from 2005 to 2013. Out of 256 maternal deaths in the specified period, 32 deaths were associated with pre-eclampsia and eclampsia, representing 12.5% of the total maternal deaths. Pre-eclampsia was 37.5% and eclampsia was 62.5%. The highest number of maternal deaths due to pre-eclampsia and eclampsia per year was 21.9% in 2010 and the lowest was 3.13% in 2011 and 2013 (KHANUM et al., 2015).

Another retrospective descriptive study was made from 1996 to 2005. During the studied time 79 maternal deaths related to hypertension occurred. This number represents 20% of maternal deaths in the period. Deaths related to eclampsia were (59,5%) 43.3/100,000 born alive. Maternal deaths related to hypertension till represent 20% of maternal death in Santa Catarina. Gestational hypertension may be prevented by the broadening of prenatal coverage, training of personnel, early diagnosis of high-risk patients and a quick and efficient reference system on the third health-attention level (SAVIATO et al., 2008).

Demographical, clinical and social risk factors for hypertensive disorders are shown in Figure 5. The family history of pre-eclampsia, previous pre-eclampsia history, high body mass index (BMI), diabetes, chronic hypertension, schooling and prenatal were demonstrated to be more frequent in hypertensive disorders in pregnancy when compared to normotensive women. Regarding nulliparity, multifetal gestation and smoking habits, there were no significant differences between patients and controls.

2.2 CLINICAL ASPECTS OF PRE-ECLAMPSIA AND ECLAMPSIA

2.2.1 Etiology and risk factors of Pre-eclampsia and Eclampsia

Prevention of any disease requires knowledge of its etiology and pathogenesis, as well as the availability of methods to predict people at high risk for this disease. The mechanisms responsible for the development of eclampsia remains poorly understood (WARRINGTON, 2015). Genetic predisposition, immunology, endocrinology, nutrition, abnormal trophoblastic invasion, coagulation abnormalities, vascular endothelial damage, cardiovascular maladaptation, dietary deficiencies or excess, and infection have been proposed as etiologic factors for preeclampsia and eclampsia (GABBE et al., 2016). Furthermore, it is a clinical syndrome rather than a single disease. Therefore, the pathophysiologic abnormalities of this syndrome are heterogeneous and

variable among different women (DEKKER; SIBAI, 1991; WARRINGTON, 2015).

Table 2 - Risk factors for hypertensive disorders of pregnancy in southern Brazil.

Characteristic	Hypertensive disorders n = 161	Control n = 169	p
Family history of PE	44%	20%	< 0.001
Previous PE history	57%	7%	< 0.001
Multifetal gestation	6%	3%	0.530
Body Man Index (kg/m ²)	32.9 ± 6.1	28.2 ± 4.6	< 0.001
Null parity	27%	22%	0.300
Diabetes	26%	6%	< 0.001
Chronic hypertension	30%	5%	< 0.001
Smoking	18%	23%	0.327
Schooling	34%	57%	0.003
Prenatal	88%	97%	0.007

Source: Dalmáz et al., (2011, p.694).

Although accurate prediction of pre-eclampsia remains difficult, there are a number of maternal risk factors which can be easily assessed in early pregnancy that is known to be associated with an increased risk of developing pre-eclampsia. Most risk factors were the previous history of pre-eclampsia, pre-existing diabetes, multiple pregnancies, null parity, family history, raised blood pressure, raised body mass index before pregnancy, or increasing maternal age (SHAMSI; SALEEM; NISHTER, 2013).

2.2.2 Pregnancy Conditions

Null parity

Null parity, never having previously given birth, is believed to be the most common risk factors for pre-eclampsia. Null parity has been shown to almost triple the risk of pre-eclampsia (DUCKITT; HARRINGTON, 2005). The protective effect due to a previous birth is lost when a subsequent pregnancy is conceived with a new partner, or when there is a long interval between pregnancies. This had led to the theory that prior exposure to paternal antigens has a protective role against pre-eclampsia. This theory was supported by a study of nulliparous women, whereby women with the previous termination of pregnancy with the same partner as the index pregnancy were nearly

half as likely to develop pre-eclampsia as women who had a previous termination with a different partner (SALAFIA; SHIVERICK, 1999). Reduced exposure to paternal antigen, by limited exposure to their sperm, is also a risk factor for pre-eclampsia. Women who conceive after a short period of sexual relations, or by alternative techniques such as non-partner donor insemination or intracytoplasmic sperm injection (ICSI) are also at increased risk of the disease (ILEKIS; REDDY; ROBERTS, 2007).

Multiparity

Change of partners increases the risk of preeclampsia in subsequent pregnancies (TUBBERGEN et al., 1999). Poor immune adaptation in the maternal-fetal interface may be an underlying mechanism. Multiparous women with a new partner must be addressed as primigravidas women. Pre-eclampsia was diagnosed in 3.2 % of nulliparas, 3.0 % of multiparous with altered paternity and 1.9 % of multiparas with no change (TRUPIN; SIMON; ESKENAZI, 1996). The adjusted attributable risk of preeclampsia in multiparous women connected to a change of paternity was 29 %. Although these results partially support the immunologic theory of pre-eclampsia, which also suggest that a subsequent pregnancy with a partner is associated with a lower risk of preeclampsia.

2.2.3 Preexisting Morbidity

Associated with Weight

Obesity increased body mass index or increased abdominal circumference before pregnancy or in early pregnancy are well-established risk factors for the condition (RODIE et al., 2004). The maternal risk of pre-eclampsia increases with increasing degree of obesity, which persists after accounting for other potential confounding factors (SEBIRE et al., 2001). This is likely to be related to the altered metabolic state associated with marked obesity rather than the obesity itself. Maternal obesity results in alteration of the plasma lipid profile with higher serum triglyceride and VLDL cholesterol, and lower HDL-cholesterol concentrations than those observed in lean pregnant women. This pattern of dyslipidaemia is similar to that of the metabolic syndrome described in the non-pregnant population (SATTAR et al., 1997). Obesity is also associated with chronic low-grade inflammation, a feature common to many of the other risk factors for the condition.

Diabetes

The association of pre-gestational diabetes and pre-eclampsia is well recognized, and women with a history of diabetes have an up to 4-fold increased risk of development of pre-eclampsia compared to the general population. Recent data from both the UK and the USA suggest that 0.5 - 0.75% of pregnant women have pre-existing type 1 or type 2 diabetes (MIDDLETON et al., 2010). In keeping with the general population, rates of gestational, type 1 and type 2 diabetes in pregnant women rose significantly between 1994 and 2004 in all age groups (ALBRECHT et al., 2010). The increase in rates of type 2 diabetes in pregnant women has been the most striking and is likely to be related to increased rates of obesity.

Diabetes in pregnancy increases the risk of poor maternal and neonatal outcomes. As well as the increased risk of pre-eclampsia, the condition is also associated with elevated risk of pregnancy loss, maternal infection, polyhydramnios, premature labor and failure to progress in the first or second stage of labor. Fetal and neonatal complications associated with diabetes include congenital malformation, macrosomia, respiratory distress syndrome, hypoglycaemia and jaundice. Further, the babies born to diabetic mothers have been shown in long-term follow-up studies to be at increased risk of future obesity and type 2 diabetes themselves (MIDDLETON et al., 2010).

Genetic Influences

There are clearly genetic factors involved in the development of pre-eclampsia. Women with a family history of pre-eclampsia in their mother or sister are at nearly 3 times higher risk of development of the condition compared to those without a family history (DUCKITT; HARRINGTON, 2005). A Swedish study examining over 700,000 pregnancies from 240,000 sibling pairs reported a 35% contribution of maternal genes to the risk of development of pre-eclampsia. The fetal genes, with the similar contribution of genetic effects from both parents, were responsible for 20% of the risk (CNATTINGIUS et al., 2004).

In a further Swedish family study in which 2.8% of women studied were affected by pre-eclampsia, odds ratios of 3.3 (95% CI 3.0-3.6) for sisters and 2.6 (95% CI 1.6-4.3) for daughters of those affected were reported, compared to odds ratios of 1.4 (95% CI 0.9-2.2) for maternal half-sisters and 1.0 (95% CI 0.6 to 1.6) for paternal half-sisters of those affected. Full sisters of women with pre-eclampsia were also reported to be at increased risk of pregnancy-induced hypertension without proteinuria, with a reported odds ratio of 2.5 (95% CI 2.2 to 2.8)

(NILSSON et al., 2004).

From these and other epidemiological studies, there is clear evidence of a genetic component to the development of pre-eclampsia, and several modes of inheritance have been suggested. One of the problems of researches in this field, however, is the rarity of the condition. The magnitude of genetic influence in disease is often assessed using twin studies; the rarity of pre-eclampsia has meant that very few twin studies have been possible. The Swedish group did report on 928 monozygotic twin pairs, reporting a substantial increase in the risk of pre-eclampsia (odds ratio 33.6, 95% CI 7.8 to 145) in the identical twins of those affected (NILSSON et al., 2004).

2.2.4 Other factors

Ethnicity

Pre-eclampsia rates vary significantly around the world, whether this is related to different diagnostic criteria, or whether there are true differences between different ethnic populations remains uncertain. Further, whether both maternal and paternal ethnicity play a role in determining pre-eclampsia risk is also unclear. A retrospective American cohort study of 127,000 low-risk pregnant women reported that rates of pre-eclampsia were higher among African-American women (5.2%, OR 1.41, 95% CI 1.25-1.62), and lower amongst Latina (4.0%, OR 0.9, 95% CI 0.84-0.97) and Asian women (3.5%, OR 0.79, 95% CI 0.72-0.88) compared to white women (CAUGHEY et al., 2005). Paternal ethnicity followed a similar pattern, with highest rates in African-American fathers, and lowest rates in Asian fathers. When maternal and paternal ethnic discordance were examined, the overall rate of pre-eclampsia was higher among mothers whose ethnicity differed from the father.

Smoking

Smokers appear to be relatively protected against pre-eclampsia, and the reasons for this remain poorly understood. Smoking is associated with reduced levels of sFLT-1 in non-pregnant women (SCHMIDT-LUCKE et al., 2005). It has been hypothesized, therefore, that reduced levels of sFLT-1 in smoking pregnant women would put them at lower risk of pre-eclampsia since sFLT-1 is thought to be a key factor in the development of the condition. To examine this relationship Kamareinen et al. (2009) compared third-trimester plasma sFLT-1 levels

and first-trimester placental sFLT-1 levels (obtained at termination of pregnancy) between pregnant smokers and non-smokers; no significant differences between the two groups was found. The molecular mechanisms regulating the release of sFLT-1 and sENG remain poorly understood. This is an important area of research since mechanisms to block their release may help to delay or even prevent the onset of pre-eclampsia, improving both maternal and fetal outcomes.

2.2.5 Relative risk of individual risk factors

Established risk factors associated with pre-eclampsia, along with relative risk and 95% confidence interval are shown in Table 2.

In addition to these well-established risk factors, others have more recently been reported to be associated with pre-eclampsia. Asthma, another condition characterized by chronic inflammation, has been implicated; in a study of 650 asthmatics and 1000 non-asthmatic pregnant women, women with moderate to severe asthma symptoms had an increased risk of developing pre-eclampsia, regardless of treatment, compared to those without symptoms (TRICHE et al., 2004). Moreover, a history of coronary heart disease in the pregnant woman's father has been recently reported as conferring an almost 2-fold increased risk of pre-eclampsia (NORTH et al., 2011).

Table 3 - Maternal risk factors for pre-eclampsia.

Risk Factor	Relative Risk (95% CI)
Null parity	2.91 (1.28 to 6.61)
Previous pre-eclampsia	7.19 (5.85 to 8.83)
Age > 40 yrs	1.96 (1.34 to 2.87)
Body Mass Index \geq 35 kg/m ²	1.55 (1.28 to 1.88)
Twin pregnancy	2.93 (2.04 to 4.21)
Diastolic BP > 80 at booking	1.38 (1.01 to 1.87)
Pre-existing diabetes	3.56 (2.54 to 4.99)
Family history (mother or sister)	2.90 (1.70 to 4.93)
Antiphospholipid antibody	9.72 (4.34 to 21.75)

Source: Adapted from Duckitt and Harrington (2005, p.4).

The problem with using these factors to stratify pre-eclampsia risk is that many of them are extremely common in the pregnant population. Further, the majority of these risk factors are non-modifiable. The relationship between different risk factors is also

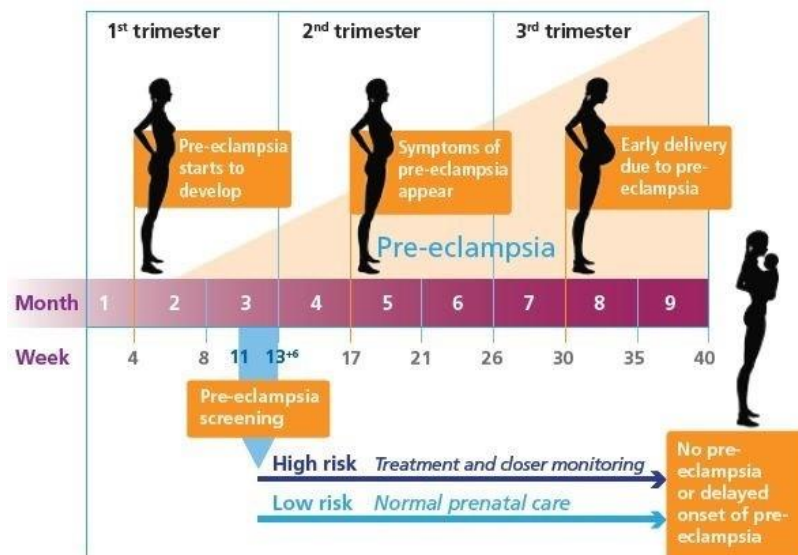
uncertain. For instance, it is not known whether a multiparous woman with high BMI remains at increased risk of pre-eclampsia if her previous pregnancies were uncomplicated.

As women in modern Western society begin to have children at a later stage in life, and as the population as a whole becomes more obese, these risk factors will become less useful in risk stratification. There is now, therefore, more of a clinical need than ever to identify clinical or biochemical parameters that will help to inform clinicians which women are at increased risk of developing pre-eclampsia.

2.2.6 Diagnostic Tests for Pre-eclampsia / Eclampsia

There have been many screening tests evaluated in the literature over the years for predicting pre-eclampsia. These screening tests have been comprehensively reviewed in a World Health Organization publication (CONDE-AGUDELO; VILLAR; LINDHEIMER, 2004). A further summary of predictive tests, including a review of preventative interventions and economic modeling, has been published by the UK National Institute for Health Research (MEADS et al., 2008).

Figure 4 – Pregnancy, Signs and Symptoms of Pre-eclampsia.



Source: Weebly Preeclampsia (2015).

Uterine Artery Doppler

The advent of ultrasound has revolutionized the practice of obstetrics in the past 50 years, offering a window into the uterus through which it can assess the anatomical structures of the fetus. The latest addition of Doppler flow studies of maternal and fetal vessels provides more useful information, allowing the evaluation of maternal-fetal physiology unit. Doppler studies are non-invasive and acceptable to patients and can be performed at the same time as a detailed anomaly scan, and have therefore been widely studied for its role in the detection of adverse maternal and fetal outcomes.

In the non-pregnant state, there is a rapid increase and decrease in the rate of flow of the uterine artery during systole and a notch in the form of the downward wave at the start of diastole. The remodeling of the spiral arteries in early pregnancy is an important step in regulating and maintaining placental perfusion. Reducing the resistance of the spiral arteries as a result of remodeling during pregnancy can be reflected in uterine artery Doppler studies, by a high-speed constant flow throughout diastole, and the loss of the diastolic notch at 20 to 24 weeks' gestation (SCISCIONE; HAYES; SMFM, 2009).

In pre-eclampsia, the remodeling of the spiral arteries is impaired. This pathological resistance to placental flow can be detected by Doppler studies of the maternal uterine vessels, offering the potential to detect women at risk not only of pre-eclampsia but also of intra-uterine growth restriction. Abnormalities are detectable as early as 12 weeks of gestation; for women with abnormal first trimester testing the likelihood ratio (LR) for the development of pre-eclampsia is approximately 5, while normal Doppler studies carry an LR of 0.5 (SCISCIONE; HAYES; SMFM, 2009). Although this relationship persists into the second trimester, the optimal timing for performing these studies remains uncertain.

The use of uterine artery Doppler was perhaps best summarized in a comprehensive meta-analysis. Cnossen et al., (2008) reviewed 74 uterine artery Doppler studies including nearly 80,000 pregnant women, of whom 2,500 developed pre-eclampsia. The majority of Doppler indices had poor predictive characteristics, but this varied with patient group studied and severity of the disease. For all women, the overall risk of pre-eclampsia was best predicted by an elevated second trimester PI accompanied by persistent bilateral uterine artery notching. As a result of these findings, the authors concluded that Doppler studies were more accurate for prediction of future preeclampsia when performed in the second trimester rather than the first trimester. Since the false positive

rate was relatively high, they felt that the increased anxiety and expense associated with abnormal results could not justify their use for screening in low-risk women.

The majority of studies using uterine artery Doppler studies to predict pre-eclampsia have been performed in large centers with significant experience and expertise in their use. It remains to be seen whether these findings are applicable in smaller centers, or in the developing world where they would be more likely to be clinically useful. The tests are also relatively time-consuming, taking around 20 minutes to perform (SCISCIONE; HAYES; SMFM, 2009), which may preclude their use in the general pregnant population. The combination of these studies with maternal risk factors, or with analysis of serum markers such as antiangiogenic factors (YU et al., 2006) may ultimately be more clinically useful.

Arterial Stiffness

Normal pregnancy is associated with a number of changes to the maternal circulation, with an increase in heart rate and cardiac output and a corresponding reduction in vascular resistance and arterial blood pressure. In contrast, pre-eclampsia is characterized by an increase in vascular resistance and generalized vasoconstriction (ELVAN-TASPINAR et al., 2004).

The traditional measurement of blood pressure using sphygmomanometry means that much of the information contained in the shape of the arterial waveform is lost. The assessment of central pressures and arterial stiffness can give more information on the risk of developing preeclampsia. Although the waveform of the arterial pulse has been used as an evaluation tool since the late nineteenth century, it is only recently that technological advances have enabled the recording and detailed analysis of waveforms for clinical use. Applanation tonometry is one such technique that allows non-invasive assessment of the various components of the pulse wave, which is simple, validated, reproducible and non-invasive (MACEDO et al., 2008).

Pulse Wave Analysis in Pre-eclampsia

It is well established in the non-pregnant population that arterial stiffness is associated with traditional risk factors for cardiovascular disease. Given that pre-eclampsia and cardiovascular disease share a number of common mechanisms, several studies have examined the relationship between arterial stiffness and pre-eclampsia. In non-pregnant women, AIx decreases during the luteal phase of the menstrual

cycle and rises at the beginning of the menstrual cycle (ROBB et al., 2009). AIx is lower in pregnant women compared to non-pregnant controls, and within pregnancy, AIx decreases further (MACEDO et al., 2008). This fall is thought to be related to NO-mediated vasodilatation. Several studies have shown that, at term, women with pre-eclampsia have increased AIx, indicating increased arterial stiffness, compared to non-pregnant controls (SPASOJEVIC et al., 2005). Women with pre-eclampsia have a higher AIx compared to women with gestational hypertension without proteinuria, an increase that persists after correction for blood pressure (SPASOJEVIC et al., 2005). No difference has been reported by women with pre-eclampsia at term and those with pre-eclampsia requiring preterm delivery (ROBB et al., 2009), nor has a difference been reported between different ethnic groups studied (KHALIL; COOPER; HARRINGTON, 2009).

Uric Acid

Hyperuricemia has been reported to be elevated in preeclampsia in 1917 (SCHACKIS, 2004) and remains one of the most common blood tests to assess the condition in clinical practice in the UK. Uric acid is a marker of oxidative stress, tissue injury, and renal dysfunction, and several studies have reported a positive correlation between high levels of uric acid in maternal serum and adverse pregnancy outcomes (THANGARATINAM et al., 2006). In view of this, the National Heart, Lung and Blood Institute (NHLBI) of the United States, recommends measuring serum uric acid in high-risk women with normal blood pressure (CNOSSEN et al., 2006).

A systematic review of the literature, however, examining 18 studies of 4,000 pregnant women, consistently observed the poor performance of uric acid in predicting various maternal and fetal outcomes (THANGARATINAM et al., 2006). Furthermore, a study designed to examine the impact of the uricosuric agent Probenacid in lowering uric acid in 40 women with pre-eclampsia did not demonstrate any effect on maternal blood pressure, nor on any other fetal or maternal outcomes (SCHACKIS, 2004). It, therefore, appears that while uric acid may be of value in the detection of pre-eclampsia, it is not useful in the early prediction of disease.

Blood Pressure Measurement

Although blood pressure measurement is clearly essential for the detection of hypertensive disorders of pregnancy, it remains to be seen whether measurement of blood pressure in the first or second trimesters

can predict which women will develop problems later on. Increased diastolic blood pressure is associated with an increased risk of preeclampsia (DUCKITT; HARRINGTON, 2005), but studies using assessment of blood pressure in the first or second trimester for prediction of pre-eclampsia have reported false-positive rates ranging from 7 - 52% and detection rates ranging from 8 - 93% (POON et al., 2008). It is likely that these differences relate to differences in the populations studied, different techniques used to measure blood pressure, and different definitions of pre-eclampsia. A meta-analysis of 34 studies evaluated the role of systolic pressure (SBP), diastolic pressure (DBP), mean arterial pressure (MAP) and increase in blood pressure during the first or second trimester to predict pre-eclampsia in low and high-risk women (CNOSSEN et al., 2008). MAP was shown to be superior to SBP, DBP and increase in blood pressure between the first and second trimester in predicting pre-eclampsia; second trimester MAP of ≥ 90 mmHg was associated with a positive likelihood ratio of 3.5 for pre-eclampsia and a negative likelihood ratio of 0.46.

Ambulatory blood pressure monitoring (ABPM) allows multiple readings to be taken using automated blood pressure devices, in a nonclinical environment. As such this may provide a better estimate of true blood pressure since it is not confounded by the “white coat” effect (HIGGINS et al., 1997). Few studies have examined ABPM in the context of pre-eclampsia prediction, and the majority of these are suboptimal (CONDE-AGUDELO; VILLAR; LINDHEIMER, 2004).

One study which examined over 1100 women who had 24 hour ABPM between 18 and 24 weeks’ gestation did not find ABPM to be a useful predictor of hypertension later on in pregnancy (HIGGINS et al., 1997) since absolute differences in ABPM measurements were small, and overlap between hypertensive and normotensive women was high.

2.2.7 Other social determinants of Maternal Death

The probability of women dying during pregnancy and childbirth is closely linked to their social and economic status, norms and values of their culture and distance from their home. In fact, maternal mortality rates reflect the gap between rich and poor countries more than other health measures (WHO, 2008).

The high rate of maternal mortality is an indication of not only a substandard health system, but also of deep gender inequalities that leave women with limited control over decision-making and limit their

access to social support, health, and economic opportunities (WHO, 2008).

In many developing countries, legal systems provide little help to women and girls to protect their reproductive rights. In some cases, the laws deliberately denies such rights, such as laws that prohibit adolescent girls from accessing contraception or require permission from their parents or husbands (TEMIN; LEVINE, 2009).

In some communities, women's health is valued less than that of men. Parents may prioritize their sons' over their daughters' lives and health. Girls and women often do not have control over financial resources or access to transportation and are thus dependent on male relatives or mothers-in-law for mobility and access to health services (WHO, 2008).

Across the developing world, girls' health is determined more by social forces than biological ones. Poverty and gender inequality put girls at risk for exploitation, physical abuse, early pregnancy (TEMIN; LEVINE, 2009).

Education is a critical determinant of women's health. Education allows women to make informed choices and seek proper health care. A World Health Organization report on Asia and the Pacific shows that female literacy rates are a strong predictor of maternal mortality rates (WHO, 2008).

Pakistan has made progress in achieving the health targets. But despite reductions in the Maternal Mortality Rate, Pakistan is still behind other developing countries with respect to these indicators. This is due to the interplay between various factors such as the low societal status of women, poor nutrition, poverty, illiteracy, inappropriate health-seeking behavior, a poorly functioning health system, poor access to health services and a rapidly growing population (MAHMUD et al., 2011).

The need for contraception is higher among less educated, younger, poor and living in rural areas. In many developing countries, women with high income are twice as likely to use modern contraceptives than women with low-income (SINGH, 2009).

Lack of education and poor knowledge about maternal health care can contribute to delays in seeking care during pregnancy and childbirth. Poor mothers are at high risk of developing pregnancy related complications. Almost all maternal deaths that occur in low and middle-income countries are mainly among the poorest of the poor (WHO, 2015b). Most obstetric complications cannot be predicted, but it can be prevented and treated if women have access to adequate health care. The

lack of access to emergency obstetric care and delay for emergency referral are factors that contribute to high maternal mortality.

The lack of access and control of resources, limited educational opportunities, poor diet and lack of decision-making ability significantly contribute to adverse outcomes related to pregnancy. Factors such as cultural beliefs, socio-demographic status, empowerment of women, economic conditions, physical and financial accessibility are important determinants of use of maternal health services (SHAIKH; HATCHER, 2005).

In India, the low utilization of maternity services seems to be due to low levels of household income, high illiteracy and ignorance, and a host of traditional factors (SHARIFF; SINGH et al., 2002). A study realized in Pakistan described the poor socio-economic status, lack of physical accessibility, cultural beliefs and perceptions, low literacy level of the mothers and large family size as the leading causes of poor utilization of primary health care services (SHAIKH; HATCHER, 2005).

