HULA: HABITUAL URINALYSIS IS A LABORIOUS ACTIVITY

Noreen MURRAY

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CERTIFICATE OF AUTHORSHIP / ORIGINALITY

I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of the requirements except as fully acknowledged within the text.

I also certify that the thesis is written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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DEDICATION

I wish to dedicate this thesis to my mother who died on 28th Jan 1997. Mum, your unconditional love, encouragement, and constant support of all of my endeavours and those of my brothers and sister, still fills me with inspiration and confidence to always embrace a challenge. I thank you.

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ABBREVIATIONS

ADIPS	Australasian Diabetes in Pregnancy Society
ANC	Antenatal Clinic
ASSHP	Australasian Society into the Study of Hypertension in Pregnancy
BC	Birth Centre
BP	Blood Pressure
DAU	Day Assessment Unit
GDM	Gestational Diabetes Mellitus
GH	Gestational Hypertension
GP	General Practitioner
GTT	Glucose Tolerance Test
IUGR	Intrauterine Growth Restriction
ISSHP	International Society into the Study of Hypertension in Pregnancy
MSU	Mid Stream Urine
NHMRC	National Health and Medical Research Council
PC	Protein/Creatinine ratio
RCT	Randomised Controlled Trial
PE	Pre-eclampsia
SGA	Small for Gestational Age
SLE	Systemic Lupus Erythematous
STOMP	St. George Outreach Maternity Program
UTI	Urinary Tract Infection
WHO	World Health Organization

ABSTRACT

Objectives: The objective was to determine whether routine urinalysis in the antenatal period facilitates diagnosis of pre-eclampsia