In India, the low utilization of maternity services appears to be due to low levels of household income, high rates of illiteracy and ignorance, and a number of traditional factors (SHARIFF; SINGH et al., 2002; THIND et al., 2008). Similarly, a study (SHAIKH; HATCHER, 2005) in Pakistan has described the poor socioeconomic status, lack of physical accessibility, cultural beliefs and perceptions, the low level of literacy of mothers and the large size of the family as the main causes of poor utilization of primary health care services (SHAIKH; HATCHER, 2005). A study (MEKONNEN, Y.; MEKONNEN, A., 2002) in Ethiopia observed that the use of maternal health services can be influenced by the sociodemographic characteristics of women, the cultural context, and the accessibility to these services.

2.3 PRENATAL OR ANTENATAL NURSING CARE

Antenatal nursing care includes the care of pregnant women and their families at all stages of pregnancy and childbirth, as well as the first 4 weeks after birth (ALDEN et al., 2013). The main objective is to provide regular check-ups that allow midwives or nurses to prevent possible health problems during pregnancy. Throughout the antenatal period, nurses provide care to women in primary health centers, clinics, and hospitals and prepare them for childbirth. Nurses teach women and their families about pregnancy, the process of labor, birth, and recovery

and parenting skills. They provide continuity of care throughout the childbearing cycle.

Prenatal nursing may reduce the risk of complications during pregnancy. Following a healthy diet, getting regular exercise as advised by a nursing care provider, and controlling existing conditions, such as high blood pressure and diabetes, is important in order to avoid serious complications in pregnancy such as pre-eclampsia. The prenatal visits are designed to increase checkup frequency later in the pregnancy, which increases the assessment of blood pressure, urine tests, and other nursing care activities.

If the blood pressure is increased at any time before the delivery, the nursing care emphasizes on more frequent blood pressure readings. They might be asked to stay until the blood pressures are taken for a few hours rather than a one-off reading.

If only blood pressure is increased, nursing care may start tablets (defined in protocols) to lower it and prevent it from further increase. If other features of preeclampsia occur, such as headaches or liver pain, the nurse forwards the woman to the hospital and suggest support from other professionals.

Prenatal care is a program of care for a pregnant woman before she gives birth to her baby. It's very important for women to start their prenatal care in the first trimester of pregnancy followed by at least 4 antenatal visits (WHO, 2015b). The nursing care improves the access to antenatal care and promotes all the support in the networking care. Appropriate nursing care during pregnancy and childbirth is essential to reduce the maternal mortality. One-quarter of maternal deaths are due 1/4 to inadequate delivery of health care from the beginning of pregnancy (CHRESTANI et al., 2008).

In developed countries, mostly pregnant women receive visits to the nurse or midwifery about once a month during the first six months. The frequency of visits increases to every two or three weeks for the remainder of the pregnancy. In the prenatal period, pregnant women need nursing care for her, her baby and the family. During prenatal nursing care visits, nurse or nurse-midwife will make sure the pregnant women, developing fetus are healthy and strong. These regular checkups are necessary for pregnancy because, if there are any danger signs, it will be easy to manage at the initial stage. The prenatal period provides an excellent opportunity for nurses to influence family health. During this period, essential healthy women seek regular care and guidance. The nurse's health promotion interventions can affect the well-being of the pregnant women (CORBETT; CALLISTER, 2000).

Caring of a primary pregnancy with eclampsia is a challenge to any nurse and interdisciplinary team. The nurse's keen observation and prompt decision-making ability to use lifesaving procedures and referral to the right place, at the right time, can save the mother. Skilled midwives are valuable members of the community. They are more than a nursing care provider they are educators, mentors, and guardians of new life. A nurses needs to know the danger signs of pregnancy and educate women about these risks:

- Dizziness: hypertension, low blood pressure, malnutrition;
- Visual disturbance: Pre-eclampsia;
- Epigastric pain: Pre-eclampsia, heartburn;
- Reduced urine out: Pre-eclampsia, dehydration;
- A severe headache, Pre-eclampsia.
- Edema of hands of feet, Pre-eclampsia, diastolic blood 90 mm Hg or more after 20 weeks' gestation, Pre-eclampsia, convulsions, Pre-eclampsia, epilepsy;
- Fever, chills, muscle joint pain, infection, history of malaria, meningitis.

Nurses have the opportunity to identify women at risk of pregnancy and create a plan for their care that will reduce mortality of women (DAVIS, 2004). Ongoing prenatal care is important in achieving a healthy pregnancy and birth, and positively influencing the health of the child in the early years. It provides a pregnant woman with the opportunity to access health information and identify risks and underlying factors that can influence her health and the health of her fetus.

The purpose of prenatal care is to identify existing risk factors and other deviations from normal so that pregnancy outcomes may be enhanced. Major emphasis is placed on preventive aspects of care, primarily to motivate the pregnant women to practice optimal self-care and to report unusual changes early so that the problem can be minimized or prevented. If health behavior must be modified in early pregnancy, the nurse needs to understand psychosocial factors that may have an influence on the women (CHOU et al., 2003).

In Brazil, the Unified Health System provides universal, integrated and free health care services. Antenatal care has been given high priority since 2000 when implemented many programs (BRASIL 2012a,b; 2013; SERRUYA; LAGO; CECATTI, 2004).

2.3.1 Importance of nursing care to prevent pre-eclampsia

All pregnant women should have proper access to effective nursing antenatal care irrespective of their social, economic, cultural and geographical background. Appropriate care during pregnancy and childbirth is essential to reduce the maternal mortality. One-quarter of maternal deaths are due to inadequate delivery of health care from the beginning of pregnancy (CHRESTANI et al., 2008).

Prenatal care visits are the proper time for nurses to advise pregnant women about their diet, exercise, and other lifestyle changes during pregnancy. Prenatal care visits are the proper time for nurses to advise pregnant women to change her lifestyle during pregnancy and promote awareness to improve the well-being of the pregnant women (CORBETT; CALLISTER, 2000; DAVIS, 2004).

Major emphasis is placed on preventive aspects of nursing care, especially to encourage the pregnant women to practice optimal self-care and to report unusual changes early so that the problem can be minimized or avoided.

Nursing management plays a vital role in the care of the mother during pregnancy related complications. According to (WAGNER, 2004), pre-eclampsia affects approximately 5-7% of pregnancies and complications of hypertension and are together the third leading cause of pregnancy-related deaths. Early recognition of the signs and symptoms of this syndrome is vital for an optimal outcome for both mother and fetus. Because this the nursing observation is very important throughout the course of pregnancy.

Nurses must understand the pathophysiology of pre-eclampsia to provide an optimal nursing care management (ARAFEH, 2006). Once the diagnosis of pre-eclampsia is confirmed, nurses must utilize assessment skills, proper nursing interventions, and patient teaching to promote a safe environment for labor and delivery.

Nursing management is a key variable in promoting a positive outcome for the mother. It begins with a review of prenatal records and an interview with the patient to clarify the history and observation of any severe headaches, visual disturbances or severe pain. The physical examination and observation by the nurses must be consistent when taking and recording blood pressure. Assessing edema, deep tendon reflexes, breath sounds for crackles, the level of consciousness, and intake and output is essential when caring for a pre-eclamptic patient (PERRY et al., 2014).

Furthermore, nursing care includes assessing uterine toxicity for

signs of abruption. Nursing care is essential to monitor cervical changes to evaluate and document the progression of labor. The nurse should be aware of ongoing laboratory results, taking into account any changes compared to the previous levels. It is also essential that the nurse is prepared at any time for an emergency delivery due to the risk of complications.

The most common antihypertensive used during labor is hydralazine IV in five to ten-milligram doses or labetalol IV twenty milligram bolus, followed by forty milligrams after ten minutes. Magnesium Sulfate is the drug of choice to prevent and treat eclamptic seizures during labor (SCHROEDER et al., 2002). Many authors suggest administering Magnesium Sulfate piggyback with a loading dose of four to six grams diluted in a hundred milliliters of intravenous fluid infused over fifteen to thirty minutes, followed by a maintenance dosage according to the provider's orders (PERRY et al., 2014).

In the inpatient setting, educating the patient and her significant other on the disease process and the management rationale is a primary nursing action. It is important for the woman and her family to understand what is physiologically happening within the body to have a greater understanding of the treatment plan and the compromise with her pregnancy.

In the context of hospital admission, educating the patients and their families about the disease process and management is one of the primary nursing care actions. It is important for the woman and her family to understand what is happening physiologically inside the body to have a greater understanding of the treatment plan and commitment to her pregnancy.

The nurse should review the signs and symptoms of pregnant women that require immediate attention and assess current patient knowledge about pre-eclampsia and other pregnancy related complications and add more information to an extent which patient can understand. The nurse should explain the treatment plan in progress and the variables that will change the care plan. This ensures that the patient will be prepared for any other complications that may arise. Women and her partner should be involved in managing and controlling the situation. In turn, this can help reduce the anxiety associated with the complication in pregnancy.

The nurse is responsible for taking care of the mother and fetus during labor and delivery, which requires nursing care to promote the most favorable outcome. Understanding maternal and fetal effects of preeclampsia help nurses to perform comprehensive assessments. The

information provided by the network of nursing care that is in the evaluation will determine nursing care and the steps needed to support the woman and fetus.

2.3.2 Nursing Care During Pregnancy

Nursing care for women has contributed to making the health system more responsive to the needs of women. Nurses have been crucial to the development of strategies to improve the welfare of women and their babies and have led the efforts to implement the guidelines of clinical practice. Nurses can have a voice in setting standards and influence health policy, actively participating in public education (ALDEN et al., 2013).

The prenatal period is a time of physical and psychological preparation for childbirth and motherhood. The nurse's interventions can improve the well-being of the pregnant woman and her unborn child for many years. The ideal regular prenatal visit starts immediately after the first menstrual period. Prenatal health care allows the discovery, diagnosis and treatment of pre-existing maternal diseases and other disorders that develop during pregnancy. Prenatal care is designed to monitor the growth and development of the fetus and detects abnormalities that interfere with the normal course of labor. Prenatal care also provides education and support for self-management. Healthcare professionals refer to early, middle, and late pregnancy as trimesters. The first trimester lasts from weeks 1 to 13, the second from weeks 14 to 26 and the third, from weeks 27 to 40 (ALDEN et al., 2013).

Health Needs during Pregnancy

Adaption to Pregnancy

Pregnancy affects all family members, and each family member has to adapt to the pregnancy and interpret its meaning in light of his or her own needs. This process of family adaptation to pregnancy takes place within a cultural environment influenced by societal trends. According to the cultural background, nurse must be prepared to support not only traditional families in the childbirth experience but also single-parent families, reconstituted families, and alternative families (ALDEN et al., 2013).

Maternal Adaptation

During pregnancy, all women adapt to the maternal role, a complex process of social and cognitive learning. Early in pregnancy nothing seems to be happening but with the perception of fetal movement in the second trimester, the woman focus on her pregnancy and her relationships with her mother and other women who have been or who are pregnant. Nurses being aware and knowledgeable can play a vital role in fulfilling the information need of women regarding the pregnancy and motherhood (ALDEN et al., 2013).

Care Management

The purpose of prenatal care is to identify existing risk factors and other anomalies so that pregnancy outcomes may be enhanced (GREGORY; NIEBYL; JOHNSON, 2016). Emphasis is placed on the preventive aspects of care, especially to motivate pregnant women to practice good self-management and report unusual changes early so that problems can be avoided or minimized. If health behaviors need to be changed early in pregnancy, nurses need to understand the psychosocial factors that can affect a woman. In holistic care, nurses provide information and guidance on not only the physical but also the psychological and social impact of pregnancy on women and family members (ALDEN et al., 2013).

The current conventional model to provide prenatal care has been used for over a century. The first visit usually occurs in the first trimester, with monthly visits until the 28th week of pregnancy. The visits are then scheduled every 2 weeks until week 36 and then every week until the birth (AAP; ACOG, 2012).

Prenatal care is ideally a multidisciplinary task in which nurses work with nutritionists, physicians, social workers, and others in order to provide a integral care to pregnant women. To emphasize the nursing role, care management for the initial visit and follow-up visits is organized around the central elements of the nursing process which is assessment, nursing diagnoses, expected outcomes, plan of care and interventions, and evaluation (ALDEN et al., 2013).

Nursing Assessment of Pregnant Women - Initial Visit

Nursing care needs to be guided by the current scientific evidence since nurses are the first professionals to have contact with pregnant women during pregnancy (WHO, 2015b). Prenatal care begins when the presence of pregnancy and the desire of its continuation is confirmed. The assessment process starts from the first prenatal visit and is

continued throughout the pregnancy. Assessment techniques include interview, physical examination, and laboratory tests. The therapeutic relationship between the nurse and the woman is established during the initial assessment interview (ALDEN et al., 2013).

History

The history of health includes those physical conditions, use of medications or procedures that may affect the pregnancy or that may be affected by the pregnancy. The dietary assessment shows special dietary practices, food allergies and eating behaviors. Similarly, a woman's past and present use of drugs and prescription medications are assessed. In addition, the family history provides information about the woman's immediate family, including parents, siblings, and children. These data help identify genetic disorders or conditions that could affect the present health status of the woman or her fetus. Situational factors such as the family's ethnic background, cultural trends, and socio-economic status are also assessed (ALDEN et al., 2013).

Interview

Women should be interviewed about their psycho-social and mental health symptoms they are experiencing. During interviews throughout the pregnancy, nurses should be alert to the emergence of potential problems, such as depression, lack of family support and inadequate living conditions. Nurses should assess women's attitudes to health, particularly during fertility, their expectations of health care providers, and their view of the relationship between women and the nurse. At the beginning of pregnancy, the nurse must determine the knowledge and awareness of pregnant women regarding pregnancy, maternal changes, fetal growth, self-care, dangerous signs, and food. Before planning nursing care, the nurse needs information about women's lifestyle, exercise habits, sleep pattern, diet, interests, personal hygiene and clothing behaviors. Similarly, the nurse should ask the woman to identify and characterize existing or simultaneous problems in all systems of the body and assess their mental state (ALDEN et al., 2013).

Physical Examination

Physical examination includes reviewing the body systems, vital signs, weight, pelvic examination, and fetal heart rate. The initial physical examination provides the baseline for assessing subsequent changes. The nurse should fulfill the information need of the woman and should explain the basic information along with a demonstration of the equipment and procedure that may be used. The interaction requires a hassle-free, sensitive, and gentle approach. The physical examination

begins with the assessment of vital signs and body mass index. During the examination, the nurse should remain attentive to the woman's suggestions that provide guidance for further evaluation. Each time a pelvic exam is performed, the tone of the pelvic muscles and the woman's knowledge of Kegel exercises is assessed. Particular attention is paid to the size of the uterus because this is an indication of the duration of pregnancy. During the examination, the nurse can coach the woman in breathing and relaxation techniques, as needed (ALDEN et al., 2013).

Laboratory Tests

The laboratory data obtained from the analysis of the samples obtained during the examination, provide important information about the symptoms of pregnancy and the health status of the women. Samples are collected at the initial visit so that the cause of any potential risks can be treated. Blood and urine may be collected for several tests. The finding of risk factors during pregnancy may indicate the need to repeat some laboratory tests at different times (ALDEN et al., 2013).

Nursing Assessment of Pregnant Women - Follow-up Visit

In traditional prenatal care, monthly visits are scheduled during the first and second trimesters, although women may set up additional appointments if necessary. During the third trimester, however, the risk of complications increases, and the need for closer follow-up become necessary. From week 28, maternity visits are scheduled every two weeks until week 36 and then every week until birth. Visits can occur more or less frequently, often depending on the individual needs, complications and risks of pregnant women (ALDEN et al., 2013).

Follow-up visits are less intense than the first prenatal visit. At each of these follow-up visits, the woman is asked to summarize relevant developments since the previous visit. All suspicious signs or symptoms and review of the physical systems of women are performed in detail. Subsequent evaluation is a constant procedure in the care of a pregnant woman. Physiological changes are documented as the pregnancy progress and are checked for any deviation from the normal course. At each visit, physical parameters are measured. The weight of the woman is evaluated and the adequacy of a weight gain during gestation is evaluated in relation to her body mass index. Urine may be checked by dipstick, and the presence and degree of edema are noted (ALDEN et al., 2013).

The number of routine laboratory tests performed during follow-up visits in pregnancy is limited. A clean urine sample is collected to

measure glucose, proteins, nitrites and leukocytes at each visit. Urine samples are obtained for culture and sensitivity, and vaginal and blood samples are taken to repeat a test, if necessary. The nurse-client relationship is essential to set the tone for further interaction. The techniques of listening with an attentive expression, using eye contact and recognizing the woman's feelings and her right to express these feelings, is very important. The interaction can take place in diverse formal and informal contexts. A clinical setting, home visits or telephone conversations provide opportunities which can be used effectively (ALDEN et al., 2013).

The nurse can help a woman to gather relevant information, explore her options, decide on a course of action, and take responsibility for the results. These options may include living with a problem, as it is, to alleviate the effects of a problem so that it can be more easily accepted, or eliminate the problem. Educational literature describing fetal and maternal changes is available and can be used to explain the changes as that occur. A knowledgeable and observant nurse knows the typical concerns of the prospective parents, anticipate the questions that will be asked and encourage women to discuss what is in their minds. Often, printed literature and brochures can be used to complement individualized nursing education related to the women experience (ALDEN et al., 2013).

Assessing the nutritional status of a woman and providing information about nutrition are part of the responsibilities of nurses in prenatal care. This includes assessing weight gain during pregnancy and prenatal nutrition. Education may include discussion about iron-rich foods, prenatal vitamins, and recommendations to moderate or limit caffeine intake and smoking (ALDEN et al., 2013). Most studies on pregnancy in humans showed no association between caffeine intake and birth defects or low birth weight, however, some studies have documented an increase in the risk of miscarriage with increased caffeine consumption at 200 mg/d (WENG; ODOULI; LI, 2008).

2.3.3 Interventions for a woman with mild pregnancy induced hypertension

Women with mild pre-eclampsia can be managed at home with frequent follow-up care. Regardless of the setting, the care is similar.

Monitor Antiplatelet Therapy

Due to the increasing trend of platelets aggregation along the

arterial walls, an antiplatelet agent such as low-dose aspirin may prevent or delay the development of preeclampsia (DULEY et al., 2007).

Promote Bed Rest

When the body is in the supine position, sodium tends to be excreted at a higher rate during activity. Bed rest is the best way to help increase sodium evacuation and promote diuresis. Rest should always be in a lateral recumbent position in order to prevent uterine pressure on the vena cava and avoid supine hypotension syndrome (GABBE et al., 2016).

Promote Good Nutrition

Women needs to continue their normal pregnancy nutrition. At one time, rigorous salt restriction was recommended to reduce edema. However, it is no longer true, because heavy sodium restriction can activate the reninangiotensin-aldosterone system and cause an increase in blood pressure (PERRY et al., 2014).

Provide Emotional Support

It is difficult for a woman with preeclampsia to assess the possible severity of the symptoms, as they are so uncertain. Neither high blood pressure nor protein level in urine is something she can see or feel (PERRY et al., 2014). It is not always easy to follow the instruction of getting an additional rest during the day on the basis of a few uncertain symptoms since most women contribute financially to the running of their household (GABBE et al., 2016). Therefore, stress, anxiety, and ups and downs often develop during the course of pregnancy. Family, friends and health care providers can play their role in comforting women if they are feeling vulnerable.

2.3.4 Nursing interventions for a woman with severe pregnancy induced hypertension

Support Bed Rest

In the case of severe pre-eclampsia, most women are hospitalized so the rest can be enforced and a woman can be more closely observed. Visitors in such a case are generally restricted to husband, father or older children. Because a loud noise such as a baby's crying or a dropped tray may be enough to trigger a seizure initiating eclampsia (GABBE et al., 2016). A dark and quiet room is highly recommended because a bright light can also trigger seizures. However, the room should not be so dark that healthcare professionals have to use a flashlight to do evaluations. Flashlight targeting into the woman's eyes

is the kind of sudden stimulation to be avoided. Stress is another stimulus capable of increasing blood pressure and cause seizures in a woman with severe pre-eclampsia. Make sure that women are given clear explanations of what is happening and what is expected (PERRY et al., 2014).

Monitor Maternal Well-being

Blood pressure should be measured at least every 4 hours, or with a continuous monitoring device to detect any increase. Blood tests such as blood count, platelet count, liver function, blood urea nitrogen and creatinine and fibrin degradation products should be obtained in order to assess renal and hepatic function and development of ICD. Since a woman is at high risk of premature separation of the placenta and resulting hemorrhage, a blood sample for type and cross-match is usually also obtained (PERRY et al., 2014).

Daily hematocrit levels are used to observe blood concentration. This level will increase if more fluid is leaving the bloodstream for interstitial tissue (edema). On the other hand, anticipating the need for frequent plasma estriol levels (a test of placental functioning) and electrolyte levels is also essential. A woman's optical fundus should be evaluated daily for signs of arterial spasm, edema, or hemorrhage. Obtain daily weights at the same time in order to re-assess fluid retention (GABBE et al., 2016).

A permanent urinary catheter may be inserted to allow accurate recording of output and comparison with intake. Urine output should be greater than 600 ml per 24 hours. Proteins in urine and specific gravity are measured and recorded. A 24-hour urine sample can be collected for protein measurements and creatinine clearance to assess renal function. A woman with mild pre-eclampsia that spills from 0.5g to 1g protein for 24 hours (1+ a random sample). Similarly, a woman with severe pre-eclampsia spills approximately 5 g for 24 hours (3+ to 4+ an exemplary individual) (PERRY et al., 2014).

Monitor Fetal Well-being

In general, a single doppler auscultation at intervals of approximately 4 hours is sufficient at this stage of treatment. However, fetal heart rate can be measured continuously with an external fetal monitor. A woman can have a stress test or a biophysical profile done every day to assess utero-placental sufficiency. Administration of oxygen to the mother may be necessary to maintain adequate oxygenation and prevent fetal bradycardia (PERRY et al., 2014).

Support a Nutritious Diet

A woman needs a diet rich in protein and moderate in sodium to

compensate for the protein she is losing in urine. An intravenous fluid line is usually initiated and maintained to serve as an emergency route for drug administration as well as to administer fluid to reduce hemoconcentration and hypovolemia (ALDEN et al., 2013).

Administer Medications to Prevent Eclampsia

A hypotensive drug such as hydralazine (Apresoline), labetalol (Normodyne), or nifedipine may be prescribed to minimize hypertension. These medications work to reduce blood pressure by peripheral dilatation and thus do not interfere with placental circulation. Pulse and blood pressure should be assessed since these medications can cause maternal tachycardia. Diastolic pressure should not be lowered below 80 to 90 mm Hg or inadequate placental perfusion could occur. Even with these new drugs, magnesium sulfate, however, still remains the drug of choice to prevent eclampsia (SHILVA SAHA; KALRA; PRASAD, 2007). This medication reduces edema by causing a change in fluid from the extracellular spaces into the intestine. It also acts as a central nervous system depressant which lowers the possibility of seizures (KARCH, 2015). To lower the blood pressure immediately, magnesium sulfate is first administered intravenously in a loading or bolus dose. The drug acts almost immediately but its effect remains only for 30 to 60 minutes, so administration must be continuous.

2.3.5 Nursing interventions for a woman with eclampsia

Severe pre-eclampsia deteriorates to eclampsia when cerebral irritation from increasing cerebral edema becomes so acute that a seizure occurs. This usually occurs at the end of pregnancy, but can also happen up to 48 hours after delivery. Immediately before a seizure, a woman's blood pressure and temperature increase suddenly. She also experiences blurring of vision or a severe headache and her reflexes become hyperactive. Vascular congestion of the liver or pancreas may lead to severe epigastric pain and nausea. The urinary output may drop sharply to less than 30 mL/hour. Eclampsia, however, actually occurs only when a woman experiences a seizure (ALDEN et al., 2013).

Tonic-Clonic Seizures

An eclamptic seizure occurs in stages. After the preliminary signal that something is happening, all the muscles of the woman's body contract. It arches her back, stiffens her arms and legs. Respirations may stop since her thoracic muscles get contracted. This phase of the seizure is called the tonic phase which happens approximately for 20 seconds

(ALDEN et al., 2013).

During the second stage of seizure which is called the clonic stage, the woman's bladder, and bowel muscles contract and relax which result in the incontinence of urine and feces. Breathing is not quite effective even if the woman is breathing during this stage. The clonic stage of a seizure lasts up to 1 minute. The primary care for a woman with a tonic-clonic seizure is to maintain her airway and supply oxygen by face mask to protect the fetus. To prevent aspiration, lie woman on her side in order to drain the secretions from her mouth. Magnesium sulfate or diazepam may be given intravenously as an emergency measure. Apply an external fetal heart monitor if one is not already in place to assess fetal status. If labor is required to progress despite the seizure, fetal heart sounds and uterine contractions should be continuously assessed (ALDEN et al., 2013).

The third phase of the seizure is called postictal stage. During this phase, a woman is semi-comatose and cannot be awakened, except for painful stimuli of 1 to 4 hours. Extremely close observation is as important during the third stage as during the first two phases. If the seizure causes premature separation of the placenta, labor may begin during this period, but woman will not be able to report the sensation of contraction. In addition, painful stimulation of contractions may initiate another seizure. Hold the woman's hand so that the secretions from the mouth can be drained. Do not give him anything to eat or drink. Remember that in coma, hearing is the last sense to be lost and the first one to be regained. Conversation with patient may be helpful as she may be able to listen, even if she does not respond (ALDEN et al., 2013).

Nursing Interventions During the Postpartum Period.

Postpartum hypertension can occur within 10 to 14 days after birth, although it usually does not occur more than 48 hours after birth (CANTEY; TECKLENBURG; TITUS, 2007). Monitoring blood pressure in the postpartum period and making sure that eclampsia can occur up to 2 or 3 weeks after birth is essential residual hypertensive or renal disease (CANTEY; TECKLENBURG; TITUS, 2007).

2.3.6 Networking

Networking is defined as "*the exchange of information or services among individuals, groups, or institutions*" (MERRIAM-WEBSTER.COM, 2016). It describes interactions and communication activities between individuals, groups, communities and organizations

operating in a variety of settings and contexts.

Information and knowledge is a valuable resource and has become the key to success in all fields of life. Communities, organizations, and companies need to understand precisely what information and knowledge will give them a competitive advantage. They then need to keep this knowledge, use it, share it and evolve it across the organization. Information and knowledge need to be managed, used, shared and evolved like a key asset. Gathering information and transforming it into useful knowledge require a great deal of collaboration, networking and focus on the community of practice (CoP) (WENGER; MCDERMOTT; SNYDER, 2002).

Since the boom in communication and information technologies (ICT), the field of eHealth has emerged into many forms and its potential has been discussed globally. eHealth has increasingly become part of people's everyday lives and has the ability to change how health care is delivered, the quality of the patient experience, and the cost of health care (WANG; LIU, 2009). It enables, among other things, the exchange of healthcare and administrative data and the transfer of medical images and laboratory results. The use of ICT in the health sector has the potential to change the face of global health systems and can deliver life-saving information even in the most remote and resource-poor settings (WHO, 2011). It is now reasonable to expect that by 2020 every inhabitant of our planet will, from any location and at any time, be able to access the medical information necessary to maintain his or her health or seek a cure for his or her illness. Improvement in ICT, development of smaller components with higher levels of security, decreasing costs and increasingly user-friendly features are the main reasons for adopting eHealth solutions in our daily lives (PIETTE et al., 2012).

Nurses need to adapt to the new ways of communication using information technology. This will not only enhance nurse-to-nurse collaboration but also nurse-to-patient interaction and will improve quality and safety of healthcare (VAN DE CASTLE et al., 2004). Collaboration means interpersonal interaction or collective action toward a common goal (D'AMOUR et al., 2005). It enables the sharing of knowledge and expertise and improves timeliness, quality and access to a broad range of health care services for individuals, families, and communities. In order for nursing to develop and excel as a profession, professional networking and interaction between nurses need to be strengthened. Such collaboration can help move the profession forward and ultimately improve clinical care (WASHER, 2002).

Networking provides access to countless opportunities for nurses and patients and allows them to communicate, interact and collaborate with each other in order to enhance nursing care practice and improve health. The ubiquity of information and communication technologies have the potential to improve access to both health information and services in health care. Networking tools play a central and supportive role in nursing practices and patient well-being. These tools can be divided into three main categories based on the nature of collaboration and their potential users. These categories are: “*Collaboration between Health Professionals*”, “*Nurse-to-Patient interaction*” and “*Patient-to-Patient interaction*”. (text already published by the author in Societies. For more detail please refer to (KHANUM et al., 2016).

3 METHODOLOGY

In this chapter the author described the aspects related to the study designs and methodology of the research work developed.

3.1 A SYSTEMATIC REVIEW WITHOUT META-ANALYSIS

PRISMA guidelines (MOHER et al., 2009) were used as a basis for the overall study approach. A systematic search was conducted from May 2015 to May 2016 to answer the research question of: What are the available best technologies and techniques for the prevention and control of pre-eclampsia and eclampsia? PubMed / MEDLINE, CINAHL, and COCHRANE were searched for articles published between 1985 to 2015, reporting on the available technologies and techniques for the prevention and control of pre-eclampsia and eclampsia in pregnant women. The question was adjusted according to the PICO acronyms; P (population/participants) representing all pregnant women; I (intervention) represent the use of available technologies and techniques; C shows comparison in the control group, the placebo group or non-existence of the comparison group; and O represented the outcomes of interest which was prevention and control of pre-eclampsia and eclampsia and reduction in maternal mortality. The search strategy was based on a number of medical subject headings MESH terms and text words.

Inclusion Criteria

Systematic Reviews and RCTs published in the English language between 1985 to 2015 based on the prevention and control of pre-eclampsia and eclampsia were eligible for inclusion in this review.

Exclusion Criteria

Studies, except systematic reviews and RCT's, were excluded. Studies not published in the English language, or whose topics were irrelevant to the objective of this study were also excluded.

Search Outcome

A total of 1,808 articles were initially identified using the search criteria from all the three databases, of which 14 were duplicate. Titles screening of the remaining 1,794 articles resulted in 330 relevant articles being selected for abstract screening. The abstracts of these 330 papers were then examined resulting in 58 papers being examined in full. Of these, 11 were excluded after quality assessment. The remaining 47 studies were fully read and were included in the review.

Each article was screened by two independent reviewers and disagreement between them was resolved by discussion. The aim was to identify as many articles as possible which have reported the use of different techniques and technologies for the prevention of pre-eclampsia and eclampsia in past 30 years.

Quality Appraisal

We assessed the quality of each paper meeting the inclusion criteria using the following: (a) relevance to the systematic review (b) validity and appropriateness of methodology (c) quality of evidence generalizability of results (d) quality of reporting (e) limitations of the study and how it was adjusted. The quality of the outcome was assessed using the Evidence Level: Joanna Briggs from Level I to II.

Data Extraction and Synthesis

All 47 papers were independently assessed by two reviewers. The following information was extracted from the included studies. General information about authors, journal, publication date, country, research design, location, participants, aim, sample size, evidence of use of the available technologies and techniques in pregnant women for the prevention of pre-eclampsia or eclampsia, results and descriptive summaries of numerical data. Synthesis of the studies involved categorizing technologies and techniques by their characteristics, narrating and summarizing its effectiveness and presenting data visually.

3.2 INTEGRATIVE REVIEW

This review was conducted from February 2015 to December 2015 to answer the research question: what does the scientific literature published between 2000 to 2015 report about the maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan? PUBMED/MEDLINE, CINAHL, and COCHRANE databases were

searched for the articles reporting on the maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan. The search was limited to articles published between January 2000 and December 2015 in the English language. The search strategy was based on a number of medical subject headings MESH terms and text words aiming to include as many relevant articles as possible.

Inclusion Criteria

Studies published in the English language between 2000 to 2015 which were reporting on the maternal mortality associated with preeclampsia and eclampsia in KPK Pakistan were eligible for inclusion in this review.

Exclusion Criteria

Articles that were published in a language other than English; studies reporting on maternal mortality associated with other complications of pregnancy and studies reporting on maternal mortality in other provinces of Pakistan were excluded.

Search Outcome

A total of 621 articles were initially identified using the search criteria from all the selected databases, of which 25 were duplicated. Title screening of the remaining 596 studies was completed which resulted in 95 studies to be selected for abstract reading. After abstract screening 08 studies were selected for full-text reading, of which all were included in the review, as shown in PRISMA flowchart. Each article was screened by two independent reviewers and disagreement between them was resolved by discussion. The aim was to identify as many relevant articles as possible which have reported on maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan.

Quality Assessment

We assessed the quality of each paper using the following: (a) relevance to this review (b) validity and appropriateness of the study methodology (c) quality of evidence (d) sampling method and quality of reporting (e) and limitations of the study. The quality of the outcome was assessed using the Evidence Level from Joanna Briggs Institute (from Level I to V).

Data Extraction and Synthesis

Extracting and synthesizing data from heterogeneous sources is a complex process (GOLDSMITH; BANKHEAD; AUSTOKER, 2007). All selected studies were independently assessed by two reviewers. The information was extracted from the included studies: general information about authors, journal, publication date, country and region; research design, location, participants, aims; maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan; results and descriptive summaries of numerical data.

Synthesis of the data involved categorizing and tabulating data and presenting it visually.

3.3 INTEGRATIVE REVIEW

This review was conducted from October 2015 to March 2016 to answer the research question of; what does the scientific literature published between 2005 to 2016 report about the nursing care practices in the prevention and control of pre-eclampsia and eclampsia? PUBMED/MEDLINE, CINAHL and COCHRANE databases were searched for relevant studies on nursing care practices in the prevention and control of pre-eclampsia and eclampsia. The search was limited to articles published between January 2005 to March 2016 in the English language. The search strategy was based on a number of medical subject headings MESH terms and text words aiming to include as many relevant articles as possible.

Inclusion Criteria: All types of qualitative and quantitative studies published in the English language between 2005 to 2016 which were reporting on nursing care practices for the prevention and control of pre-eclampsia and eclampsia, were eligible for inclusion in this review.

Exclusion Criteria: Studies that were published before 2005, reporting on nursing care practices in pregnancy-related complications other the pre-eclampsia and eclampsia and studies not reporting on the nursing care practices, were excluded.

Search Outcome: A total of 2,895 articles were initially identified using the search criteria from all the selected databases and through manual searching using Google Scholar, where 215 were

duplicated. The remaining 2,680 articles were selected for title-wise screening which resulted in 153 studies to be selected for abstract reading. After the abstract screening, 15 studies were selected for full-text reading, of which 14 were included in the review. All screening was done by three independent reviewers. Each article was screened by three reviewers and disagreement between them was resolved by discussion. The aim was to identify all relevant articles which have reported on the nursing care practices in the prevention and control of pre-eclampsia and eclampsia.

Quality Assessment: It is always difficult to analyze the quality of heterogeneous and distinctive primary sources in an effective manner (WHITTEMORE; KNAFL, 2005). The methodological quality assessment was not conducted in this review because the assignment of such quality score in different studies is an arbitrary and unscientific process (MEADE; RICHARDSON, 1997). However, tools like (CASP, 2002) and the Joanna Briggs Institute (JBI) were used to assess the quality of included studies. Similarly, assessment of studies was not summarized due to the inherited methodological complexity (WHITTEMORE; KNAFL, 2005). Articles were classified according to (MELNYK; FINEOUT-OVERHOLT, 2011).

Data Extraction and Synthesis: Extracting and synthesizing data from heterogeneous sources is a complex process (GOLDSMITH; BANKHEAD; AUSTOKER, 2007). All selected studies were independently assessed by two reviewers. The following information was extracted from each included study: general information about authors, journal, publication date, country and region; research design, location, participants, aims; nursing care practices in the prevention of pre-eclampsia and eclampsia; results and descriptive summaries of numerical data.

Synthesis of the data involved categorizing and tabulating data and then narrating, summarizing and presenting it visually.

3.4 THEORETICAL DESIGN

The application development life-cycle is a term used in systems engineering, information systems, and software engineering to describe a process for planning, creating, testing, and deploying an information system. It is a splitting of software development work into distinct

phases (or stages) containing activities with the intent of better planning and management. The iterative and incremental development (LARMAN; BASILI, 2003) methodology is to be followed in this work.

The basic idea behind this method is to develop a system through repeated cycles (iterative) and in smaller portions at a time (incremental), allowing developers to take advantage of what was learned during the development of earlier parts or versions of the system. Learning comes from both the development and use of the system, where possible key steps in the process start with a simple implementation of a prototype and then iteratively improving the system. At each iteration, design modifications are made and new functional capabilities are added.

It must be noted that during this thesis, I have focused and completed only the first two phases (Requirements and Design) of the development process of this network model. The others phases are intended to be completed in partnership with my advisor in a future research project.

The development of Pregnancy Nursing Care Virtual Network (PNCN) will involve a process consisted of the following steps (LARMAN; BASILI, 2003):

Requirements: This phase consist of gathering information about the target population, determining the needs or conditions to meet, deciding the contents and knowledge to be delivered, the tasks and function to be completed, and analysis of available technologies feasible for development and implementation.

Design: The design phase consists of planning, creating specifications, conceptualizing and framing material and production of content, preparing the storyboard and layout design and user interface (color, fonts, images and buttons).

Develop: The third phase, development, involves the creation of the activities that will be implemented. It consists of developing and programming the navigation structure, user interface, settings, images, content, and animations.

Test: Testing ensures that the materials achieved the desired goals and basic functionality. It is used to verify whether the component meets the requirements decided earlier, responds correctly to all kinds of inputs, performs its functions in an acceptable manner, is sufficiently usable, can be installed and used in its intended environments, and achieves the general result its end users require.

Debug: Debugging is the process of identifying and removing errors that prevent correct operation of computer software or a system.

Deployment: This stage consists of the installation of PNCN files to a central server and making available the client app through different mobile platforms.

Evaluate and Maintain: This phase involves review, evaluation and modification in a component after deployment to correct faults, add features, improve the performance or other attributes.

Expected Results

It will make possible, easy and useful communication between pregnant women, community, and nurses and will improve women knowledge and awareness regarding pre-eclampsia, eclampsia and other pregnancy-related complications and maternal health. It will increase antenatal care visits through application reminders and enable access / call to emergency obstetric care when complications arise and will improve referral communication and will increase access to quality care. This network will make it possible for pregnant women to communicate with midwives/nurse for useful information. It will improve antenatal, postnatal care and record keeping and will serve as maternal health indicators for policy makers. This network will enable monitoring, follow-up, referrals and interactive information for pregnant women along with continuity of care from the start of the pregnancy all the way through her post-partum period.

However, it must be noted that during this thesis, I have focused and completed only the first two phases (Requirements and Design) of the development process of this network model. The others phases are intended to be completed in partnership with my advisor in a future research project.

3.5 ETHICAL CONSIDERATIONS

This study was developed in the context of project TO 13075/2012 - FAPESC, Opinion N°. 120.343 and N°. 169.110 of the year 2012 (Annexes A and B) and for that reason, it respects what is set out the Resolution no. 466/2012 of the Ministry of Health Brazil (BRASIL, 2013). However, the completion of this research work did not involve any human subjects. Financial support was also granted by the CNPq and TWAS (CNPq process 190141/2012-3) to pursue PhD study in the Postgraduate Program in Nursing at Federal University of Santa Catarina (PEN-UFSC), Brazil.

4 RESULTS

Considering the goals previously set for the study, the result and discussion obtained are presented in four manuscripts according to the PEN/UFSC Normative Instruction 01/PEN/2016 attending the criteria for the format of presentation of work for completion of Doctoral degree in Nursing. Titles of the manuscripts are:

- *Technologies and techniques for the prevention of pre-eclampsia and eclampsia: a systematic review without meta-analysis;*
- *Maternal mortality associated with pre-eclampsia and eclampsia in Khyber Pakhtunkhwa province of Pakistan: an integrative review;*
- *Nursing care practices in the prevention and control of pre-eclampsia and eclampsia: an integrative review;*
- *Pregnancy nursing care virtual network: a theoretical design.*

4.1 MANUSCRIPT 1 - TECHNOLOGIES AND TECHNIQUES FOR THE PREVENTION OF PRE-ECLAMPSIA AND ECLAMPSIA. A SYSTEMATIC REVIEW WITHOUT META-ANALYSIS

TECHNOLOGIES AND TECHNIQUES FOR THE PREVENTION OF PRE-ECLAMPSIA AND ECLAMPSIA. A SYSTEMATIC REVIEW WITHOUT META-ANALYSIS

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Maria de Lourdes de Souza²

Abstract. Pregnancy, the most valuable period of every woman's life, requires continuous, prompt and supportive care throughout during pregnancy and also after childbirth for safe motherhood. **Objectives.** To assess the technologies and techniques used for the prevention of pre-eclampsia and eclampsia. **Methods.** The standard methodology of systematic review without meta-analysis was followed and only Random Controlled Trials and Systematic Reviews were included in this systematic review. Three electronic data sources (PubMed/Medline, Cinahl, and Cochrane) were searched for studies, published between 1985 and 2015 on the prevention and control of pre-eclampsia and eclampsia. **Results.** 47 studies were included in the review, of which 18 were systematic reviews and 29 were Random Controlled Trials. Technologies and techniques used in the included studies for the prevention and control of pre-eclampsia and eclampsia are Magnesium Sulfate, Aspirin, Antioxidant (Vitamin C, E and Lycopene), Calcium supplementation, Chinese Herbal Medicine, Physical Activities, Nitric Oxide, Marine Food Oils, Low Salt Diet, Garlic, Plasma Volume Expansion, Low-dose Dopamine, Progesterone, Smoking, and Diuretics. **Conclusion.** Magnesium Sulfate appears to be the most promising technique which reduces the risk of eclampsia by more than 50%. However, its best dose and route is still controversial and need further

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research. The knowledge and experience in properly using the protocols and evidence-based interventions are necessary for patient care.

Keywords: Pre-Eclampsia. Eclampsia. Maternal Mortality. Women's Health. Pregnancy.

BACKGROUND

Women are the source of all human life on this planet. The pleasure and excitement of being a mother cannot be expressed in words. In all cultures and societies being pregnant or to give birth to a child is considered as an important, beautiful and divine event (DUTTA, 2001). Pregnancy, the most precious period of every woman's life, requires continuous, prompt and supportive care throughout during pregnancy and also after childbirth for safe motherhood.

Pre-eclampsia is a hypertensive disorder of pregnancy, a serious condition that occurs typically after 20 weeks of pregnancy. It is a combination of hypertension (raised blood pressure) and proteinuria (the presence of protein in the urine) (DULEY; HENDERSON-SMART; WALKER, 2009). Most women with pre-eclampsia give birth without problems. However, severe pre-eclampsia can cause problems such as stroke, kidney failure, liver failure, and blood clotting (DULEY; HENDERSON-SMART; WALKER, 2009).

On the other hand, eclampsia, which is usually rare but potentially life-threatening, is characterized by the occurrence of a seizure in association with pre-eclampsia, swelling feet, sudden weight gain, headaches, and changes in vision (DULEY et al., 2010a). Approximately 1 out every 200 women who had pre-eclampsia, eventually develop more serious condition of eclampsia which causes about 50,000 maternal deaths each year (KHAN et al., 2006).

Globally 300,000 women die each year from complications of pregnancy and more than 95% of these women are in Africa and Asia (WHO, 2015). Pre-eclampsia and eclampsia together affect about 10% of all pregnant women around the world (MYLES; BENNETT; BROWN, 1993; GHULMIYYAH; SIBAI, 2012). In Africa and Asia, about one-tenth of all maternal deaths and in Latin America one-quarter of all maternal deaths are associated with hypertensive disorders of pregnancy. More than half of the maternal deaths occur in sub-Saharan Africa and about one third occur in South Asia (WHO, 2015). Among

the hypertensive disorders of pregnancy, pre-eclampsia and eclampsia remain one of the major causes of maternal mortality (DULEY, 2009; WHO, 2015). In Australia alone, it was estimated that between 4% to 10% of pregnant women develop pre-eclampsia, causing four to five maternal deaths and up to 300 to 500 perinatal deaths per year (ROBERTS et al., 2011).

OBJECTIVES

To assess the technologies and techniques for prevention of pre-eclampsia and eclampsia.

MATERIALS AND METHODS

Design

PRISMA guidelines (MOHER et al., 2009) was used as a basis for the overall study approach. A systematic review without meta-analysis search was conducted from May 2015 to May 2016 to answer the research question of: *What are the available technologies and techniques for the prevention and control of pre-eclampsia and eclampsia?* PubMed / MEDLINE, CINAHL, and COCHRANE were searched for articles published between 1985 to 2015, reporting on the available technologies and techniques for the prevention and control of pre-eclampsia and eclampsia in pregnant women. The question was adjusted according to the PICO acronyms; **P** (population/participants) representing all pregnant women; **I** (intervention) represent the use of available technologies and techniques; **C** shows comparison in the control group, the placebo group or non-existence of the comparison group; and **O** represented the outcomes of interest which were prevention and control of pre-eclampsia and eclampsia and reduction in maternal mortality. The search strategy was based on a number of medical subject headings MESH terms and text words, summarized in Table 1.

Inclusion Criteria

Systematic Reviews and Random Controlled Trials (RCT's) published in the English language between 1985 to 2015 based on the prevention and control of pre-eclampsia and eclampsia were eligible for inclusion in this review.

Exclusion Criteria

Papers whose topics were irrelevant to the objective of this study were excluded and all qualitative research.

Table 1 - Database, Filters and Keywords.

Database	Filters	Keywords
PUBMED	Text: Complete; Publication Date: 19850101-20150131; Language: English; Sex: Female; Age: 19-44 years	("eclampsia/prevention and control"[Mesh]) OR "pre-eclampsia/prevention and control"[Mesh]
COCHRANE	Total review 1,085 Complete review 179	Prevention and control of pre-eclampsia or eclampsia
CINAHL	Text: Complete; Publication Date: 19850101-20150131; Language: English; Sex: Female; Age: 19-44 years	Prevention and control of pre-eclampsia or eclampsia)

Source: Made by the author (2016).

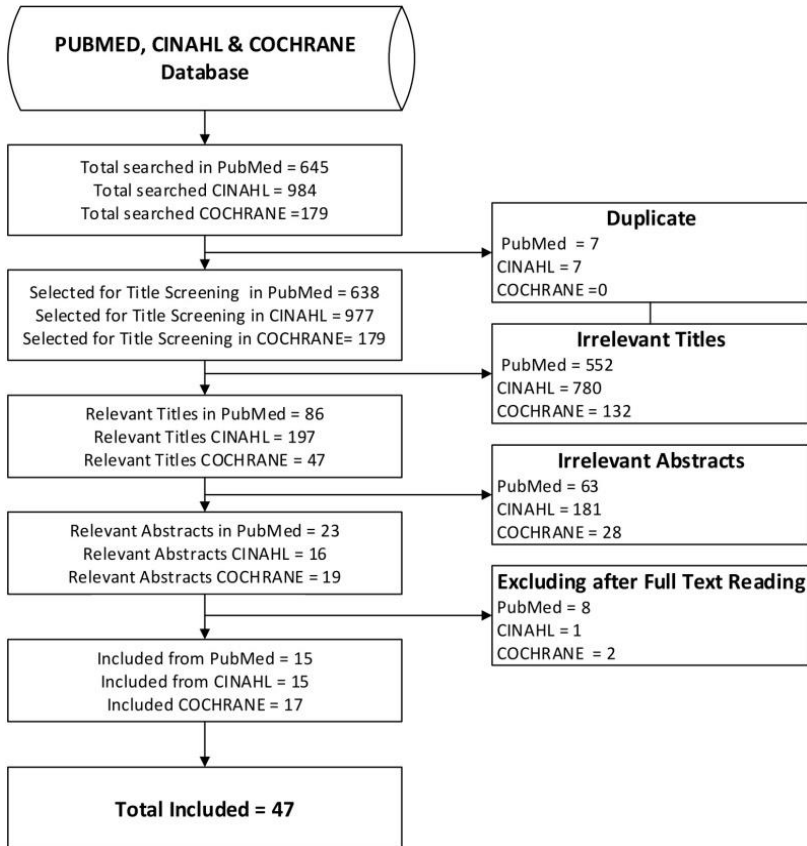
Search Outcome

A total of 1,808 articles were initially identified using the search criteria from all the three databases, of which 14 were duplicate. Titles screening of the remaining 1,794 articles resulted in 330 relevant articles being selected for abstract screening. The abstracts of these 330 papers were then examined resulting in 58 papers being examined in full. Of these, 11 were excluded after quality assessment. The remaining 47 studies were fully read and were included in the review as shown in Figure 1.

Each article was screened by two independent reviewers and disagreement between them was resolved by discussion. The aim was to identify as many articles as possible which have reported the use of

different techniques and technologies for the prevention of pre-eclampsia and eclampsia in past 30 years.

Figure 1 - Flow diagram showing the process of identification and screening for this systematic review.



Source: Made by the author (2016).

Quality Appraisal

We assessed the quality of each paper meeting the inclusion criteria using the following: (a) relevance to the systematic review (b) validity and appropriateness of methodology (c) quality of evidence generalizability of results (d) quality of reporting (e) limitations of the study and how it was adjusted. The quality of the outcome was assessed

using the Evidence Level: Joanna Briggs from Level I to II as outlined in Table 2.

Table 2 - Level of Evidence.

Level	Description
I	Evidence obtained from a systematic review of all relevant randomized controlled trials.
II	Evidence obtained from at least one properly deigned randomized controlled trial.
III.1	Evidence obtained from well-designed controlled trials, not randomized.
III.2	Evidence obtained from comparative studies such as cohort studies, case-control studies preferably from more than one center or research group.
III.3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments.
IV	Evidence from the opinion of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Source: Adapted from the Joanna Briggs Institute (2002).

Data Extraction and Synthesis

All 47 papers were independently assessed by two reviewers. The following information was extracted from the included studies. General information about authors, journal, publication date, country, research design, location, participants, aim, sample size, evidence of use of the available technologies and techniques in pregnant women for the prevention of pre-eclampsia or eclampsia, results and descriptive summaries of numerical data. Synthesis of the studies involved categorizing technologies and techniques by their characteristics, narrating and summarizing its effectiveness and presenting data visually.

Ethical Considerations

This study was developed in the context of project TO 13075/2012 - FAPESC, Opinion No. 120.343 and No. 169.110 of the year 2012 (Annexes A and B) and for that reason, it respects what is set out the resolution no. 466/2012 of the Ministry of Health Brazil (BRASIL, 2013). However, the completion of this research work did not involve any human subjects.

RESULTS

Among the 47 articles included in this study, 18 were systematic reviews, 29 were RCTs, including 9 multicenter RCTs. All the identified articles for systematic review were based on quantitative research studies. All included studies in this systematic review, restricted sampled participants to nulliparous or multiparous pregnant women (between 12 and 34 weeks of gestation), with hypertension, pre-eclampsia or eclampsia. Age of the participants vary between 14 to 45 years and sample size of the selected studies vary from 30 in (NIROMANESH; LAGHAI; MOSAVI-JARRAHI, 2001) to 37,560 in (DULEY et al., 2007) participants.

The included 29 RCTs were conducted and based in countries; UK=3, Italy=1, Brazil=1, Iran=1, South Africa=2, Barbados=1, India=2, Finland=2, USA=4, Mexico=1, Japan=1, Australia=1. Similarly, the multicenter studies were conducted in countries; 1 Multicenter RCT in South Africa, Turkey, Brazil, Argentina, Philippine, Dominican, America; 1 Multicenter RCT in France and Belgium; 1 Multicenter RCT in America and Europe; 1 Multicenter RCT in India, Peru, South

Africa, Vietnam; 1 Multicenter RCT in Argentina, Brazil, Colombia, Ghana, India, Uganda, Venezuela, Zimbabwe; 1 Multicenter RCT in England, Ireland, Scotland; 1 Multicenter RCT in Peru, Argentina, India, Egypt, South Africa, UK; 1 Multicenter RCT in Australian and New Zealand; 1 Multicenter RCT in Canada and Mexico.

The included studies used different technologies and techniques to intervention for the prevention and treatment of pre-eclampsia, eclampsia and its complications in pregnant women. These include *Magnesium Sulfate (8 studies)*, *Aspirin (9 studies)*, *Antioxidant including Vitamin C and E (9 studies)*, *Calcium Supplementation (4 studies)*, *Physical Activity and Exercise (3 studies)*, *Nitric Oxide (3 studies)*, *Marine Food Oils (2 studies)*, *Low Salt Diet (1 studies)*, *Garlic (1 studies)*, *Chinese Herbal Medicine (1 studies)*, *Plasma Volume Expansion (1 studies)*, *Low-dose Dopamine (1 studies)*, *Progesterone (1 studies)*, *Antioxidant Lycopene (1 studies)*, *Smoking (1 studies)* and *Diuretics (1 studies)*. A detail discussion on these interventions is presented in section 4 while their summarized results are provided from Table 3 to Table 8.

DISCUSSION

This study gives an overview of the available technologies and techniques for the prevention of pre-eclampsia and eclampsia in the past 30 years. The review has identified evidence about the central and supportive role of Magnesium Sulfate in the prevention of pre-eclampsia and eclampsia in pregnant women (BELFORT et al., 2003; DULEY; GULMEZOGLU; CHOU, 2010; DULEY et al., 2010b). Although, there is little evidence about the size of the effective dose, in order to draw any firm conclusions. Technologies and techniques including Magnesium Sulfate and many others identified in this study used for the prevention of pre-eclampsia and eclampsia are discussed in details, as follows.

It is generally believed that anticonvulsant is effective in managing eclampsia and that why Magnesium Sulfate, the most commonly used anticonvulsants, is considered a treatment of choice for eclampsia (DULEY et al., 2010b; SIBAI, 1990). Table 3 shows the summary of magnesium sulfate related studies included in this systematic review.

Magnesium Sulfate is the most promising technique and reduces the risk of eclampsia by more than 50%, as concluded by a systematic review (DULEY et al., 2010b) with 15 trials and more than 12,000 women. Similarly, Magnesium Sulfate is also effective in reducing the incidence of eclampsia in women with severe pre-eclampsia (COETZEE; DOMMISSE; ANTHONY, 1998). Magnesium Sulfate performs better than a lytic cocktail (DULEY; GULMEZOGLU; CHOU, 2010) and is more effective than nimodipine (BELFORT et al., 2003) in preventing maternal death, further seizures and other serious maternal morbidity in pregnant women with eclampsia.

Magnesium Sulfate had a 52% lower risk of recurrent convulsions (95% CI 64% to 37% reduction) than that allocated diazepam (60 (13.2%) vs 126 (27.9%). Similarly, Magnesium Sulfate had a 67% lower risk of recurrent convulsions (95% CI 79% to 47% reduction) than that allocated phenytoin (22 (5.7%) vs 66 (17.1%) (WHICH ANTICONVULSANT..., 1995). Low dose i.v. Magnesium Sulfate regimen is equally effective in the prevention of convulsion recurrence and maternal deaths in eclamptic women compared with an i.m. magnesium sulfate regimen (CHOWDHURY et al., 2009).

Despite the strong evidence in favor of Magnesium Sulfate for prevention of eclampsia, trials comparing alternative techniques

regimens are too small for a reliable conclusion. There was not enough evidence to show what is the best dose for Magnesium Sulfate for women with pre-eclampsia or eclampsia, and what is its best route. Magnesium Sulfate has also been associated with increased risk of PPH and respiratory difficulties (BELFORT et al., 2003), flushing (DULEY et al., 2010b) and overdose adverse effects (primarily from medication and administration errors) and may increase the rates of cesarean delivery (RANTONEN et al., 2001).

Antiplatelet agents, in particular, Aspirin, are among the most promising candidates for prevention of pre-eclampsia. They keep a good balance between prostacyclin, a vasodilator, and thromboxane, a vasoconstrictor, and stimulant of platelet aggregation (VILLA et al., 2013). However, according to the studies included in this review, Aspirin does not show any significant benefits in the incidence of proteinuric pre-eclampsia, preterm delivery, birthweight or of stillbirth, placental abruption, and neonatal death (ROTCHHELL et al., 1998; HAAPSAMO et al., 2010; SUBTIL et al., 2003; YU et al., 2003; CARITIS et al., 1998).

Although, a meta-analysis suggested that low-dose Aspirin initiated before 16 weeks of gestation reduces the risk of pre-eclampsia (RR 0.6, 95% CI 0.4-0.8) and severe pre-eclampsia (RR 0.3, 95% CI 0.1-0.7) (VILLA et al., 2013). Similarly, the results obtained in another review (DULEY et al., 2007) shows that antiplatelet agents, mostly low-dose Aspirin, have little benefits when used for prevention of pre-eclampsia and its complications. The role of Aspirin in the prevention of pre-eclampsia continues to be debatable and unclear. Its benefits and effectiveness are from small to moderate depending on the outcome. Table 4 shows the summary of Aspirin-related studies included in this review.

There are several evidences which support the hypothesis that oxidative stress, an imbalance between pro-oxidant and antioxidant forces, plays a key role in the development of pre-eclampsia during pregnancy (XU et al., 2010). However according to the results of this review no promising results has yet been shown by antioxidants including vitamin C and E in reducing the complications of pre-eclampsia or eclampsia. Table 5 shows the summary of antioxidants related studies included in this systematic review.

Table 3 - Summary of Magnesium Sulfate related studies (SR=Systematic Review; RCT=Randomized Control Trial; MgSo4=Magnesium sulfate).

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
(WHICH ANTICONVULSANT...., 1995)	Multicenter RCT	MgSo4 Versus Diazepam Versus Phenytoin	1,680 women with eclampsia from 9 countries	MgSo4 has 52% and 67% lower risk of recurrent convulsions than diazepam and phenytoin respectively	Not Reported
(COETZEE; DOMMISSE; ANTHONY, 1998)	RCT	IV magnesium sulfate (4g) versus Placebo	685 Women with Severe pre-eclampsia	IV MgSo4 is effective in reducing the incidence of eclampsia	Not Reported
(BELFORT et al., 2003)	Unblinded Multicenter Trial	Nimodipine (60mg/4h orally) and IV MgSO4 of 2g/h and 1g/h	1,650 women with severe pre-eclampsia	MgSo4 is more effective and has lower mortality rate than Nimodipine in women with severe pre-eclampsia	Increases the risk of PPH and respiratory difficulty
(LIVINGSTON et al., 2003)	RCT	IV MgSo4 (6g), followed by 2g/h	222 Women with mild pre-eclampsia	No major impact on disease progression. Does not seem to increase rates of cesarean delivery, infectious morbidity, obstetric hemorrhage.	Not Reported
(CHOWDHURY et al., 2009)	Prospective Trial	4g IV MgSO4 followed by i.m. injections or IV 0.6g/h	630 women with eclampsia	Both interventions are equally effective in the prevention of convulsion recurrence and maternal deaths	Not Reported
(DULEY et al., 2010a)	SR	MgSo4 with different dose	6RCTs - with 866 women	Strong evidence in favor of MgSo4. Lack of clarity for best dose size/route	Not Reported
(DULEY et al., 2010b)	SR	MgSO ₄ and Other Anticonvulsants	15 RCTs with more than 12000 women	MgSo4 reduce (50%) the risk of eclampsia and is more effective than phenytoin, diazepam or nimodipine	Flushing
(DULEY; GULMEZOGLU; CHOU, 2010)	SR	MgSo4 Compared with Lytic Cock-tail	3 small trials involving 397 women	MgSo4 is more effective in reducing MM and serious maternal morbidity than Lytic cocktail.	Recurrence of seizures.

Source: Made by the author (2016).

Table 4 - Summary of Aspirin-related studies included in this review (SR=Systematic Review; RCT=Randomized Control Trial; PC = placebo-controlled; DB = double blinded).

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
(SIBAI et al., 1993)	RCT	60 mg Aspirin per day	3,135 nulliparous women (13–26 week pregnancy)	Low-dose aspirin decreases the incidence of pre-eclampsia among nulliparous women	Increasing the risk of abruption placentae
(ROTCHHELL et al., 1998)	Randomized PC Trial	75 mg controlled release Aspirin	3,647 women (12–32 week pregnancy)	Do not support the routine use of low-dose aspirin for prevention of pre-eclampsia or its complications.	Not Reported
(CARITIS et al., 1998)	Randomized DB PC Trial	60 mg Aspirin per day	2,503 women (13–26 week pregnancy)	Low-dose aspirin did not reduce the incidence of pre-eclampsia significantly or improve perinatal outcomes in pregnant women.	Not Reported
(SUBTIL et al., 2003)	Randomized DB PC Trial	100 mg low-dose Aspirin per day	3,294 women (14–20 week pregnancy)	Does not reduce the incidence of pre-eclampsia in nulliparous women	increase in bleeding complications
(YU et al, 2003)	RCT	150mg low-dose Aspirin per day	560 Women (22– 24 week pregnancy)	No significant differences between the aspirin and placebo groups	Not Reported
(CHIAFFARINO et al., 2004)	Randomized Trial	100 mg low-dose Aspirin per day	40 women (14 week pregnancy)	Limited data show some support for early treatment with Aspirin in pregnant women	Not Reported
(DULEY et al., 2007)	SR	Antiplatelet Agents (low-dose aspirin)	59 trials with 37,560 women	Antiplatelet Agents, largely low-dose aspirin, have moderate benefits when used for prevention of pre-eclampsia	Not Reported
(HAAPSAMO et al., 2010)	Randomized DB PC Trial	100 mg low-dose Aspirin per day	487 Women	No statistical difference between low-dose aspirin and placebo groups	Not Reported
(VILLA et al., 2013)	Randomized DB PC Trial	100 mg low-dose Aspirin per day	152 women (12 week pregnancy)	Showed no statistically significant effect of aspirin in preventing pre-eclampsia	Not Reported

Source: Made by the author (2016).

Table 5 - Summary of Antioxidant and Vitamin C, E related studies (SR=Systematic Review; PC = placebo-controlled; DB = double blinded).

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
(GÜLMEZOĞLU; HOFMEYR OOSTHUISEN, 1997)	Randomized DB PC Trial	(800IU Vitamin E, 1g Vitamin C and 200g allopurinol) daily	54 women with severe pre-eclampsia (24–32 weeks pregnancy)	Do not encourage the routine use of antioxidants against pre- eclampsia	Increase in acne, transient weakness and skin rash
(POSTON et al., 2006)	Randomized PC Trial	1g vitamin C and 400IU of Vitamin E or placebo	2,410 Women (14– 22 weeks pregnancy)	does not prevent preeclampsia in women at risk	Increase rate of low birth- weight babies
(RUMBOLD et al., 2006)	Multicenter PC Trial	1g vitamin C and 400IU of Vitamin E or placebo daily	1,877 women from two countries (14–22 weeks pregnancy)	No reduction in the risk of pre- eclampsia, intrauterine growth restriction, or other serious outcomes in their infants.	Not Reported
(SPINNATO et al., 2007)	Randomized DB PC Trial	1g vitamin C and 400IU Vitamin E or placebo	739 Women (12– 19 weeks pregnancy)	No benefits in reducing the rate of pre-eclampsia among patients with chronic hypertension	Not Reported
(RUMBOLD et al., 2008)		Antioxidant (with Vitamin C , E, selenium and lycopene)	10 RCT with 6,533 women (12–28 eeks pregnancy)	No reduction in the risk of pre- eclampsia and its complications	Not Reported
(VILLAR et al., 2009)	Multicenter PC Trial	1g vitamin C and 400 IU of Vitamin E or placebo daily	687 women (14– 22 weeks pregnancy)	No reduction in the rate of pre- eclampsia high- risk pregnant women with low nutritional status	Not Reported
(MCCANCE et al., 2010)	Multicenter PC Trial	1g vitamin C and 400IU of Vitamin E or placebo	762 diabetic pregnant women (8–22 weeks)	No reduction in the risk of pre- eclampsia in women with type I diabetes	Not Reported
(ROBERTS et al., 2010)	Multicenter PC Trial	1g vitamin C and 400IU of Vitamin E or placebo	10,154 Women (9– 16 weeks pregnancy)	No reduction in the rate of adverse maternal or perinatal outcomes	Not Reported
Continues...					

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
Conclusion					
(XU et al., 2010)	Multicenter RCT	1g vitamin C and 400 IU of Vitamin E or placebo daily	2,647 women from 27 centers	No reduction in the rate of pre- eclampsia	increased fetal loss and preterm rupture of membrane

Source: Made by the author (2016).

Table 6 - Summary of Calcium related studies included in this review (PC = placebo-controlled; DB = double blinded).

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
(LEVINE et al., 1997)	Randomized DB PC Trial	2g calcium/day or placebo	4,589 women (13–21 weeks pregnancy)	No prevention in preeclampsia, or its severity or delay its onset	Not Reported
(NIROMANESH; LAGHAI; MOSAVIJARRAHI, 2001)	Randomized DB PC Trial	2g calcium/day or placebo	30 women (28 to 32 weeks of gestation)	Limited data shows reduction of in the risk of pre- eclampsia	Not Reported
(VILLAR et al., 2006)	Randomized DB PC Trial	1.5g calcium/day or placebo	8,325 women of 20 week pregnancy	did not prevent pre-eclampsia but did reduce its severity and maternal morbidity	Not Reported
(HOFMEYR; DULEY; ATALLAH, 2007)	Systematic Review	1.5g to 2 g calcium/day	12 RCTs with 15,528 women	Appears to reduce the risk of pre- eclampsia and serious morbidity	No other clear benefit or harms

Source: Made by the author (2016).

Results obtained in (XU et al., 2010; GÜLMEZOĞLU; HOFMEYR; OOSTHUISEN, 1997; VILLAR et al., 2009; RUMBOLD et al., 2006; 2008; MCCANCE et al., 2010; POSTON et al., 2006; ROBERTS et al., 2010; SPINNATO et al., 2007) fails to demonstrate the benefits of antioxidant supplementation in reducing the rate of pre-eclampsia and hence do not encourage its routine use against pre-eclampsia. Previous research also does not support the use of vitamin C and E supplementation in pregnancy to reduce the risk of pre-eclampsia

or its complications (ROBERTS et al., 2010). However, the possibility that vitamin supplementation might be beneficial in women with a low antioxidant status at baseline needs further research and trials.

Historically, a relationship between calcium deficiency and homeostasis and pre-eclampsia was suggested (VILLAR; BELIZÁN, 2000). In this regard, nutrient supplements consisting of calcium are prescribed to treat deficiencies or for pharmacologic effects during pregnancy. The use of calcium supplementation in the light of this review did not show strong evidence in favor of its routine use (VILLAR et al., 2006; LEVINE et al., 1997). However, a systematic review (HOFMEYR; DULEY; ATALLAH, 2007) with 12 good quality RCTs involving 15,528 women and an RCT in (NIROMANESH; LAGHAI; MOSAVI-JARRAHI, 2001) show promising results in favor of calcium supplementation in the prevention of preeclampsia and related problems.

Overall it seems that calcium supplementation appears to reduce the risk of pre-eclampsia and reduce the rare occurrence of the serious morbidity. However, further research is needed in different settings and trials to explain its role in the prevention of pre-eclampsia. Table 6 shows the summary of calcium related studies included in this systematic review.

It can be possibly believed that increased physical activities and exercise may help pregnant women in the prevention of developing preeclampsia as its benefits are many for non-pregnant people (MEHER; DULEY, 2006a). There are, however, also concerns that there may be adverse effects of exercise taken during pregnancy and hence the role of increased physical activity and exercise is controversial and not clear. Table 7 shows the summary of physical activities and exercise related studies included in this review.

For inactive pregnant women, a stretching exercise may be more effective than walking in mitigating the risk of pre-eclampsia due to higher adherence and possible cardiac-physiologic effects (YEO, 2009). However, the results do not deny the effects of walking exercise on risk of pre-eclampsia. In the light of this review, no firm conclusion can be drawn about recommending rest or increased activity to women, due to the insufficient evidence obtained in (MEHER; DULEY, 2006a,c). However, further research is needed in different settings and trials to explain its role in the development and prevention

In the Table 8 show the summary of included studies related to miscellaneous interventions.

The salt consumption during pregnancy should remain a matter of

personal choice. The effects of salt consumption during pregnancy were assessed in a systematic review (DULEY; HENDERSON-SMART; MEHER, 2005) with two trials involving 603 women. Both trials compared reduce dietary salt intake with normal diet. However, the review did not show any evidence of benefit for the mother or baby.

Traditional Chinese Medicine (TCM) believes that during pregnancy most of the blood of the mother flows to the placenta to provide the fetus with the required blood circulation and nutrition and as a result, other organs of the mother get weak. The effectiveness of TCM in pre-eclampsia was assessed in a systematic review (ZHANG; WU; LIU, 2006) in which the authors identified 45 studies but none could be classified as a randomized controlled trial. The usefulness of Chinese herbal medicines for treating pre-eclampsia hence remains unclear due to insufficient evidence.

Population studies have shown that higher intakes of marine foods during pregnancy are associated with higher infant birth weights and a low incidence of pre-eclampsia (MAKRIDES; DULEY; OLSEN, 2006). The Marine food contains fatty acids which are believed to be helpful in preventing the incidence of pre-eclampsia. However, there is insufficient evidence to support the routine use of marine food and oil during pregnancy in order to minimize the risk of pre-eclampsia and its related complications (ZHOU et al., 2012; MAKRIDES; DULEY; OLSEN, 2006).

Similarly, there is insufficient evidence to recommend increased garlic intake for preventing pre-eclampsia and its complications during pregnancy as evident from a systematic review (MEHER; DULEY, 2006b) with one included trial (100 women). Further large randomized trials evaluating the effects of garlic are needed before any recommendations can be made to guide clinical practice.

Nitric oxide drugs (glycerol trinitrate) or their precursors (Arginine) relaxing the walls of the blood vessel and may play an effective role in the prevention of pre-eclampsia. However, there is insufficient evidence to draw reliable conclusions about whether nitric oxide drugs or their precursors prevent pre-eclampsia and its related complications (LEES et al., 1998; MEHER; DULEY, 2007).

Although, one randomized, blinded, placebo-controlled clinical trial (VADILLO-ORTEGA et al., 2011) show some evidence of a reduction in the incidence of pre-eclampsia. Participants in this trial were pregnant women with a history of a previous pregnancy pre-eclampsia. 222 women were allocated to the placebo group, 228

received L-arginine plus antioxidant vitamins, and 222 received antioxidant vitamins alone. The incidence of pre-eclampsia was reduced significantly ($X^2 = 19.41$; $P < 0.001$) in L-arginine plus antioxidant vitamins compared with placebo (absolute risk reduction 0.17 (95% CI 0.12 to 0.21)). L-arginine plus antioxidant vitamins compared with antioxidant vitamins alone resulted in a significant effect ($P = 0.004$; absolute risk reduction 0.09, 0.05 to 0.14). Supplementation with L-arginine plus antioxidant vitamins needs to be further evaluated in a low-risk population in order for the firm conclusion to be drawn.

Blood plasma volume increases gradually in women during the second half of pregnancy and is reduced in women with pre-eclampsia (DULEY; WILLIAMS; HENDERSON-SMART, 2000). It is possible that women with pre-eclampsia might benefit from expanded plasma volume if it were to increase blood circulation for the mother and baby. However, the results of a systematic review (DULEY; WILLIAMS; HENDERSON-SMART, 2000) are inconclusive about the effects of plasma volume expansion for the treatment of women with pre-eclampsia.

Cigarette smoking adversely affects every organ system (SHEA; STEINER, 2008). However very strangely, smoking during pregnancy has been associated with a reduction in the risk of pre-eclampsia (ENGLAND; ZHANG, 2007).

A review based on the relation between smoking and pre-eclampsia was conducted from 1959 to March 2006 with a total of 48 epidemiologic studies (ENGLAND; ZHANG, 2007). Overall, smoking during pregnancy reduces the risk of pre-eclampsia by up to 50% with a dose-response pattern. This result was consistent with all nulliparous and multiparas women, singleton and multifetal pregnancies, and in all cases of mild and severe pre-eclampsia. However, the underlying mechanisms and the exact ingredients in cigarette smoke that influence the risk preeclampsia is unclear. Further research may enhance our understanding of the disease and contribute to the development of prevention strategies.

The role of low-dose dopamine in the management of pregnant women with severe pre-eclampsia was assessed in a systematic review in (STEYN, D. W.; STEYN, P., 2007). Only one Randomized placebo-controlled trial of six hours' duration, including 40 postpartum women, was found. However, it remained unclear whether low-dose dopamine therapy for pre-eclamptic women with oliguria is beneficial.

According to one theory the shortage of progesterone might be

the cause of pre-eclampsia, hence it is believed that progesterone during pregnancy might help them to avoid pre-eclampsia. However, no reliable conclusions could be made about the effects of progesterone in preventing pre-eclampsia and its complications according to the result of a review in (MEHER; DULEY, 2006d).

Table 7 - Summary of physical activities & exercise related studies included in this review.

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
(MEHER; DULEY, 2006a)	Systematic Review	Physical Activity and Exercise	2 small, good quality trials with 45 women	Insufficient evidence for reliable conclusions	Insufficient evidence
(MEHER; DULEY, 2006c)	Systematic Review	Physical Activity and Exercise	2 small, low quality trials (106 women)	Insufficient evidence for reliable conclusions	Insufficient evidence
(YEO, 2009)	Randomized Control Trial	Physical Activity and Exercise	124 women (≥ 14 weeks Pregnancy)	Stretching exercise may be more effective than walking in reducing the risk of pre-eclampsia.	Not Reported

Source: Made by the author (2016).

Table 8 - Summary of other interventions related studies (SR = systematic review; PC = placebo-controlled; DB = double blinded).

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
(LEES et al., 1998)	Randomized DB PC Trial	glyceryl trinitrate 5mg daily	40 women (24–26 weeks pregnancy)	No reduction in preeclampsia, preterm delivery or fetal growth restriction	Not Reported
(DULEY; WILLIAMS; HENDERSON-SMART, 2000)	SR	Plasma Volume Expansion	3 trials with 61 women	Insufficient evidence to draw reliable conclusions	Not Reported
(DULEY; HENDERSON-SMART; MEHER, 2005)	SR	Low Salt Diet	2 Trials with 603 women	No Effect (Insufficient Data)	Not Reported
Continues...					

Ref.	Study Type	Intervention	Population/ Sample Size	Results/Benefits	Adverse Effects
Conclusion					
(ZHANG; WU; LIU, 2006)	SR	Chinese herbal medicines	No trials suitable for inclusion	Insufficient evidence	Insufficient evidence
(MAKRIDES; DULEY; OLSEN, 2006)	SR	Marine oil & prostaglandin precursor	6 trials with 2,783 women	Not enough evidence to support the routine use of marine oil, or other prostaglandin precursor	Not Reported
(MEHER; DULEY, 2006b)	SR	Garlic	1 trial (100 women)	Insufficient evidence	Odor
(CHURCHILL et al., 2007)	SR	Diuretics	5 studies (1,836 women)	Insufficient Evidence	Nausea, Vomiting
(ENGLAND; ZHANG, 2007)	SR	Cigarette smoking	48 epidemiologic studies	Smoking during pregnancy reduces the risk of pre-eclampsia by up to 50%	Not Reported
(MEHER; DULEY, 2007)	SR	nitric oxide donors or precursors	6 trials with 310 women	Insufficient evidence to draw reliable conclusions	Headache with little evidence
(STEYN, D. W.; STEYN, P., 2007)	SR	Low-dose dopamine	1 trial (40 women)	Insufficient Evidence	Not Reported
(BANERJEE; JEYASEELAN; GULERIA, 2009)	Randomized DB PC Trial	Lycopene oral 2mg daily	159 Women (12 to 20 weeks of gestation)	No significant difference between the two groups in developing pre-eclampsia	Increased preterm labor
(MEHER; DULEY, 2006d)	SR	progesterone	4trials (1,445 women)	Insufficient Evidence	Not Reported
(VADILLO-ORTEGA et al., 2011)	Randomized DB PC Trial	L-arginine plus antioxidant vitamins	672 pre-eclamptic women (14–32 weeks pregnancy)	Reduced the incidence of pre-eclampsia.	Not Reported
(ZHOU et al., 2012)	DB RCT	n-3 LCPUFA (fish oil)	2399 Pregnant women of >21 week pregnancy	No meaningful effect on the risk of pre-eclampsia	Not Reported

Source: Made by the author (2016).

Diuretic drugs result in reducing the blood pressure by excreting more urine and hence relaxing blood vessels. Due to these effects, it has been believed that Diuretic drugs might lower the risk of pre-eclampsia in pregnant women. However, the result drew in a systematic review (CHURCHILL et al., 2007) (5 studies involving 1,836 women), showed insufficient evidence to draw reliable conclusions about the effects of diuretics on prevention of pre-eclampsia and its related complications. The risk of nausea and vomiting was also increased, therefore the use of diuretics for the prevention of pre-eclampsia and its related complications cannot be suggested.

A randomized double-blind placebo-controlled trial (BANERJEE; JEYASEELAN; GULERIA, 2009) with 159 primigravidas (similar physical and social parameters) was conducted in India to evaluate the efficacy of antioxidant lycopene in preventing pre-eclampsia. 77 women received 2mg/day oral lycopene until delivery. There was no significant difference in developing pre-eclampsia. The results confirm that lycopene is not effective in preventing pre-eclampsia in healthy primigravidas. Rather, they result in the incidence of the adverse effects of preterm labor and low birth weight babies.

CONCLUSIONS

There are a number of evidences that have been identified and assessed for its role in the prevention of pre-eclampsia and eclampsia. Magnesium Sulfate so far has shown a great success in this regards and can be called as treatment of choice. It is more effective than diazepam, phenytoin, aspirin, calcium supplementation or lytic cocktail. However, despite the strong evidence, trials comparing alternative techniques are too small for reliable conclusions. There is insufficient evidence to show what is the best dose and route for magnesium sulfate for women with pre-eclampsia or eclampsia.

Similarly, the role of Aspirin, Calcium supplementation, and Larginine plus antioxidant vitamins continues to be controversial. Its benefits and effectiveness range from small to moderate depending on the outcome. Further research is needed to assess which women are most likely to benefit. There is also insufficient evidence about whether to recommend rest or increased physical activity to women during pregnancy. Further research is highly desirable in different settings to explain its role in the development and prevention of pre-eclampsia and

its complications.

There is evidence in the light of the included studies in this review as well as previous studies that supplementation with vitamins C and E did not reduce the risk of pre-eclampsia in both nulliparous and multiparous women. However, further research is needed to analyze the possibility that vitamin supplementation might be helpful in women with a low antioxidant status.

Another puzzling evidence we obtained from this review is that smoking during pregnancy reduces the risk of pre-eclampsia by up to 50% with a dose-response pattern. This result was consistently found in both nulliparous and multiparas, singleton and multifetal pregnancies for both mild and severe pre-eclampsia. Current literature does not give us a clear explanation for this supportive effect of smoking in pregnant women. More epidemiologic studies are needed to further clarify this puzzling relationship. Understanding the underlying mechanisms and finding which ingredients in cigarette smoke influence the risk of preeclampsia can enhance our understanding and can contribute to the development of prevention strategies.

We also recommend further research into assessing the role and importance of current and new technologies and techniques in the reduction of pre-eclampsia and eclampsia. All nurses or midwives should know the evidence about the prevention and treatment of pre-eclampsia and eclampsia to identify the nursing care that is essential to guide the pregnant woman and family and prevent adverse events related to the use of techniques and technologies.

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4.2 MANUSCRIPT 2 - MATERNAL MORTALITY ASSOCIATED WITH PRE-ECLAMPSIA AND ECLAMPSIA IN KHYBER PAKHTUNKHWA PROVINCE OF PAKISTAN: AN INTEGRATIVE REVIEW

MATERNAL MORTALITY ASSOCIATED WITH PRE-ECLAMPSIA AND ECLAMPSIA IN KHYBER PAKHTUNKHWA PROVINCE OF PAKISTAN: AN INTEGRATIVE REVIEW

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Maria de Lourdes de Souza²

Abstract. Background: Pre-eclampsia and eclampsia are pregnancy-related disorders, associated with significant maternal mortality. They are the second leading causes of maternal deaths particularly in developing countries. **Objective:** To show the maternal mortality associated with pre-eclampsia and eclampsia in Khyber Pakhtunkhwa province of Pakistan, from the scientific literature published between 2000 to 2015. **Method:** An integrative review was conducted. Three electronic databases, PUBMED/MEDLINE, COCHRANE, CINAHL, were searched for published studies on the maternal mortality related to pre-eclampsia or eclampsia in the Khyber Pakhtunkhwa province of Pakistan. Synthesis of the data involved categorizing and tabulating data and presenting it visually. **Results:** After identification and screening, eight studies were included in the review, of which four were cross-sectional and 4 were descriptive. These studies were conducted in Khyber Pakhtunkhwa in Gynecology and Obstetrics Units of the four tertiary care hospitals. Maternal mortality associated with pre-eclampsia and eclampsia reported in the included studies vary between 8% in Lady Reading Hospital and Medical Teaching Institute Peshawar to 30% in Ayub Medical and Teaching Institution Abbottabad. **Conclusion:** Maternal mortality associated with pre-eclampsia and eclampsia

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continue to remain high in one Province of Pakistan. Low-socioeconomic status, accesses to health care services and quality of nursing care of the obstetrics emergency were the main causes. Provision of adequate, timely and effective nursing care for the safe motherhood are vital for the prevention of pre-eclampsia and eclampsia.

Keywords: Pre-eclampsia. Eclampsia. Maternal Mortality. Nursing Care. Khyber Pakhtunkhwa. Pakistan.

INTRODUCTION

Maternal mortality indicates the quality of women's health and the life quality of a population and provides a measure of human and social development (MAGALHAES; BUSTAMANTE-TEIXEIRA, 2012). Information on maternal mortality is essential for setting priorities for policy making and research strategies.

Every day in 2015, about 830 women died due to pregnancy complications and childbirth complications (WHO, 2015b). Of these 830 daily maternal deaths, 550 occurred in sub-Saharan Africa and 180 in Southern Asia, compared to 5 in developed countries. Almost all of these deaths occurred in low-resource settings, and most could have been prevented. The risk of a woman in a developing country dying from a pregnancy-related complication during her lifetime is about 33 times higher compared to a woman living in a developed country (WHO, 2015b).

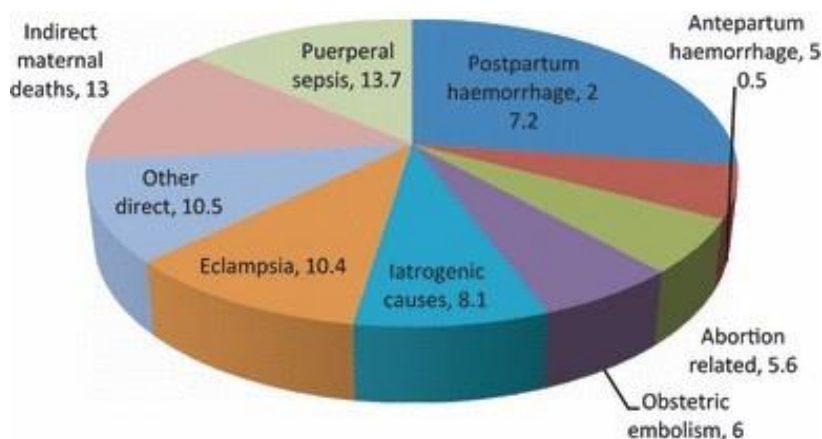
Pregnant women die as a result of complications which either develop during pregnancy or may exist before but are aggravated during pregnancy. The primary causes of death are hemorrhage, hypertension and infections. The major complications that account for nearly 75% of all maternal deaths consist of pre-eclampsia and eclampsia (together 14%), Severe bleeding (27%) and Infections (11%) (SAY et al., 2014).

Hypertensive disorders of pregnancy are causing one out of ten maternal deaths in Africa and Asia, and nearly one-quarter in Latin America (CAMPBELL et al., 2006). Ten million women develop preeclampsia each year around the world (KUKLINA; AYALA; CALLAGHAN, 2009). About 1 in 200 women who had pre-eclampsia, eventually also progress to a dangerous condition known as eclampsia which is responsible for about 50,000 maternal deaths each year worldwide (KHAN et al., 2006).

Maternal Mortality Rate and health care quality vary among low and middle-income countries (KIDANTO et al., 2012; WHO, 2015b). Preeclampsia and eclampsia are one of the leading cause of maternal mortality in pregnant women in the developing countries. Among the developing countries in Pakistan eclampsia is a common cause of maternal deaths (MAHMUD et al., 2011).

Organized data on routine health outcomes do not exist in most part of Pakistan. The World Health Organization's estimate of maternal mortality in Pakistan (350 per 100,000 live births in 1995) which was lowered to 178 in 2015 (WHO, 2015a). According to the Pakistan Demographic and Health Survey, 73% of mothers receive antenatal care from skilled health care providers, 1% of mothers receive prenatal care from a traditional birth attendant, and 25% of women no received antenatal care at all (NIPS, 2014). Nevertheless, there is a large difference between urban and rural women. Urban women are more than twice (88%) as likely to seek antenatal care compared with rural women (67%) (NIPS, 2014). In Pakistan, the Maternal Mortality Rate is associated with, low skilled birth attendance, illiteracy, malnutrition and insufficient access to emergency obstetric care services. Hemorrhage (32.7%), eclampsia (10.4%) and sepsis (13.7%) are the main direct causes of maternal deaths according to (MAHMUD et al., 2011) as shown in Figure 1.

Figure 1 - Causes of maternal mortality in Pakistan (2006-7).



Source: Mahmud et al., (2011).

There has been a significant improvement over the past 20 years in the proportion of mothers who receive prenatal care from a health care provider, increasing from 33% in 1996 to 61% percent in 2006-07 and 73% in 2013 (ZAFAR; ANWAR, 2006; NIPS, 2013; 2014). More than 35% of pregnant women make four or more antenatal visits during pregnancy. The urban population has more tendency to have four or more visits than the rural population. The median duration of pregnancy at the first prenatal care visit is 3.7 months. The most common reasons reported for not receiving prenatal checkups are a lack of concern, problems of accessibility and costs of services (NIPS, 2013; 2014).

Although the overall health status of Pakistan's population has improved over the past few decades, however, it is still poor when compared to most low-income countries. The slow pace of improvement in the health sector is largely due to poverty, low literacy rate, and lack of civic facilities such as proper sanitation (NIPS, 2014).

This study aims to investigate the available scientific literature published between 2000 to 2015 and estimate the cases of maternal mortality associated with pre-eclampsia and eclampsia in the Khyber Pakhtun Khwa (KPK) province of Pakistan.

MATERIALS AND METHODS

Search Strategies and Sources

This review was conducted from February 2015 to December 2015 to answer the research question of; *how the maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan, was showed in the scientific literature published between 2000 to 2015?* PUBMED/MEDLINE, CINAHL and COCHRANE databases were searched for the articles reporting on the maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan. The search was limited to articles published between January 2000 and December 2015 in the English language. The search strategy was based on a number of medical subject headings MESH terms (shown in Table 1) and text words aiming to include as many relevant articles as possible.

Inclusion Criteria

Quantitative studies published in the English language between 2000 to 2015 which were reporting on the maternal mortality associated with preeclampsia and eclampsia in KPK Pakistan were eligible for

inclusion in this review.

Table 2 - Search strategies for the identification of selected studies published in 2000-2015.

Database	Keywords and Descriptors
PUBMED	((“eclampsia”[Mesh] OR “Preeclampsia”[Mesh]) AND (“Maternal Mortality”[Mesh] OR “Maternal Death”[Mesh]) AND (“Pakistan”[Mesh]))
Cochrane	(Maternal mortality or maternal death) and (Preeclampsia or eclampsia) and (Khyber Pakhtunkhwa or Pakistan)
CINAHL	(Maternal mortality or maternal death) and (Preeclampsia or eclampsia) and (Khyber Pakhtunkhwa or Pakistan)

Source: Made by the author (2016).

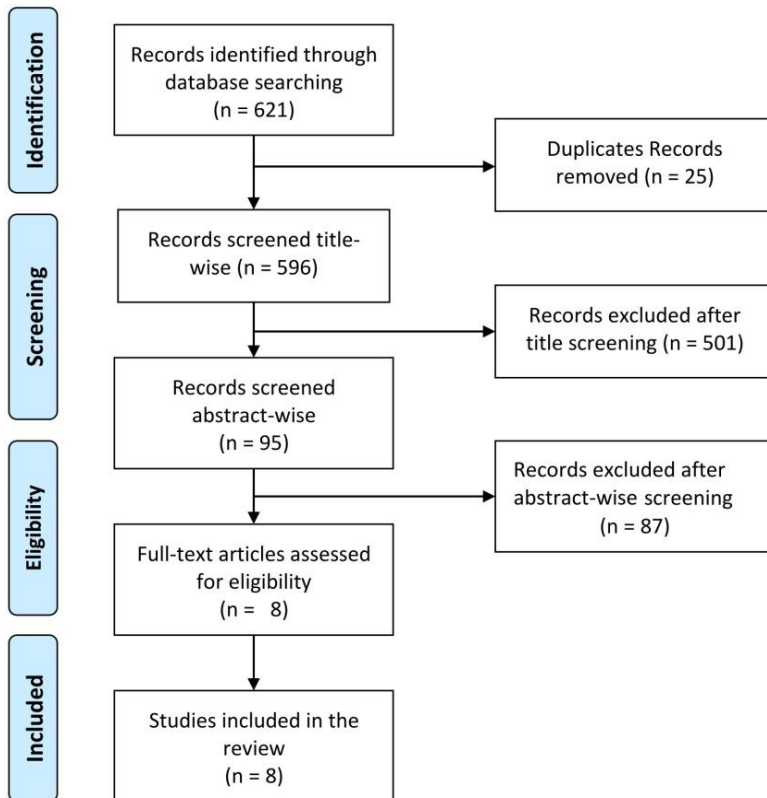
Exclusion Criteria

Articles that were published in a language other than English; studies reporting on maternal mortality associated with other complications of pregnancy and studies reporting on maternal mortality in other provinces of Pakistan were excluded.

Search Outcome

A total of 621 articles were initially identified using the search criteria from all the selected databases, of which 25 were duplicated. Title screening of the remaining 596 studies was completed which resulted in 95 studies to be selected for abstract reading. After abstract screening 08 studies were selected for full-text reading, of which all were included in the review, as shown in PRISMA flowchart (see Figure 2). Each article was screened by two independent reviewers and disagreement between them was resolved by discussion. The aim was to identify as many relevant articles as possible which have reported on maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan.

Figure 2 - Flowchart showing the process of identification and screening of studies.



Source: Made by the author (2016).

Quality Assessment

We assessed the quality of each paper using the following: (a) relevance to this review (b) validity and appropriateness of the study methodology (c) quality of evidence (d) sampling method and quality of reporting (e) and limitations of the study. The quality of the outcome was assessed using the Evidence Level from Joanna Briggs Institute (from Level I to V).

Data Extraction and Synthesis

Extracting and synthesizing data from heterogeneous sources is a

complex process (GOLDSMITH; BANKHEAD; AUSTOKER, 2007). All selected studies were independently assessed by two reviewers. The information was extracted from the included studies: general information about authors, journal, publication date, country and region; research design, location, participants, aims; maternal mortality associated with pre-eclampsia and eclampsia in KPK Pakistan; results and descriptive summaries of numerical data.

Synthesis of the data involved categorizing and tabulating data and presenting it visually.

Ethical Considerations.

The development of this research work did not involve any human subject. Thus it is considered that Resolution 466/2012 was respected (Brazil 2013).

RESULTS

The included 8 articles in this study were based on quantitative research where data is collected from hospitals records documents. Among them 4 studies were cross-sectional, 1 was descriptive and 3 were retrospective descriptive. All included studies were based on data collected from four tertiary care hospitals, named Medical Teaching Institute Lady Reading Hospital Peshawar (MTILRH), Khyber Teaching Hospital Peshawar (MTIKTH), Hayatabad Medical Complex Peshawar (HMCTI), and Ayub Medical and Teaching Institution Abbottabad (AMTI).

Two studies were based in each of these four hospitals. All studies restricted sampled participants to pregnant women with hypertension, pre-eclampsia or eclampsia. The sample size of the studies reviewed varied from 25 to 740 patients. All these studies were conducted in the period of 2000 to 2015, the first being in 2001 (GILLANI; HASSAN, 2011) and the latest being in 2013 (IQBAL et al., 2014). Maternal mortality associated with pre-eclampsia and eclampsia reported in the included studies vary between 8% in Lady Reading Hospital and Medical Teaching Institute Peshawar (JAMIL; AKHTAR, 2005) to 30% in Ayub Medical and Teaching Institution Abbottabad (BEGUM, S.; AZIZ-UM-NISA; BEGUM, I., 2003). Summary of the included studies are presented in Table 2.

Studies Conducted in Peshawar Region

Peshawar is the capital of Khyber Pakhtunkhwa Province and one of the biggest cities in Pakistan. This city has modern and excellent health facilities. It has three government hospitals and accommodates patients from all around the province. Peshawar is known for its good health system. It has created many new well-equipped hospitals in the last decade. The leading hospitals in Peshawar city are Medical Teaching Institute Lady Reading Hospital Peshawar (MTILRH), Medical Teaching Institute Khyber Teaching Hospital Peshawar (MTIKTH), and Hayatabad Medical Complex Peshawar Teaching Institute (HMCTI). They are all modern public health care organizations that provide high-quality health services to the community. They provide acute hospital services and specialist services to people living in KPK, Federally Administered Tribal Areas (FATA) and adjoining areas of Afghanistan. These hospitals offer a full range of emergency and high dependency care in Maternity, Pediatrics, Surgery and much more.

A cross-sectional study (GILLANI; HASSAN, 2011) was conducted in Hayatabad Medical Complex Teaching Institute (HMCTI) Peshawar in 2000 to evaluate maternal mortality from eclampsia. It reported that out of 30 eclamptic women 5 women died. The prevalence of eclampsia was 10.4% per 1,000 and case fatality of eclampsia was 16.66% which accounted for 29.4% of total maternal deaths. Most of the patient (56%) were less than 20 years.

A Cross-sectional study (SHAHEEN; HASSAN; OBAID, 2003) was conducted in the same institute of Hayatabad Medical Complex Teaching Institute (HMCTI) Peshawar in 2001-2002 to observe pregnancy outcome in eclamptic women and to explore the avoidable factors contributing to the adverse outcome. The study reported that according to the results, 12 out of 71 patients died due to eclampsia. Mortality rate was 16.9% and it accounted for 48% of total mortality. Reasons were poverty, illiteracy, and poor access to health facility.

A Cross-sectional study (NAIB; SIDDIQUI; AJMAL, 2011) was done in Medical Teaching Institute Khyber Teaching Hospital (MTIKTH) Peshawar from Jan 2001 to Dec 2001 to estimate the maternal mortality and due to eclampsia. It shows that 4 women died out of 25 eclamptic patients. It reported that maternal mortality rate was 4 (28.57%) related to eclampsia. The majority of the patient (60%) were 17 to 30 years.

Table 2 - Summaries of included studied from 2000 to 2015 in KPK Pakistan.

Ref.	Design	Objectives	Sample Size	Outcome
(GILLANI; HASSAN, 2011)	Cross-sectional	To estimate maternal mortality due to eclampsia	30 eclamptic women	5(16.6%) eclamptic women died
(SHAHEEN; HASSAN; OBAID, 2003)	Cross-sectional	To explore the avoidable factors in pregnancy outcome in eclamptic patients	71 eclamptic women	35(16.9%) eclamptic women died
(JAMIL; AKHTAR, 2005)	Cross-sectional	To study the determinants of maternal outcome	50 eclamptic women	4(8%) eclamptic women died
(MALIK et al., 2015)	Retrospective descriptive	To evaluate maternal mortality and identify causes with age groups	277 maternal deaths analyzed	44(15.8%) eclamptic women died
(NAIB; SIDDIQUI; AJMAL, 2011)	Cross-sectional 2001	To estimate maternal mortality due to eclampsia	25 eclamptic patients	4(28.5%) eclamptic women died
(IQBAL et al., 2014)	Descriptive	To determine the perinatal mortality rate and its related obstetric risk actors	740 perinatal deaths analyzed	118 (15.9%) eclampsia and preeclampsia 80 (10.8%)
(BEGUM, S.; AZIZ-UM-NISA; BEGUM, I., 2003)	Retrospective descriptive	To determine preventable factors responsible for maternal mortality.	27 maternal deaths analyzed	8(30%) eclamptic women died
(JAMIL; ABBASI; ZAMAN, 2013)	Retrospective descriptive	To determine the outcome of eclampsia patients	116 eclamptic patients	18(15.5%) eclamptic women died

Source: Made by the author (2016).

A cross-sectional study (comprising of six months) (JAMIL; AKHTAR, 2005) was conducted in Medical Teaching Institute Lady Reading Hospital Peshawar (MTILRH) in 2003. In 50, eclamptic women, total 19 maternal deaths occurred of which 4 were due to eclampsia. Maternal mortality rate due to eclampsia was 4(8%) and eclampsia accounted for 21% of maternal deaths. Prevalence of eclampsia was 2.2%. Main causes were poor antenatal care, emergency obstetric care, and referral system.

A retrospective descriptive study (MALIK et al., 2015) was done in Medical Teaching Institute Lady Reading Hospital (MTILRH) in 2009-2011 to find the occurrence of maternal mortality and identify causes with age groups in tertiary care hospital of Peshawar, Pakistan. It

reported that out of 277 maternal deaths 44 (15.88%) women deaths were due to eclampsia. Most of the maternal deaths were in the age group 26 to 35 years.

Another descriptive study (IQBAL et al., 2014) was conducted in 2014 in Medical Teaching Institute Khyber Teaching Hospital (MTIKTH) Peshawar to determine the perinatal mortality rate and its related obstetric risk factors. Out 11,260 perinatal there were 740 perinatal deaths, where (26.7%) were due to hypertensive disorders of pregnancy. Eclampsia was 118 (15.9%) and severe pre-eclampsia was 80 (10.8%). The study reported that inadequacy and inaccessibility of maternity services and the poor socio-economic status and cultural pattern are the main reason of high maternal mortality.

Studies Conducted in Abbottabad Region

Abbottabad is a city located in the Khyber Pakhtunkhwa province, in northeastern Pakistan. Ayub Medical Teaching Institution Abbottabad is a 1,000-bedded tertiary care hospital in Abbottabad and is the largest health care facility in the Northern region receiving patients from all districts of the northern side of the province.

A Retrospective descriptive study (BEGUM, S.; AZIZ-UM-NISA; BEGUM, I., 2003) was conducted in Ayub Medical and Teaching Institution (AMTI) Abbottabad in 2000-2001 to identify the causes and preventable factors of maternal mortality. The study reported that 26 maternal deaths occurred of which 8(30%) were due to eclampsia. There were 16 (61.5%) patients with age > 30 years. The age was between 18–42 years. Main reasons for maternal mortality were age, high parity, lower socioeconomic status, illiteracy, socio-cultural factors and poor access to health facility.

Similarly, another retrospective descriptive study (JAMIL; ABBASI; ZAMAN, 2013) was conducted in Ayub Medical and Teaching Institution (AMTI) Abbottabad in 2010-2011. It determines the outcome of eclampsia patients admitted to intensive care unit (ICU). It reported that total 18 patients died out of 116 eclamptic patients. Maternal mortality rate due to eclampsia was 15.52%.

DISCUSSION

This review gives an overview about maternal mortality related to pre-eclampsia and eclampsia in KPK Pakistan. Pre-eclampsia and

eclampsia remain a major cause of maternal mortality in the KPK region of Pakistan. The combined figure of Maternal Mortality Rate associated with pre-eclampsia and eclampsia in KPK, from all included studies turn out to be 18% (236 out of 1,336 women with pre-eclampsia or eclampsia died). Most of the mother died at the age of 20 to 30 years. The low socio-economic condition, poor access to the health care services, and low quality of health care of the obstetrics emergency, were the main causes.

The information revealed from the included studies truly reflect the situation in the community, and highlights the continuing high ratios of maternal mortality associated pre-eclampsia and eclampsia. All included studies report no decrease in the Maternal Mortality Rate due to pre-eclampsia and eclampsia over different time periods during the last fifteen years. This is of deep concern for government officials and health care providers in the region.

However, there is a need for large and high quality studies to be reporting on maternal mortality. Studies need to conform to a uniform standard of reporting. More data, at the provincial and national level, need to be readily available. It is of vital importance that all births and deaths at each district and province are registered.

Maternal health policy should be carefully revised and should consist of comprehensive short and long-term goals. All motherhood programs, both in the public and private sector, need to be critically evaluated. Health awareness, particularly about mothers and newborn should be increased at the community level. Nurses and midwives should be appropriately trained in order to provide maternal care during pregnancy, labor and the postpartum period (TABASSUM; UMBER; KHAN, 2010). In addition to proper education and training, nurses and midwives need to be motivated to work in the rural and remote areas of the province.

No matter how trained and knowledgeable a nurse and midwife is, very little can be done when serious complications arise during delivery and labor if access to emergency care or drugs, essential supplies and equipment are not available. Support services like a blood bank, laboratories and proper referral system should be in place and readily available to pregnant women.

The maternal mortality is high in the developing countries and the major cause of those deaths are pre-eclampsia and eclampsia. In those countries where maternal mortality is low, pre-eclampsia and eclampsia are the cause of a substantial proportion of deaths (GOLDENBERG et

al., 2011). The incidence of pre-eclampsia and eclampsia can be minimized by introducing comprehensive programs with a focus on health education and a network of easily available healthcare facilities. Deaths associated with pre-eclampsia and eclampsia are preventable by the provision of effective antenatal nursing care to the pregnant women in all health care services (KHANUM; SOUZA, 2016).

Limitations

This is study based on the limited and small number of studies conducted in KPK, Pakistan. Since organized data on routine health outcomes in KPK do not exist and there is also a scarcity of published studies on the subject matter, this small but equally representative study gives a glimpse of the high maternal mortality ratio associated with pre-eclampsia and eclampsia in the KPK province.

CONCLUSION

Available data shows that the Maternal Mortality Ratio associated with pre-eclampsia and eclampsia in KPK Pakistan continue to remain high. To address the unacceptable state of maternal health, a systematic and organized data collection of all births and deaths and other health outcome at the district and province level is of utmost importance. Qualifying emergency obstetric nursing care and increasing the number of well-equipped health care facilities are a more viable and fastest way to cope with pregnancy-related complications.

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4.3 MANUSCRIPT 3 - NURSING CARE PRACTICES IN THE PREVENTION AND CONTROL OF PRE-ECLAMPSIA AND ECLAMPSIA: AN INTEGRATIVE REVIEW

NURSING CARE PRACTICES IN THE PREVENTION AND CONTROL OF PRE-ECLAMPSIA AND ECLAMPSIA. AN INTEGRATIVE REVIEW

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Abstract: Background: Deaths associated with pre-eclampsia and eclampsia are preventable by the provision of effective antenatal nursing care to the pregnant women in all health care services. Effective nursing care practices, including the confidence of decision-making and timely referrals of the pregnant women in emergency cases to the right place, to higher level facilities can prevent pre-eclampsia and eclampsia and reduce maternal mortality. **Objective:** To assess the nursing care practices for the prevention and control of pre-eclampsia and eclampsia. **Method:** An integrative review was conducted. Google Scholar and three electronic databases of Pubmed/Medline, Cochrane and Cinahl were searched for articles published between 2005-2016, on nursing care practices for the prevention of pre-eclampsia and eclampsia. Numerical and descriptive data from included studies was extracted, categorized, tabulated and presented visually. **Results:** A total of 2,895 articles were initially identified using the search criteria from all the selected databases where 14 studies were finally selected to be included in the review. Several key aspects of nursing care practices which play an important role in the prevention of pre-eclampsia and eclampsia were identified. These includes a physical examination of pregnant women, early detection of signs and symptoms of pre-eclampsia and eclampsia, monitoring laboratory tests, fetal assessment, blood pressure

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measurement techniques, early identification and treatment of hypertension through institutional protocols, standardization of care and instruments and decision-making abilities. **Conclusion:** Nursing practices have an important role in the prevention of pre-eclampsia and eclampsia. Midwives and nurses are the main antenatal care providers. Professional training and continuing education, as well as review of cases and work processes, are necessary for nurses in order to play a better role in providing quality nursing care to pregnant women.

Keywords: Pre-eclampsia. Eclampsia. Maternal Mortality. Nursing Care. Nursing Practice.

INTRODUCTION

Pre-eclampsia is defined as high blood pressure and the presences of protein in the urine after 20 weeks of pregnancy. Pre-eclampsia is one of the three main cause of death in pregnant women (WHO, 2015b). Detection of pre-eclampsia in early stages is important and helpful to manage it effectively and prevent its further development to eclampsia (DULEY, 2009). Eclampsia is a serious complication of pregnancy characterized by a serious condition of life-threatening acute tonic-clonic seizures in a pregnant woman (DULEY, 1992). Worldwide pre-eclampsia affects up to 7.6% of pregnancies (BARTSCH et al., 2015) and eclampsia occurs in 1.4% of pregnancies. Globally, pre-eclampsia and eclampsia are the primary cause of more than 10% of maternal deaths (WHO, 2015a; SAY et al., 2014).

Maternal Mortality Ratio in developing countries is high than the developed countries due to the provision of differences in quality of health care among low and middle-income countries (KIDANTO et al., 2012). In developed countries due to the provision of timely and effective nursing care services and extensive research now pre-eclampsia and eclampsia are in control and has become a rare complication of pregnancy (KEELING et al., 1991).

Deaths associated with pre-eclampsia and eclampsia are preventable by provision of effective antenatal nursing care to the pregnant women in all health care services (WHO, 2015a,b). A skilled nurse's effective nursing practice, the confidence of decision-making and timely referral of the pregnant women in emergency cases to the right place, to higher level facilities can prevent pre-eclampsia and

eclampsia and reduce maternal mortality (WHO, 2011).

Prenatal nursing care is a program for pregnant woman until she gives birth to her baby. Some pregnant women received prenatal care in the first trimester of pregnancy, some received later in pregnancy and some pregnant women could not receive Prenatal nursing care because of several factors. But for a safe childbirth, all pregnant women should have proper access to elective antenatal care, whatever of their social, economic, cultural and geographical background. Effective nursing care throughout pregnancy and during childbirth is essential for reduction of maternal mortality. One-quarter of maternal deaths are due to inadequate delivery of nursing care from the onset of pregnancy (CHRESTANI et al., 2008).

The Nurse's eager observation, quick decision-making ability to use lifesaving procedures and referral to the right place, at the right time, can save the pregnant women (FULLERTON, 2011). Skilled Nurses are valuable members of the community. They are more than a healthcare provider - they are educators, mentors, and guardians of new life. Nurses need to know the danger signs of pregnancy and educate women about these risks.

The skilled and effective nursing care in the antenatal period can help, to prevent pre-eclampsia and eclampsia and reduce maternal mortality rates (DAVIS, 2004). Nurses are providing health care services in primary health care centers. They are the frontline health care providers. So they are expected to provide skilled and effective nursing care to the pregnant women. They should have the ability to detect any pregnancy complications, initial management, and referral of maternal and newborn complications to higher level facilities.

The objective of this study is to assess the nursing care practices for the prevention and control of pre-eclampsia and eclampsia.

MATERIALS AND METHODS

Search Strategies and Sources

This integrative review was conducted from October 2015 to March 2016 to answer the research question of; *what does the scientific literature published between 2005 to 2016 report about the nursing care practices in the prevention and control of pre-eclampsia and eclampsia?* PUBMED/MEDLINE, CINAHL and COCHRANE databases were searched for relevant studies on nursing care practices in the prevention

and control of pre-eclampsia and eclampsia. The search was limited to articles published between January 2005 to March 2016 in the English language. The search strategy was based on a number of medical subject headings MESH terms (see Table 1) and text words aiming to include as many relevant articles as possible.

Table 1 - Search terms used to identify studies.

Database	Descriptors Set
PUBMED	((“eclampsia”[Mesh] OR ”Pre-eclampsia” [Mesh]) AND (“Nursing Care” OR ”Nursing Practic”[Mesh] OR ”Obstetric Nursing and Nursing”[Mesh]))
Cochrane	(Pre-eclampsia or eclampsia) and (Nursing Care or Obstetric Nursing or Nursing Practice)
CINAHL	(Pre-eclampsia or eclampsia) and (Nursing Care or Obstetric Nursing or Nursing Practice)
Google Scholar	Nursing care or nursing practices or Obstetric Nursing for the prevention of Pre-eclampsia or eclampsia

Source: Made by the author (2016).

Inclusion and Exclusion Criteria

All types of qualitative and quantitative studies published in the English language between 2005 to 2016 which were reporting on nursing care practices for the prevention and control of pre-eclampsia and eclampsia, were eligible for inclusion in this review.

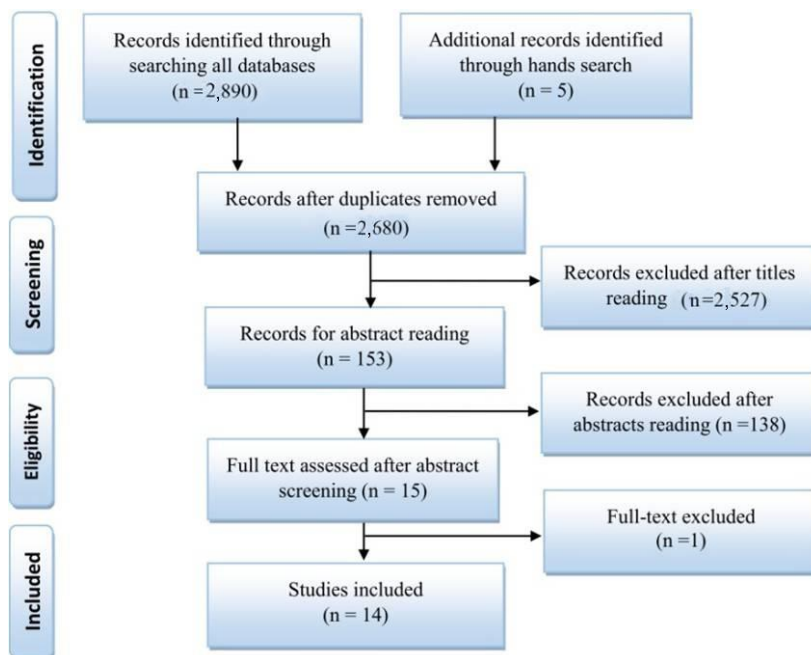
Studies that were published before 2005, reporting on nursing care practices in pregnancy-related complications other the pre-eclampsia and eclampsia and studies not reporting on the nursing care practices, were excluded.

Search Outcome

A total of 2,895 articles were initially identified using the search criteria from all the selected databases and through manual searching using Google Scholar, where 215 were duplicated. The remaining 2,680 articles were selected for title-wise screening which resulted in 153 studies to be selected for abstract reading. After the abstract screening, 15 studies were selected for full-text reading, of which 14 were included in the review (see Figure 1). All screening was done by three independent reviewers. Each article was screened by three reviewers and disagreement between them was resolved by discussion. The aim was to

identify all relevant articles which have reported on the nursing care practices in the prevention and control of pre-eclampsia and eclampsia.

Figure 4 - Flowchart showing the process of identification and screening of studies (Manuscript 3).



Source: Made by the author (2016).

Quality Assessment

It is always difficult to analyze the quality of heterogeneous and distinctive primary sources in an effective manner (WHITTEMORE; KNAFL, 2005). The methodological quality assessment was not conducted in this review because the assignment of such quality score in different studies is an arbitrary and unscientific process (MEADE; RICHARDSON, 1997). However, Joanna Briggs Institute (JBI) were used to assess the quality of included studies. Similarly, assessment of studies was not summarized due to the inherited methodological complexity (WHITTEMORE; KNAFL, 2005). Articles were classified

according to (MELNYK; FINEOUT-OVERHOLT, 2011) as defined in Table 2.

Table 2 – Levels of Evidence for identification studies.

Level	Description
I	Evidence from systematic review and meta-analysis of all relevant RCTs
II	Evidence derived from well-designed evidence RCTs
III	Evidence obtained from well-designed clinical trials without Randomization
IV	Evidence from well-designed cohort studies and case control studies
V	Evidence from systematic review of descriptive and qualitative studies
VI	Evidence derived from a single descriptive or qualitative study
VII	Evidence from opinion of authorities or expert committees report

Source: Melnyk and Fineout-Overholt, (2011).

Data Extraction and Synthesis

Extracting and synthesizing data from heterogeneous sources is a complex process (GOLDSMITH; BANKHEAD; AUSTOKER, 2007). All selected studies were independently assessed by two reviewers. The following information was extracted from each included study: general information about authors, journal, publication date, country and region; research design, location, participants, aims; nursing care practices in the prevention of pre-eclampsia and eclampsia; results and descriptive summaries of numerical data.

Synthesis of the data involved categorizing and tabulating data and then narrating, summarizing and presenting it visually.

Ethical Considerations

This study was developed in the context of project TO 13075/2012 - FAPESC, Opinion No. 120.343 and No. 169.110 of the year 2012 (Annexes A and B) and for that reason, it respects what is set out in the Resolution no. 466/2012, of the Ministry of Health Brazil (BRASIL, 2013). However, the completion of this research work did not involve any human subjects.

RESULTS

Total 14 studies were included in the review, of which 3 were case report, 1 was randomized controlled trial, 2 were methodological studies, 1 was descriptive qualitative studies, 2 were prospective cohort studies, 1 observational, 1 quasi-experimental study, 1 was retrospective descriptive study and 2 were cross-sectional studies. The included 14 studies were conducted and based in countries shown in Table 3.

Table 3 - Countries where the selected 14 studies were conducted.

Country	Number of Studies
Australia	2
USA	5
UK	2
India	1
Egypt	1
Brazil	1
Nigeria	1
Netherland	1

Source: Made by the author (2016).

The characteristics of the primary 14 studies are summarized in Table 4. All the 14 included studies in this integrative review, were classified into four categories, on the basis of nursing practices. The details of all these four categories are discussed as follow.

Table 4 - Summaries of included studied from 2005 to 2016 on nursing practices for prevention pre-eclampsia and eclampsia.

Ref.	Country, Year	Evidence Level	Objectives	Nursing Practice
(ELLIS et al., 2008)	UK, 2008	RCT, Level II	To compare the effectiveness of training assistance to eclampsia with and without the teamwork theory	Measurement and monitoring of BP, early magnesium sulfate, Oxygen Saturations, Vaginal examination
(CHRISTIAN; KRUMWIEDE, 2013)	USA, 2013	Quasi experimental study, Level III	To assess whether training with realistic simulation is an effective strategy in the training of nurses caring for pre-eclampsia or eclampsia	Physical examination of women, Measurement and monitoring of BP, administration of Magnesium Sulfate, intake output record
Continues...				

Ref.	Country, Year	Evidence Level	Objectives	Nursing Practice
Continuation				
(REINDERS et al., 2006)	Australia, 2006	Observational, Level IV	To compare two BP scouting measures with quickly mercury release	Measurement and monitoring of BP
(IYENGAR, K.; IYENGAR, S. D., 2009)	India, 2009	Prospective Cohort, Level IV	To document the experiences of nurses and midwives and detect their decision-making abilities	Detect pregnancy complications and decision-making about the referral to further facility
(DANIELS et al., 2010)	USA, 2010	Prospective cohort study, Level IV	To compare results of simulated training and theoretic training to deal with emergencies in the delivery room	Assessing sign and symptoms, diagnose of preeclampsia, administration of Magnesium Sulfate, monitoring of blood pressure, monitor necessary fits.
(MOUSA; ALI; ADAWY, 2013)	Egypt, 2013	Cross-sectional, Level IV	To analyze nurse's knowledge about preeclampsia	Measurement of BP, physical examination, administration of Magnesium Sulfate
(BLACK; MORIN, 2014)	USA, 2014	Methodologic al study, Level, IV	To refine psychometric properties of an instrument to assess symptoms	Assessing sign and symptoms measurement and monitoring of BP, urine tests for proteinuria
(MOHAMMED et al., 2016)	Nigeria, 2015	Cross-sectional, Level IV	To assess the knowledge of nurse-midwife	Detecting and diagnosing pre-eclampsia, administration of Magnesium Sulfate
(NOBLE, 2005)	USA, 2005	Case study, Level VI	To describe a case of preeclampsia in the puerperium	Measurement and monitoring of BP, urine tests for proteinuria
(CUNHA; OLIVEIRA; NERY, 2007)	Brazil, 2007	Qualitative study, Level VI	To assess the opinion of women with pre-eclampsia on nursing care received	Measurement and monitoring of BP and administration of Magnesium Sulfate
(SCHUTTE et al., 2008)	Netherlands, 2008	Retrospective descriptive study, Level VI	To assess quality of care in cases of maternal death by hypertensive disorders	Measurement and monitoring of BP, urine tests for proteinuria, administration of Magnesium Sulfate
(AMEH; EKECHI; TUKUR, 2012)	UK, 2012	Methodologic al study, Level VI	To develop a chart to track the care of pregnant women with pre-eclampsia and eclampsia	Measurement and monitoring of BP, Monitoring of proteinuria level, number of fits, level of consciousness, ad administration Magnesium Sulfate, Calcium Gluconate
Continues...				

Ref.	Country, Year	Evidence Level	Objectives	Nursing Practice
Conclusion				
(MARTIN; MCINTOSH, 2013)	Australia, 2013	Case report, Level VI	To describe pre-eclampsia frame care simulation and eclampsia in the labor room	Measurement and monitoring of BP, early Magnesium Sulfate
(STEPHENS-HENNESSY; SENN, 2014)	USA, 2014	Case report, Level VI	To report the experience of an intervention program to reduce maternal mortality	Measurement and monitoring of BP

Source: Made by the author (2016).

Blood Pressure Measurement Technique

An observational study (REINDERS et al., 2006) was conducted in Australia in 2006, to compare two Blood pressure scouting measures with quickly mercury release. Two Blood pressure readings were obtained, one quickly (>5 mm Hg/sec) and the other with slow (≤ 2 mm Hg/sec) lowering of mercury. The Blood pressure measurement was made by nurses. The results reported that the slow descent of the mercury is the recommended method to measure blood pressure while rapid cuff deflation underestimates blood pressure.

In Stephens-Hennessy and Senn, (2014), a series of different techniques was adopted by a multidisciplinary team of a hospital to improve nursing care for pregnant women at risk of developing pre-eclampsia. The implications for nursing care indicate the need for standardization of the blood pressure measurement technique, identification of hypertensive serious condition, urgent call for the multidisciplinary team, rapid administration of the drug and review of work processes.

Training of nurses in the prevention of pre-eclampsia and eclampsia

In Ellis et al., (2008) a randomized controlled trial was conducted in the United Kingdom to compare the effectiveness of training for eclampsia in a simulation center, with and without teamwork theory. The results reported that, after training with the teamwork theory, there was a significant decrease in the mean duration of techniques in the management of eclampsia and also a significant increase in the number of professionals who performed basic nursing care actions and additional assistance in eclampsia. The main nursing care actions for eclamptic patients observed in this study includes measurement and monitoring of blood pressure, administration of the correct loading dose

of magnesium sulfate, call for help in emergency cases during attending an eclamptic patient, supporting and making access to the airways, lowering the bed to reduce the risk of falls of patients, administration of oxygen, monitoring heart rate of fetal, and establishing quality venous access.

In Martin and McIntosh, (2013), a simulation scenario of nursing care in pre-eclampsia and eclampsia in the labor room was proposed. The simulated scenarios consist of oral administration of nifedipine, labor induction, anesthesia, insertion of the airway, oxygen therapy facility with a facial mask, establishing IV access, blood pressure measurement and early doses of magnesium sulfate. The study reported that the simulation training helped participants in understanding the different perspectives and different priorities for nurses in dealing with pre-eclampsia and them to better understand the different skill set required in different situations.

In Daniels et al., (2010) prospective cohort study was conducted in the United States of America, in 2010 to investigate the impact of human simulation on the self-efficacy of nurses in the management of pre-eclampsia and eclampsia. One group was given only theoretical instructions while the second group received training instructions with simulations. During scenario, essential nursing care actions, provided to the pregnant women with pre-eclampsia were; recognizing signs symptoms of pre-eclampsia; diagnose of pre-eclampsia; administration of accurate loading dose of magnesium sulfate; monitoring of blood pressure measurement; monitoring of mother and newborn condition; monitor necessary seizure precautions. The performance of the group which was trained with simulation performed much better than the group which received only theoretical training.

Similarly, another study (CHRISTIAN; KRUMWIEDE, 2013) was conducted in the United States of America in 2013 to evaluate the skills of nurses in women with pre-eclampsia and eclampsia, after practical training. The results reported that the training significantly boosted the skill of nurses and other health professionals, particularly with regard to the early identification and adoption of appropriate nursing behaviors. Nursing practices observed and found essential for prevention of pre-eclampsia and eclampsia were recognizing the signs and symptoms of pre-eclampsia, Blood pressure monitoring, Oxygen saturations, physical examination, airway monitoring, correct dose of magnesium sulfate, maintenance of IV line, call for assistance, anesthesia and urine tests for proteinuria.

Instruments for Standardization Care

A study in Black and Morin, (2014) was conducted in the United States of America in 2014 to assess and refine the psychometric properties of an instrument designed to assess a comprehensive range of pre-eclampsia symptoms. The study reported that the use of a scale to evaluate the symptoms of pre-eclampsia during pregnancy, assists in the prediction and cause complications, allowing early implementation of nursing care. The results revealed that this instrument would be useful in nursing practice for detecting and diagnosing of pregnant women with pre-eclampsia.

Similarly, a chart was developed to track the care of pregnant women with pre-eclampsia and eclampsia in a study (AMEH; EKECHI; TUKUR, 2012) conducted in UK in 2012. The chart contains the data regarding the fetal heart rate, blood pressure, respiratory rate, proteinuria levels, number of fits, level of consciousness, water balance, deep tendon reflexes, administration of anti-hypertensives drugs, and administration of magnesium sulfate and calcium gluconate, and a summary of hospital treatment and complications in the admission and discharge. The results showed that most participants reported the graphic chart is a great alternative for monitoring women, and emphasized its usefulness in improving nursing care of pregnant women with pre-eclampsia, especially, in monitoring and provision of evidence-based nursing care and treatment.

Knowledge and Quality of Nursing Care

The standard of quality of nursing care was assessed in a study (SCHUTTE et al., 2008) in Mortality cases that occurred in the Netherlands between 2000 and 2004. In 135 deaths cases, 27 (20%) women died as a result of hypertensive disorders. All women met the criteria for the diagnosis of pre-eclampsia, of which 16 (60%) resulted in eclampsia. In 60% of cases, prenatal nursing care was performed by traditional midwives, and 96% compliance was considered low-level or below required. Late onset of prenatal nursing care and lack of blood pressure check up in the first quarter were reported. In 46% of cases, laboratory tests of urine were not carried out for the detection of proteinuria, and in all of these pregnant women, the risk factors for pre-eclampsia were present during pregnancy. There was a delay in referral (15%) and in-hospital care, and 41% did not make the relevant diagnostic tests, 85% had inadequately reported hypertension and 74% were a misdiagnosis of mild pre-eclampsia when, in fact, they would be

classified as severe cases. It was found that the low quality of nursing care was present in almost all cases of maternal death resulting from hypertensive disorders.

A pregnant woman faces physiological changes in virtually every organ of her body and hence demands specialized training to meet the requirements of her nursing care. Administration of drugs and blood products, as well as prior knowledge of the pathophysiology of pre-eclampsia and explanation of pathological changes occurring in the pregnant women body, contributes to improvement in the nurse's care for the pregnant women with pre-eclampsia (NOBLE, 2005).

Similarly, a study was conducted to describe and evaluate the nursing care received by pregnant women, hospitalized for pre-eclampsia. It is concluded that nursing care must be more human in addition to meeting the physical, social and psycho emotions needs of the patient (CUNHA; OLIVEIRA; NERY, 2007).

A cross-sectional study was conducted in Egypt in 2011 to update nurses' knowledge regarding the care of pre-eclamptic patients (MOUSA; ALI; ADAWY, 2013). A structured pre and post-test questionnaire were used on 25 nursing staff working in the Obstetrics and Gynecology Department. The result showed that regarding the definition and signs and symptoms of pre-eclampsia, 72% of the nurses have a correct answer but incomplete in pre-test and 72% of nurses have a correct and complete answer in post-test. The correct and complete answers are 16% and 0% for each question respectively in the pre-test. In relation to the time of urine collection, 48% and 64% of nurses have the right answer in pre and post-test respectively. Regarding time of blood pressure measuring, 80% of the nurses have a correct answer in both pre and post-test. In relation to deep tendon reflexes making, only 20% and 76% of the nurses have a correct answer in pre and post-test respectively. Regarding Edema, 76% and 88% of the nurses have a correct answer in pre and post-test respectively. Regarding Magnesium Sulfate administration, 96% of the nurses have a correct answer in both pre and post-test. The mean of knowledge in pre-test is 19.88 (59%) and in post-test 24.80 (74%). Data analysis revealed that in the pre-test a large proportion of the participants have incorrect, improper knowledge about pre-eclampsia, and they did not know that how to do nursing care of pregnant women with pre-eclampsia. While in the post-test knowledge of nurses, regarding pre-eclampsia was significantly improved.

A cross-sectional study was conducted in 2015 in Nigeria to

assess the knowledge of nurse educators about the major causes of maternal mortality (MOHAMMED et al., 2016). In this study 57.2% of educators could diagnose pre-eclampsia and 62.7% of educators could diagnose severe pre-eclampsia. 86% of nurse educators knew about magnesium sulfate as the “gold standard” for treating eclampsia, only 16.8% knew of calcium gluconate as an antidote to magnesium sulfate toxicity. The results indicate that Nurse/midwife educators in Nigeria are not as knowledgeable as previously thought, especially concerning the causes of maternal mortality.

Similarly, a prospective cohort study was conducted in India to document nurse’s experience in providing maternal and newborn nursing care (IYENGAR; IYENGAR, 2009). From 2000 to 2008, nurses attended about 2,771 women in labor and 202 women in maternal emergencies. The nurses independently detected and managed pregnancy-related complications and independently made decisions about the referral to the nearest hospital. Among the women in labor, 21% were in critical condition and had life-threatening complications and 16% were advised referral. The referral decision was made by the nurses, higher for maternal conditions than fetal conditions. Among the 202 women who came with maternal complications antenatally, post-abortion or post-partum, the referral was advised for 70%, of whom 72% were arranged. The referral system included counseling, arranging transport, accompanying women, facilitating admission and supporting inpatient nursing care. During the nine-year study period, there was only one maternal death. The study suggests that skilled and experienced nurses can especially improve access to skilled maternal nursing care in rural areas. Nurses have the ability to prevent and manage pregnancy-related complications with or without the need for referral.

DISCUSSION

The included studies investigated the standardization of blood pressure measurement technique, highlighting specific aspects for the early diagnosis and treatment of pre-eclampsia and eclampsia. In the twentieth week of pregnancy, high blood pressure is one of the most important diagnostic criteria for case definition, and the presence of protein in the urine, clarifying the diagnosis of pre-eclampsia (WHO, 2011). The measurement of blood pressure is an important predictor of pre-eclampsia and eclampsia. It should be correctly assessed to avoid

complications. Slowly deflation of the mercury column ≤ 2 mmHg to obtain more reliable and more precise results in the diagnosis (REINDERS et al., 2006), early identification and drug treatment of hypertensive crisis through institutional protocols are very essential (STEPHENS-HENNESSY; SENN, 2014).

Skilled and effective nursing assessments of the signs and symptoms are essential in the detection, monitoring, and effective management of Pre-eclampsia and eclampsia. In addition, patient education and awareness and friendly environment provided by nurses are also helpful for the wellbeing of mother and baby (KHANUM et al., 2016).

Many authors investigated the training of nurses with simulation to face pre-eclampsia and eclampsia (ELLIS et al., 2008; MARTIN; MCINTOSH, 2013; DANIELS et al., 2010; CHRISTIAN; KRUMWIEDE, 2013). As a strategy the realistic simulation for teaching and learning were used, characterized by a possibility of teaching that encompasses not only technical skills but the emergency management, leadership, teamwork and clinical reasoning. The results indicated improvement in the performance of professionals in simulated environments (DANIELS et al., 2010) and positive impacts on care (ELLIS et al., 2008) as the early identification of signs and symptoms of pregnant women with pre-eclampsia (CHRISTIAN; KRUMWIEDE, 2013), adoption of actions based on current protocols, more agility and performance of the multi-professional team in front of emergency situations (MARTIN; MCINTOSH, 2013). The training of professionals involved in health care at different levels of attention brought gains to users and health professionals (CHRISTIAN; KRUMWIEDE, 2013).

Similarly, instruments, which helps in follow-ups and continuous monitoring of pregnant women with pre-eclampsia and eclampsia, should be used by nurses, in order to improve the quality of nursing care (BLACK; MORIN, 2014; AMEH; EKECHI; TUKUR, 2012). Low quality of nursing care including lack of blood pressure check-ups, late urine test, and delayed referrals, for the women with pre-eclampsia and eclampsia, was also reported in (SCHUTTE et al., 2008).

Knowledge enhancement for in-service nurses and midwives, including short periods of didactic and case demonstrations, to increase their efficiency in dealing with pregnancy and its complications is very important (TEN HOOPE-BENDER et al., 2011). Knowledge of the direct and indirect causes of maternal mortality is fundamental to all practicing midwives. Nurse's knowledge regarding pre-eclampsia

definition, signs and symptoms, edema checking, time of urine collection, can be improved and updated with continuing education programs (MOUSA; ALI; ADAWY, 2013; FULLERTON et al, 2011). Skilled and experienced nursing care can improve the quality of obstetric care particularly in rural areas (IYENGAR, K.; IYENGAR, S. D., 2009).

CONCLUSION

Nursing care practices have an important role in the prevention of pre-eclampsia and eclampsia. This integrative review point out specific key nursing care practices which play an important role in the prevention of pre-eclampsia and eclampsia and in the reduction of maternal mortality. These includes a physical examination of pregnant women, early detection of signs and symptoms of pre-eclampsia and eclampsia, monitoring laboratory tests, fetal assessment, correct blood pressure measurement techniques, early identification and treatment of hypertension through institutional protocols, standardization of care and instruments and decision-making abilities.

Midwives and nurses are the main professionals who provide care to pregnant women. Professional training and continuing education as well as review of cases and work processes are necessary for nurses in order to enhance their knowledge and improve their practice and play a better role in providing quality nursing care to pregnant women.

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4.4 MANUSCRIPT 4 - PREGNANCY NURSING CARE VIRTUAL NETWORK: A THEORETICAL DESIGN

PREGNANCY NURSING CARE VIRTUAL NETWORK. A THEORETICAL DESIGN

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Maria de Lourdes de Souza²

Abstract: All pregnant women need timely access to the healthcare services and skilled nursing care. This including awareness about pregnancy-related complications, customized information, timely help and care from health care providers. Information and communication technologies can play an important role in facilitating some of these services to pregnant women. Also with efficient way and can thus prevent pre-eclampsia and eclampsia, and other pregnancy-related complications and reduce maternal mortality. **Objective:** To design a pregnancy nursing care virtual network for prevention the pre-eclampsia and eclampsia. **Methodology:** The development life-cycle was used The basic idea behind this method is to develop a system through repeated cycles (iterative) and in smaller portions at a time (incremental). In this study was developed two phases: the requirements and design process of the network. **Result:** The system will enable effective and real-time two-way communication between pregnant women and nurses, and all units the health system (ambulance, health facility staff, and other level) through smartphones. The primary expected result of the system is an improved access to antenatal, postnatal care, institutional delivery, and emergency obstetric care. **Conclusion:** Pregnant women need customized information and education according to their demands, needs and respective situation. Information and communication technologies can play an important role in facilitating these services in a

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fast and efficient way and can contribute to prevent pre-eclampsia and eclampsia and other pregnancy-related complications

Keywords: Pre-eclampsia. Eclampsia. Maternal Mortality. Nursing Care. Nursing Practice.

INTRODUCTION

Pre-eclampsia is a pregnancy-related complication and one of the leading cause of death in pregnant women in the developing countries (KHAN et al., 2006). In 2015 every day, approximately 800 women died from preventable causes related to pregnancy and childbirth complications (WHO, 2015). Maternal mortality is higher in women living in rural areas and among poorer communities. The major causes that account for nearly 75% of all maternal deaths are severe bleeding (27%), pre-eclampsia and eclampsia (14%), and infections (11%) (WHO, 2015). Since 1990 maternal deaths have dropped by 45% worldwide. However, between 1990 and 2013, the global maternal mortality ratio (the number of maternal deaths per 100,000 live birth) declined by only 2.6% per year. This was far from the annual decline of 5.5% required to achieve MDGs5 (WHO, 2015; SAY et al., 2014).

Most maternal deaths are preventable, as the health-care solutions to prevent complications of pregnancy are well-known (WHO, 2014). All women need access to antenatal care in pregnancy, skilled and timely nursing care during pregnancy, childbirth, and support in the weeks after childbirth. However, factors that prevent women from receiving care during pregnancy and childbirth are poverty, delays (in the home, in the way, and in care center), lack of information and awareness, lack of adequate health care services and skilled health professionals, home deliveries, and cultural practices (WHO, 2014). The delays also include; (i) identifying a life-threatening event and making the decision to go to the health facility, (ii) reaching the health care facility, and (iii) intervening effectively. Technologies including smartphones, computers, equipment, supplies, products, procedures, and techniques can play an important role in the prevention of pre-eclampsia and eclampsia and other pregnancy-related complications and can contribute to a significant reduction in maternal mortality around the world (TSU; FREE, 2001).

Since the boom in communication and information technologies

(ICT), the field of eHealth has emerged into many forms and its potential has been discussed globally. eHealth has increasingly become part of people's everyday lives and has the ability to change how health care is delivered, the quality of the patient experience, and the cost of health care (WANG; LIU, 2009). It enables, among other things, the exchange of healthcare and administrative data and the transfer of medical images and laboratory results. The use of ICT in the health sector has the potential to change the face of global health systems and can deliver life-saving information even in the most remote and resource-poor settings (WHO, 2011). Improvement in ICT, development of smaller components with higher levels of security, decreasing costs and increasingly user-friendly features are the main reasons for adopting eHealth solutions in our daily lives (PIETTE et al., 2012).

The number of mobile phones in the world was 97 per 100 people at the end of 2014 (THE WORLD BANK, 2016) and has exceeded the world population in 2016 and among those more than 50% are smartphones (STATISTA INC., 2016). Similarly, the number of internet user worldwide was 3 billion in 2015 (CIA, 2016; THE WORLD BANK, 2016). Mobile and wireless technologies offer exciting opportunities for a low cost, high reach health care services such as helping with chronic disease management, empowering the elderly and expectant mothers, reminding people to take medication at the proper time, extending service to underserved areas, and improving health outcomes and medical systems efficiency (WEST, 2012). In addition, it also offers significant opportunities for improving the data analysis and office operations of health care system. It can replace the paper-based work in low-resource settings where most of the clinical data is being kept by patients themselves. In the case of the paper-based work, it is very difficult and costly to develop a national overview of patient statistics and is extremely hard for individual institutions within the healthcare sector to share information between each other.

Improvement and increase in data transfer rates over networks of interconnected computers has removed all barriers to the exchange of medical data, physiological signals and medical imagery between computers. The standardization of exchange protocols between computers, such as the Internet Protocol for example, in addition to the improved structuring of medical data and data security rules, is increasingly making it possible for health professionals in different locations to understand one another and work together, despite differences in location and languages. It is now clear that the value of

these applications lies not in the technology itself, or even in the exchange of data, but in the ability to develop efficient networks and expertise in the field of health.

Networks, such as family network, social networks, and professional networks, are playing an important role in our daily lives. Social networks include our friends, those we meet in classroom settings, people we like to spend time with and those we engage in social media. Our family network includes all of our family members and extended family. Lastly, our professional network includes colleagues, coworkers, and customers. Especially in healthcare, the professional network between patients and nursing professionals can be vital to both sides. Mobile devices and other communication technologies can be used to make a network between nurse and pregnant women as a fast and easy way to pushing information to every possible pregnant woman. It helps in information sharing between pregnant women and maternity homes and improve decision making and reduce delays.

The most important contacts in health care will always be the face-to-face meetings. However, with the help of interactive tools on the Internet, patients can strengthen their influence on health care by getting both general and specific information. Health care accessibility increases when patients can contact health care professionals at any hour or are able to retrieve information and leave messages by the same media.

Mobile phones are in the hands of increasingly more women and nurses, including those in some of the poorest and most difficult to reach areas of the world (SPECIALE; FREYTSIS, 2013). Mobile phone and internet connectivity are creating unprecedented opportunities for improving maternal and child health outcomes by facilitating interactions and information sharing between nurses and patients (BOULOS; MARAMBA; WHEELER, 2006). This interactivity and connectivity are greatly improving health care accessibility by increasing contacts of patients with nursing professionals at any time anywhere and can retrieve specific information in less time.

Generally, less than 10% of mothers know about the development of the fetus they were carrying (SALAMEH et al., 2011). Not only that, the pregnant mothers do not know what is good and bad things they should do and avoid during pregnancy. There should be a way to help expectant mothers to be aware of their pregnancy development. They should be able to access pregnancy related customized information and useful tips regarding each stage of their pregnancy at their fingertips and

should be connected to health care providers whenever and where ever they want.

Nurses need a wide range of theoretical and practical knowledge to provide the appropriate level of care to patients. Their knowledge should be dynamic and continuously evolve. Partnership by the networking tools facilitates interaction and communication between nurses and patients resulting in comprehensive and more accessible nursing care. On one hand, a collaboration between nurses let them get involved and grow their skills and knowledge, while, on the other hand, the interaction between nurses and patients results in quality nursing care to patients, promote the family health and health of the societies.

As technology grows, nurses need to understand and adapt the complex ways in which society now communicates. Nurses need to further develop ways to interact, monitor and collaborate with peers and patients. They need to learn how to effectively manage these tools and leverage their benefits. However, several factors need to be taking care of, in order to make IT applications more effective in health care. These include better training and increased awareness of staff regarding the tools and applications used. In addition, the applications also need to be flexible enough to adjust to the changes in routine clinical practices. Last but not least, the privacy, security, and reliability of data are extremely important in improving the quality of nursing care practices. Breakthroughs in integrated and intelligent computer and communication systems are highly desired in future nursing care practices. We are continuously evolving and so is our knowledge and understanding. Today, we are living in an information age where we have unprecedented opportunities for communication, interaction, collaboration, and sharing. It is essential that nursing and healthcare providers effectively harness the power of these new technologies for global outreach (KHANUM et al., 2015). Based on the discussions in previous paragraphs, this study aims at proposing the designing a network model, *Pregnancy Nursing Care Virtual Network (PNCN)*, which will strengthen communication links between health care providers and pregnant women and increase education, awareness, and quality of nursing care during pregnancy. The goal is to educate mothers, monitor pregnancy, prevent pre-eclampsia and eclampsia and other pregnancy complications and improve maternal health. The PNCN, a computer, and smartphone base application will help pregnant women know about their maternal health and pregnancy related complications and connect them to maternity homes. It will enable

health care providers to collect real-time data about pregnant women and their status in a region for effective care and follow-up and policy making.

In addition, PNCN will help establish a communication and alert system, support documentation of pregnancies in the community, increase antenatal care visits and the number of facility deliveries through automated reminders, develop an overview of women statistics and sharing pregnant women data between institutions for an effective referral. Moreover, PNCN can contribute to the reduction of delay associated with transport to the referral facility and delay associated with timely intervention when the mother reaches the referral facility.

The remainder of this paper is organized as follows.

RELATED WORK

Before the arrival of smartphones, personal digital assistants (PDAs) were experimented with the electronic eHealth tools. These tools were designed to improve health surveillance, health-system management, health education and clinical decision-making, disease management and offered a significant advantage over paper data collection (AL-SHORBAJI, 2006).

Blaya et al., (2009) demonstrated that PDAs were more efficient than paper and preferred for collecting tuberculosis bacteriology data in Peru. Data were collected over a large geographical area, much of which did not have Internet access.

Similarly, systems facilitating clinical practice include electronic medical record systems, archiving and communication systems for managing digital medical data, and laboratory information systems that automate laboratory workflow and reporting, early disease warning and disaster management were introduced. These systems collect data from health facilities and patients to create community-wide views of disease trends and clinical activity (MOURA et al., 1998). In addition, systems facilitating care at remote areas were implemented to use a short message service (SMS) for reminders, monitoring, health education and asynchronous communication.

A mobile phone based system (NGABO et al., 2012) was implemented in Rwanda to monitor pregnancy and newborn information. The SMS-based project was developed to track the pregnancy lifecycle; enabling instant reporting of the pregnancy-related

event and timely notification for emergencies, alerting health facilities, hospital, and ambulances. The project helped to reduce the delay in seeking health care through a short SMS sent by a community health worker alerting the health system for timely and appropriate medical assistance. The system also served as the most remote data entry point for pregnant women and children health status, and as a unique interface to provide real-time data to health care providers.

Similarly, a cluster-randomized, controlled trial (LUND et al., 2013) was conducted in Zanzibar to evaluate the association between a mobile phone intervention and perinatal mortality in a resource-limited setting. At their first antenatal care visit, 2550 pregnant women (1311 interventions and 1239 controls) who attended antenatal care at selected primary health care facilities were included in this study and followed until 42 days after delivery. Twenty-four primary health care facilities in six districts were randomized to either mobile phone intervention or standard care. The intervention was based on a mobile phone text message. Secondary outcome measures included stillbirth, perinatal mortality, and death of a child within 42 days after birth as a proxy of neonatal mortality. Mobile phone applications were shown to improve the health of the newborn and should be considered by policy makers in resource-limited settings.

PotM, a mobile health application (LIM et al., 2015; DUNSMUIR et al., 2014) has been developed to help health workers in the management of women with pre-eclampsia. PotM is based on a decision model that combines accurate risk prediction of maternal adverse outcomes associated with pre-eclampsia with World Health Organization (WHO) recommendations for the management of pre-eclampsia. PotM combines two previously successful innovations into an mHealth app: the miniPIERS risk assessment model and the Phone Oximeter. The application guides health worker through a standardized process of antenatal assessment, including measurement of blood pressure, dipstick proteinuria, and symptoms.

There are a plenty of pregnancy-related applications on the world wide web, and Windows, Google Play and Apple App stores. However, none of them utilize mobile and wireless technologies to provide pregnant women the opportunity to enhance their pregnancy-related knowledge, prevent and control complications of pregnancy as well as connect them to nurses and other healthcare providers by establishing reliable communication and alert system. Our aim in this study is to educate mothers, monitor pregnancy and connect mothers with nurses

and other health professionals for prevention and control of pre-eclampsia and other pregnancy-related complication. Our primary focus is to design a mother care network to prevent and control pre-eclampsia and eclampsia but such system can also be used for the prevention of other pregnancy related complications.

METHODOLOGY

PNCN Overview

This section discusses the main features of the PNCN and presents the theoretical design of PNCN in details. The prevalent functionality of the PNCN is to equip nurses, health care providers, and expectant mothers with a mobile and computer-based application which will help them manage their pregnancy-related knowledge and needs. PNCN will store, query and retrieve pregnancy related information and women health records including their clinical data. Health records and clinical data of women will reside on a remote server, uploaded/stored by health care providers and pregnant women themselves through web user interface and PNCN application. Pregnancy-related information will be stored locally on the smartphones or computers where the application is installed in order to be used without an internet connection. PNCN will allow users to retrieve medical content (such as symptoms, preventions, guidance in case of danger signs and unknown conditions) as well as upload and modify clinical data and laboratory results. In addition, it will enable fast and reliable communication between nurses, health care providers, and pregnant women.

The network is designed keeping in mind both low and high resource settings, making it equally applicable in all scenarios. In low-resourced settings where there is limited availability of electricity and reliable internet connectivity, PNCN will use SMS for emergency communication and locally stored data in PNCN app. In the presence of a reliable internet connectivity, PNCN will have access to the latest data from the central server and will facilitate audio and video communication between women and health care providers. Synchronization of the data with the central server will occur when cellular or wireless internet connectivity is available.

The primary users of PNCN are pregnant women, nurses and other health professionals who provide care to pregnant women in the community in rural health care facilities or in a hospital setting. The

level of education of these users can vary significantly so the system and its use are intended to be kept as simple as possible while still being comprehensive to ensure usability at all levels of intended use.

PNCN offers a tool to health care providers for registration of new pregnancies in their respective community or hospital. Registered pregnancies will be effectively monitored up to the time of delivery and post-partum. Each area or community has selected staff in charge of Maternal and Child health. They are responsible for motivating community members to attend antenatal care and provide support and referral to the health centers for antenatal care, particularly in the case of a life-threatening event. After the registration of new pregnancies in the system, women download and install the app on their smartphone or PC, start getting customized information about their pregnancy and report all danger signs to the respective authorities through the facility provided in PNCN.

For a normal pregnancy, the PNCN system will send automated notification and reminders at a specific date for clinical appointments (medical check-ups and follow-up visits), development of the fetus, delivery date etc. through the app and by SMS. In the case of danger signs, an emergency alert system can be triggered, which provides immediate feedback to the respective health care provider, advising on immediate action. Ambulance requests are forwarded to the nearest ambulance vehicle point to ensure that mother/infant is timely transferred for emergency obstetric and neonatal care.

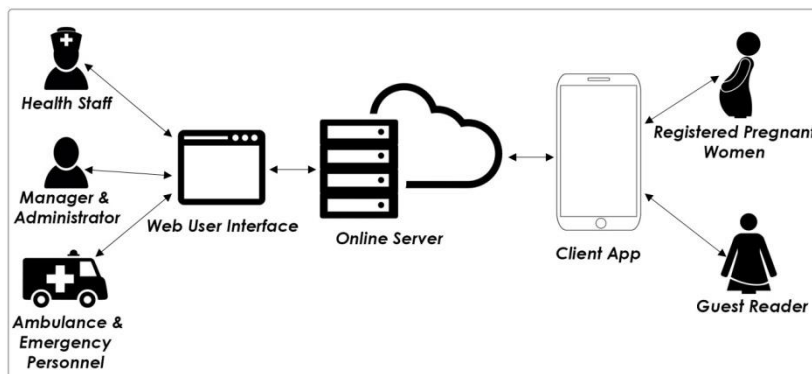
System Architecture

In the Figure 1 illustrates the theoretical design and proposed system architecture for PNCN. The main components of the PNCN are the online server, web user interface, and the client app. Two interfaces, a web client and a standalone application will allow the user to communicate and interact directly with the online server and will allow the management and storage of Women health records. Web client (web user interface) will be used by health staff, health supervisors and emergency team while the standalone application (client app) will be used by pregnant women and general interested readers. The online server manages the physical infrastructure, such as storage file and women health records and is also responsible for performing maintaining operations, such as backing up data.

Women health records at the online server is a system dedicated to collecting, storing, manipulating, and making available clinical

information important to the delivery of quality nursing care. The central focus of such systems is clinical data which consist of longitudinal record of a patient's care carried out across different institutions and time. Women health records include demographic data, health history, laboratory results, immunization history, radiology reports, and drug allergies.

Figure 1 – System Architecture of Pregnancy Nursing Care Virtual Network.



Source: Made by the author (2016).

Similarly, in client App, pregnancy-related information will be organized by time (month), by signs and symptoms and by disease name with the search facility as well, as shown in Figure 6. The locally maintained medical content will include information about female anatomy and reproductive system, health issues related to pregnancy, danger signs and precautionary measure in the form of videos, pictures and text and internet links.

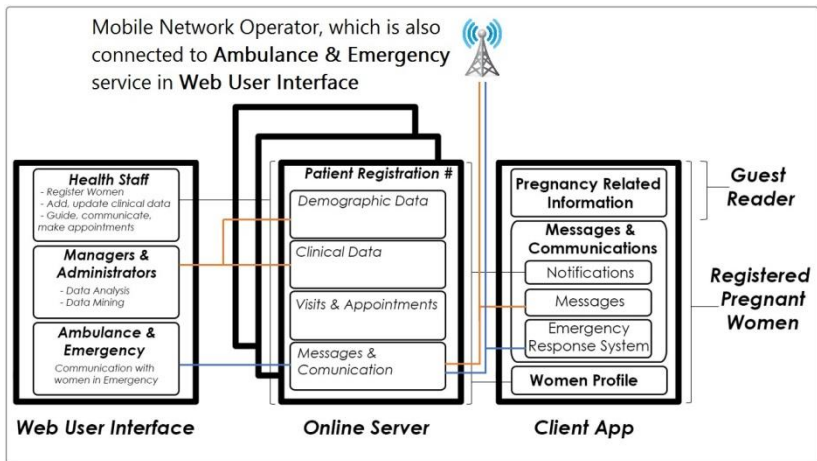
In addition to getting customized information, client App will also be used by pregnant women (if needed) to communicate with nurses and other health professionals. This communication can be real time (with video, audio, and text chat facility) or can be asynchronous where the sender and receiver reply whenever they are available. In the case of non-availability of internet coverage, pregnant women can send an important message via SMS. All she has to do is to press a button and the app will compose necessary content for the SMS and will send it to the web user interface and the pre-defined mobile number of the respective health professionals. There will also be a one click emergency

call option where the emergency team can be contacted via client app.

Similarly, the web user interface will allow nurses and other health professionals to register pregnancy, manage and maintain women health records, interact and communicate with women, send messages and reminders and schedule appointments.

The PNCN full system will consist of a client app running on the user's smartphone, a central database containing all demographic and clinical data of women on an online server, and a web-interface that allows health professionals and supervisors to enter, retrieve and analyze health data of expectant mothers as shown in Figure 2.

Figure 2 – Components and function of Pregnancy Nursing Care Virtual Network.



Source: Made by the author (2016).

System Development

The application development life-cycle is a term used in systems engineering, information systems, and software engineering to describe a process for planning, creating, testing, and deploying an information system. It is a splitting of software development work into distinct phases (or stages) containing activities with the intent of better planning and management. We use the *iterative and incremental development* (LARMAN; BASILI, 2003) methodology for PNCN. The basic idea behind this method is to develop a system through repeated cycles

(iterative) and in smaller portions at a time (incremental), allowing software developers to take advantage of what was learned during the development of earlier parts or versions of the system. Learning comes from both the development and use of the system. The development is started with a simple implementation of the system and then iteratively it is improved until its full functionality is achieved. At each iteration, design modifications are made and new functional capabilities are added, as needed.

It must be noted that during this thesis, I have focused and completed only the first two phases (*Requirements* and *Design*) of the development process of this network model. The others phases are intended to be completed in partnership with my advisor in a future research project.

The development of PNCN will involve a process consisted of the following steps (LARMAN; BASILI, 2003):

- **Requirements:** This phase consist of gathering information about the target population, determining the needs or conditions to meet, deciding the contents and knowledge to be delivered, the tasks and function to be completed, and analysis of available technologies feasible for development and implementation.
- **Design:** The design phase consists of planning, creating specifications, conceptualizing and framing material and production of content, preparing the storyboard and layout design and user interface (color, fonts, images and buttons).
- **Develop:** The third phase, development, involves the creation of the activities that will be implemented. It consists of developing and programming the navigation structure, user interface, settings, images, content, and animations.
- **Test:** Testing ensures that the materials achieved the desired goals and basic functionality. It is used to verify whether the component meets the requirements decided earlier, responds correctly to all kinds of inputs, performs its functions in an acceptable manner, is sufficiently usable, can be installed and used in its intended environments, and achieves the general result its end users require.
- **Debug:** Debugging is the process of identifying and removing errors that prevent correct operation of computer software or a system.
- **Deployment:** This stage consists of the installation of PNCN

files to a central server and making available the client app through different mobile platforms.

- **Evaluate and Maintain:** This phase involves review, evaluation and modification in a component after deployment to correct faults, add features, improve the performance or other attributes.

Technology and Tools

During design and development of PNCN, free software will be we preferred whenever possible.

We will use Visual Studio Community 2015 Edition which is a free and rich integrated development environment for creating desktop, web and mobile applications and cloud services. It contains workspace and an extensible plug-in system for customizing the environment. Visual Studio Community 2015 Edition comes with Xamarin, which is a tool used to write native Android, iOS, and Windows apps with native user interfaces and share code across multiple platforms. For the development of client app, we used Visual Studio together with C# programming language and Xamarin. C# is a general-purpose programming language used for building desktop, web and mobile applications.

For server side app and web user interface, we will use ASP.net and C# programming language. SQL Server database will be used for storing and managing demographic and health records of expectant mothers. For the production of two-dimensional graphics and manipulating and retouching photos we will MS Paint and Adobe PhotoShop CS6. For animation Adobe Flash CS6 (vector graphics program used to create interactive animations) will be used. in addition, tools like JavaScript, XML, AJAX, Web 2.0, Web-services and JSON will also be incorporated during the development of PNCN.

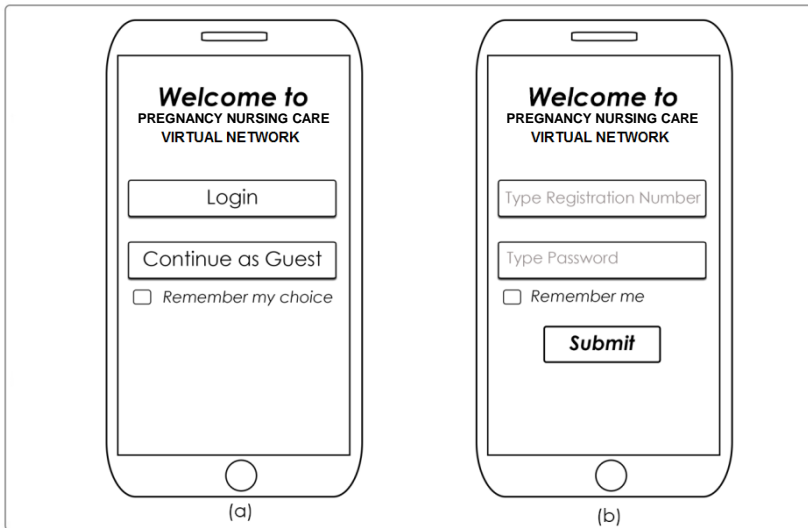
Programming files of PNCN will be installed on a central server and client app will be made available for free download on different mobile platforms (Windows, Android, and iOS), where anyone will be able to download it and use it.

User Interface

The web user interface and client app will be equally used from any computing device (mobile, tablets and desktops) with internet connectivity. The interfaces will be responsive (adjusted automatically according to the device screen size) and will look good on all devices

including small mobile devices, tablets, and desktops. The content will reside remotely on an online server but access will be presented to the user as the resources are located locally in the device. Women clinical data management, information regarding women status, related biosignals can be displayed and managed through the system's interface (web user interface and client app). Pregnancy-related information is stored locally in the client app so that it can be used without any active connection to the Internet. Connectivity to health professionals will require an active Internet connection or a mobile operator connection.

Figure 3 – User interface login.



Note: (a) show welcome screen of the client app. (b) show login screen for registered women.
Source: Made by the author (2016).

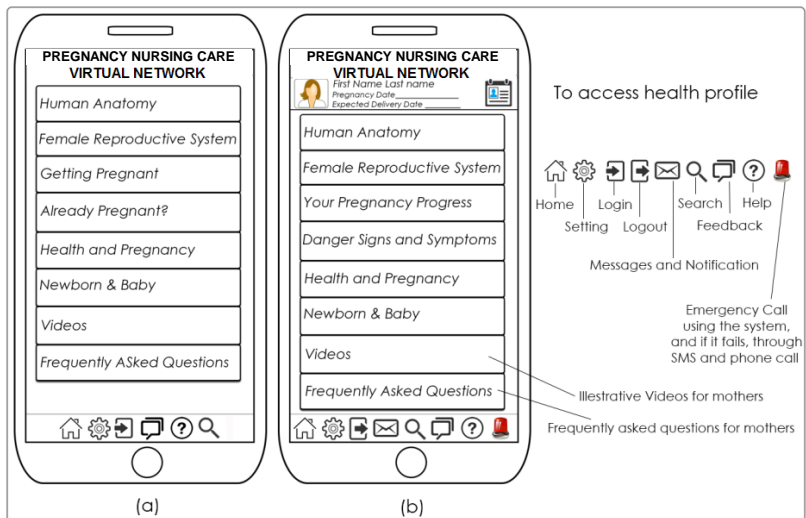
Client App

PNCN will support the ability to input, view, and edit the women history, clinical information, and current symptoms. The app will also allow viewing of past evaluations and prescribed medications. All entries will be logged with timestamps to ensure data consistency. The expected date of delivery is calculated from ultrasound measurements, last menstrual period or fundal height, in order of reliability when available.

The first screen of the client app is shown on Figure 3 (a), where the user has an option to use the app as a guest user or as a registered pregnant woman. As a guest user, only pregnancy related information are available for display. Figure 3 (b) shows the login screen for registered pregnant women. Similarly, Figure 4 (a) shows the front screen for the guest user when they enter the client app and Figure 4 (b) shows the front screen for registered users where pregnancy-related information, as well as clinical data, are available.

The app will display pregnancy related information divided into different sections. The app will educate women about female anatomy and pregnancy-related diseases and provide help and guidance regarding prevention, control, signs and symptoms of each stage and complication of pregnancy and delivery. It will provide interactive information based on text, images, videos and internet links and will keep women informed and connected anytime, anywhere.

Figure 4 – User interface start screen.



Note: (a) Main screen for guest users (b) main screen for registered pregnant women with explanation of icon bar.

Source: Made by the author (2016).

In the Figure 5 are self-explanatory and show options for communication with health staff and emergency team. The system will allow a two-way flow of information. A registered health professional

can create and send a customized message to particular women. In the same way, registered women can create and send customized messages to health professionals. Each party will be notified if they receive a message and the sender will be notified when his/her message is read. If a high priority message is not signaled read in a particular amount of time, it is assumed that the receiver is offline and an SMS will be tried to send as an alternative method. For each registered pregnancy, the system will send notification and reminders, one from the health professionals and one from the system itself (it will be automatic, based on the time and characteristics of women). In the case of danger signs (hemorrhage, in labor and at home, and unknown serious condition) during pregnancy the system can be used to send emergency requests to nearest ambulance service manager for immediate intervention. This message will include the danger sign reported, the name, address and contact details of women. A message will be sent back to the women indicating the immediate action to manage the danger sign and prepare pending ambulance arrival.

It must be noted that users can access information in a nonlinear way, without any specific order to navigate the PNCN leaving user free to establish the construction of knowledge.

Figure 5 – User interface main.



Note: (a) Main screen for triggering Pregnancy Emergency Response System. (b) Main screen for communication with health staff.

Source: Made by the author (2016).

Web User Interface

A password-protected Web user interface will be developed for use by nurses and other health professionals. Web user interface will give access to women demographic and clinical data and enables tracking history of individual woman as well as the output of reports. The password protected web user interface presents an overview of the system's outputs including individual and aggregated reports, statistics, and system administration, a log of reminders.

Figure 6 – Proposed Contents for PNCN.

Human Anatomy Skeletal System Muscular System Cardiovascular System Digestive System Endocrine System Nervous System Respiratory System Immune / Lymphatic Systems Urinary System Female Reproductive System Male Reproductive System Integumentary System Female Reproductive System Female Anatomy The Reproductive Cycle Female Breasts Lower Torso Fertilization and Pregnancy Birth and Infancy Getting Pregnant Preparing for Pregnancy Important Prenatal Vitamins Pre-pregnancy To-Do List Pregnancy After 35 Teen Pregnancy Miscarriage Fertility Improvement Understanding Conception Ways to Boost Your Fertility	Already Pregnant? Early Pregnancy Symptoms False Pregnancy Home Pregnancy Tests Due Date Calculator Ovulation Calendar Pregnancy Calculator Medication in Pregnancy Pregnancy Myths Pregnancy Discomforts Fetal Development Progress Pregnancy by Trimester Pregnancy Week by Week Pregnancy Complications Danger Signs Diet in Pregnancy Illness in Pregnancy Countdown to Baby Health and Pregnancy Healthy Pregnancy Diet What Not to Eat in pregnancy Pregnancy and Exercise Pregnancy and Fitness Weight Gain Pregnancy Week by Week Week 1 > Baby > Mom > Tip of the Week Week 2	Countdown to Baby Preparing for Baby Childbirth Options Labor and Delivery Am I in Labor? Vaginal Delivery Prolonged Labor Normal Labor Cesarean Section Pain Relief Options Inducing Labor Stages of Labor Delivery of Premature Infant Water Birth Midwives and Home Birth Newborn and Baby Baby Nutrition & Breastfeeding Vaccinations Teething Diapering Sleeping and Napping Your Baby's Skin Parenting: 3- to 6-Month Olds Parenting: 6- to 9-Month Olds Parenting: 9- to 12-Month Olds Baby's Development Tips to Lose the Baby Weight Common Symptoms in Babies Which Medicines Are Safe? How to Soothe a Crying Baby Baby Emergency?	Pregnancy by Trimester First Trimester > What to Expect > Do's and don'ts > Prenatal Tests > Health concerns Second Trimester Third Trimester Danger Signs and Symptom High Blood Pressure Swelling of feet, face, or hands Sudden weight gain Blurred vision Severe headaches convulsions/fits/ Seizures Little of no fetal movement Sudden release of water from the vagina Persistent lower back pain fever and weakness severe abdominal pain fast or difficult breathing. Pregnancy Complications Pregnancy Pains Blood Clots During Pregnancy Flu During Pregnancy High Blood Pressure Abdominal Pain Diabetes
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Source: Made by the author (2016).

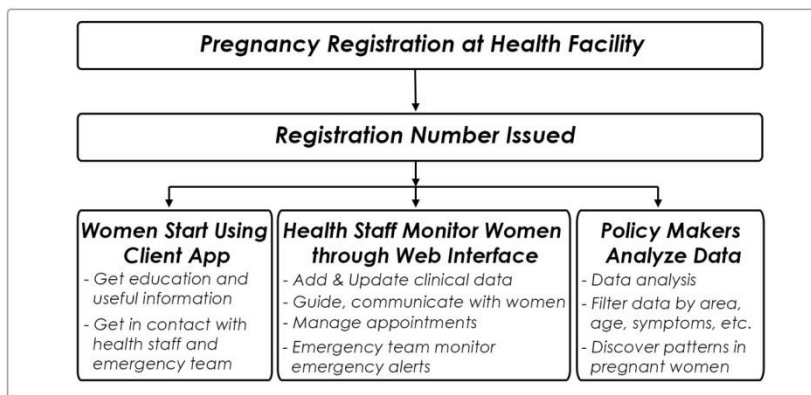
Data can be filtered by the community, age, complication and other characteristics. A user working in a health facility at the district level will be assigned an account, granting him/her permission to view and possibly modify data only from his health facility's catchment area. The web user interface will also enable dynamic data collection and sharing regarding pregnant women and maternity care centers.

Functionalities

Women will be registered in the system at her first pregnancy. Primary health care centers, maternity homes, and hospitals, which have

administrative access to the system can register pregnancy of women when it is confirmed. All details of women are inserted into the system including, name, date of birth, contact details, any medical conditions etc. Each time a woman gets pregnant, her pregnancy has to be registered into the MNCN system. If a woman is already in the system and this is the second or third time she becomes pregnant then only her pregnancy is registered and other registration details are updated (if required). At first registration, each woman will be allocated a unique username (or registration number) and a temporary password which she can change later. Figure 7 presents the system's workflow in the MNCN system.

Figure 7 – Information Flow in Pregnancy Nursing Care Virtual Network.



Source: Made by the author (2016).

Each time pregnant women have some complication and visit maternity home, her profile will be updated with the latest medical tests and treatment. After registration, women will start using the client app (using smartphone, tablet or PC). At each stage of pregnancy, women will get useful information and guidance about respective complications in pregnancy. Pregnant women and Nurses can use PNCN to communicate with each other. Real-time communication can be done in case if both parties are online at the same time, otherwise, a message will be left which can be accessed when the user become online. Details functions of the system are presented in Fig. 8.

Primary health care centers and health authorities can get statistics of pregnant women in a certain region or area which will help them in important decisions regarding women health and maternal

mortality. PNCN will automatically remind pregnant woman about each visit, follow-up visit, expected and delivery date, possible complication, nearest emergency and referral centers.

A feedback option is available for possible suggestion, improvement, and complaints about the system from potential users. MNCN will support the following task through its client app and web interface.

Figure 8 - System Features of Pregnancy Nursing Care Virtual Network.

Level of Operation	Function	Details	Responsible
Community Level	Registration	<ul style="list-style-type: none"> • Pregnancy • Birth • Death • Appointments 	CBA / CHW
	Reminders	<ul style="list-style-type: none"> • Follow-up Visits • Non-emergent Referrals • Expected Delivery date 	CBA / CHW
	Guidance	<ul style="list-style-type: none"> • Symptoms • Customized Information 	CBA / CHW
Hospital / Facility Level	Registration	<ul style="list-style-type: none"> • Pregnancy • Birth • Death 	Nurse / Health Professional
	Referral	<ul style="list-style-type: none"> • Emergent and Non-Emergent Referrals • Notification of referral center 	Data Clerk
	Guidance	<ul style="list-style-type: none"> • Symptoms • Customized Information 	Nurse / Health Professional
	Emergency Response	<ul style="list-style-type: none"> • Monitor Emergency Messages through system & SMS 	Emergency Team
District level	Monitoring, Data Analysis and Support	<ul style="list-style-type: none"> • Weekly and Monthly Reports 	Health Supervisor / Manager

Source: Made by the author (2016).

Using Client App

- Educate women;
- Immediate access to women data (only available to registered user);
- Longitudinal collection of health information of women (only available to registered user);
- Connect with Health staff and emergency service (only available to registered user);
- Feedback to the system.

Using Web User Interface (Authorized Users)

- Register pregnancies;
- Add and update clinical data;
- Provide guidance, make appointments and referrals;

- Set reminders;
- Analyze data and monitor pregnancies;
- Feedback to the system.

Security, Privacy, and Confidentiality of Women Information

In the client app, the privacy of each registered pregnant women will be taken into account by using passwords for login. Access to an online database and clinical data is granted only to authorized users to protect and maintain women's health information. On the web user, interface access can be granted by policies and job titles. Different policies can be generated for a different type of staffs according to their role in the health system. Each policy will define who can access and what type of activities are permitted. For instance, health staff is granted complete access in order to perform their care provision role. Similarly, the emergency team has no access to clinical data, they can only communicate and respond to emergency calls from authorized pregnant women. Despite particular access level, it is the health care professional's responsibility to protect and maintain the privacy of women's information and clinical data. Moreover, the online server will be configured to back up necessary data daily or weekly.

Ethical Considerations

This study was developed in the context of project TO 13075/2012 - FAPESC, Opinion No. 120.343 and No. 169.110 of the year 2012 (Annexes A and B) and for that reason, it respects what is set out the resolution no. 466/2012, of the Ministry of Health Brazil (BRASIL, 2013). However, the completion of this research work did not involve any human subjects.

EXPECTED RESULT

The PNCN system will enhance the quality, safety, and efficiency of pregnancy care during pregnancy and childbirth. It will enable effective and real-time two-way communication between pregnant women and CHW / nurses at the community level, and the rest of the health system (ambulance, health facility staff, District Hospital, and Central level) through smartphones. The primary expected result of the system is an improved access to antenatal, postnatal care, institutional delivery, and emergency obstetric care. In addition, PNCN will provide

a database for keeping clinical records of pregnant women and maternal care delivery.

PNCN will make possible, easy and useful communication between pregnant women and health care providers and will improve women knowledge and awareness regarding pre-eclampsia and eclampsia and other pregnancy-related complications and maternal health. It will reduce the different type of delays associated with pregnancy care such as in-home (due to lack of information and awareness).

It will improve antenatal, postnatal care and record keeping and maternal health indicators for policy makers. This network will enable monitoring, follow-up, referrals and interactive information for pregnant women along with continuity of care from the start of the pregnancy all the way through her post-partum period.

PNCN will replace paper-based medical records which can be incomplete, fragmented, hard to read and sometimes hard to find. It will provide a single, shareable, up to date, accurate, the rapidly retrievable source of information, potentially available anywhere and anytime. PNCN will require less space and administrative resources and has the potential for automating, structuring and streamlining clinical workflow. It will provide integrated support for a wide range of discrete care activities including, monitoring, electronic appointments and reminders, electronic referrals, real-time communications and health profile display and continuing pregnancy education and awareness. It will increase antenatal care visits through application reminders and enable access / call to emergency obstetric care when complications arise and will improve referral communication and will increase access to quality care. It will provide easy access to women clinical data and reduce medical errors.

LIMITATIONS

It must be noted that different mobile network operators and internet access are available in many parts of the world and its availability is increasing day by day. The proposed technology of PNCN and its prominent functions can be equally used in those areas where either a mobile network operator or internet access is available. However, there might be some parts of the globe where neither a mobile network operator nor internet access is available. In that case, only half

of the functionality of PNCN can be used. It's locally stored pregnancy related information can be used by pregnant women but the main feature and innovation of MNCN which is its ability to communicate remotely with nurses and health professionals, will not be available.

Similarly, in the initial phase, PNCN will be implemented in English language only and in the future it will be gradually realized in other major languages as well. Moreover, during the development and implementations phase of PNCN, some of the features and components can be modified or new ones may be added to our current design proposal. The big advantage is that women will have free access which, of course, will also encourage authors to perform adjustments to the proposed design to meet new demands.

CONCLUSION

All pregnant women need timely access to high-quality health care services. Moreover, pregnant women need customized information and education according to their demands, needs and respective situation. Information and communication technologies can play an important role in automating and facilitating these services to pregnant women in a fast and efficient way and can thus prevent pre-eclampsia and eclampsia and other pregnancy-related complications to reduce maternal mortality. In this research we have proposed a design of a PNCN, a network model which can be used to educate mothers, monitor pregnancy and improve maternal health. The network model is designed to strengthen communication links between health care providers and pregnant women and to increase education, awareness, and quality of nursing care during pregnancy, childbirth till the period of post-partum.

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5 FINAL CONSIDERATION

Maternal mortality indicates the quality of women's health and the life quality of a population providing a measure of human and social development. Information on maternal mortality is essential for setting priorities for policy making and research strategies.

Every day women die due to pregnancy and childbirth complications. The risk of a woman in a developing country dying from a maternal-related cause during her lifetime is higher when compared to a woman living in a developed country.

Pregnant women die as a result of complications which either develop during pregnancy or may exist previously but are aggravated during pregnancy. The primary causes of death are hemorrhage, hypertension, and infections.

Pre-natal nursing care support is very important for the prevention of pre-eclampsia, eclampsia and other causes of the maternal mortality. Therefore, due to the rapid improvement in information and communication technologies and the growing acceptability of mobile devices, we proposed a study theme that meets both the demands of nursing care and women health, opting to develop a Pregnancy Nursing Care Virtual Network in order to strengthen links between nurses and pregnant women and prevent pre-eclampsia and eclampsia.

A process was involved in the development of Pregnancy Nursing Care Virtual Network, but in this thesis, only two steps were applied: requirements and design. The first consists of gathering information about the target population, determining the needs or conditions to meet, deciding the contents and knowledge to be delivered, the tasks and function to be completed, and analysis of available technologies feasible for development and implementation. In the second was planning, creating specifications, conceptualizing and framing material and production of content, preparing the storyboard, layout design and user interface (color, fonts, images and buttons). For that reason we conducted a review to analyze and evaluate the available technologies, techniques and the nursing care practices used for the prevention and control of pre-eclampsia and eclampsia. When this information was acquired we defined the design of the network.

Why Nursing Care Virtual Network?

Nurses provide health care and are the frontline health care providers. So they are expected to offer skilled and effective nursing care to the pregnant women. They should have the ability to detect any pregnancy complications and conduct initial management and referral of maternal and newborn complications to higher health facilities. The nurse can promote communication between health care providers and pregnant women, increase education and quality of nursing care during pregnancy.

The most important contacts in health care will always be the face-to-face meetings. However, with the help of interactive tools on the Internet, patients can strengthen their influence on health care by getting both general and specific information. Health care accessibility increases when patients can contact health care professionals at any hour or are able to retrieve information and leave messages by the same media. This interactivity and connectivity are greatly improving health care accessibility by increasing contacts of patients with nursing professionals at any time anywhere and can retrieve specific information in less time.

The PNCN full system consist of a client app running on the user's smartphone or PC, a central database containing all demographic and clinical data of women on an online server, and a web-interface that allows health professionals and supervisors to enter, retrieve and analyze health data of expectant mothers. Client app will provide pregnant women, customized information and education according to their demands, needs and respective situation.

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ANNEXES

Annexe A – Ethical Opinion No. 120.343 of the year 2012.

UNIVERSIDADE FEDERAL DE
SANTA CATARINA - UFSC



PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: GESTÃO EM REDE: PREVENÇÃO DA MORTALIDADE MATERNA E NEONATAL

Pesquisador: MARIA DE LOURDES DE SOUZA

Área Temática: Área 4. Equipamentos, insumos e dispositivos para saúde novos, ou não registrados no país.

Versão: 1

CAAE: 03586312.0.0000.0121

Instituição Proponente: Universidade Federal de Santa Catarina

DADOS DO PARECER

Número do Parecer: 120.343

Data da Relatoria: 08/10/2012

Apresentação do Projeto:

Abrange a exploração sobre a disponibilidade dos recursos para assistência materna neonatal sob a lógica de rede. A exploração bibliográfica sobre as evidências clínicas epidemiológicas e de disponibilidade tecnológica. Esta será seguida de estudo de caso controle para a predição do Risco de Morte Materno neonatal em Santa Catarina para o período de primeiro de janeiro de 2006 e 31 de dezembro de 2010. PRODUÇÃO TECNOLÓGICA. SISTEMA DE ALERTA conforme classificação de risco materno e neonatal e medidas para evitabilidade do óbito, Modelagem do Banco de Dados e do Sistema de informação e monitoramento, Monitoramento do Nível do Risco, Causa mais prevalente, Classificação da evitabilidade, Medidas para evitabilidade na rede básica e na rede hospitalar. Impacto sobre o desfecho O desenvolvimento do sistema, em linhas gerais, observará a metodologia de desenvolvimento do ambiente computacional.

Objetivo da Pesquisa:

Objetivo Primário: Desenvolver tecnologia de gestão em rede para prevenção da mortalidade materno-neonatal. **Objetivo Secundário:** √ Realizar o diagnóstico situacional do Estado de Santa Catarina para atendimento materno e neonatal; √ Identificar os componentes clínicos, epidemiológicos e de gestão dos serviços de saúde desencadeadores do risco de insucesso da assistência materno neonatal; √ Produzir fatores de correção da informação e alertas eletrônicos para prevenção da mortalidade materno-neonatal √ Capacitar lideranças para a inovação, aplicação prática da tecnologia produzida.

Endereço: Campus Universitário Reitor João David Ferreira Lima

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UNIVERSIDADE FEDERAL DE
SANTA CATARINA - UFSC



Avaliação dos Riscos e Benefícios:

A pesquisa não traz riscos aos sujeitos, uma vez que lida com dados de pessoas já falecidas.

Comentários e Considerações sobre a Pesquisa:

Sem considerações adicionais.

Considerações sobre os Termos de apresentação obrigatória:

A folha de rosto vem assinada pela pesquisadora responsável e pela coordenadora do programa de pós-graduação em enfermagem. Foi solicitada a dispensa de TCLE devido à pesquisa ser realizada em banco de dados secundários de acesso público (SIM/SINASC/DATASUS), com consulta de informações sobre mortalidade materna e neonatal.

Recomendações:

Sem recomendações adicionais.

Conclusões ou Pendências e Lista de Inadequações:

Sem pendências.

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Sim

Considerações Finais a critério do CEP:

O presente projeto, seguiu nesta data para análise da CONEP e só tem o seu início autorizado após a aprovação pela mesma.

FLORIANOPOLIS, 11 de Outubro de 2012

Assinador por:
Washington Portela de Souza
(Coordenador)

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Bairro: Trindade CEP: 88.040-900
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Annexe B – Ethical Opinion No. 169.110 of the year 2012.

COMISSÃO NACIONAL DE
ÉTICA EM PESQUISA



PARECER CONSUBSTANCIADO DA CONEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: GESTÃO EM REDE: PREVENÇÃO DA MORTALIDADE MATERNA E NEONATAL

Pesquisador: MARIA DE LOURDES DE SOUZA

Área Temática: Área 4. Equipamentos, insumos e dispositivos para saúde novos, ou não registrados no país.

Versão: 2

CAAE: 03586312.0.0000.0121

Instituição Proponente: Universidade Federal de Santa Catarina

DADOS DO PARECER

Número do Parecer: 169.110

Data da Relatoria: 10/12/2012

Apresentação do Projeto:

Conteúdo não analisado pela CONEP.

Objetivo da Pesquisa:

Conteúdo não analisado pela CONEP.

Avaliação dos Riscos e Benefícios:

Conteúdo não analisado pela CONEP.

Comentários e Considerações sobre a Pesquisa:

Não se aplica.

Considerações sobre os Termos de apresentação obrigatória:

Não se aplica.

Recomendações:

Não se aplica.

Conclusões ou Pendências e Lista de Inadequações:

Não se aplica.

Situação do Parecer:

Devolvido

Considerações Finais a critério da CONEP:

Após análise da documentação encaminhada, a CONEP esclarece que essa pesquisa não se

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E-mail: conep@saude.gov.br

**COMISSÃO NACIONAL DE
ÉTICA EM PESQUISA**

enquadra em nenhuma Área Temática Especial do Grupo I.

Nesse caso, a aprovação ética é delegada ao Comitê de Ética em Pesquisa da instituição, devendo ser seguido o procedimento para projetos que não são do Grupo I, conforme o fluxograma disponível no site: <http://conselho.saude.gov.br> e no Manual Operacional para CEP.

Diante do exposto, esta comissão delibera por devolver o protocolo em questão.

BRASILIA, 11 de Dezembro de 2012

Assinador por:
Anibal Gil Lopes
(Coordenador)

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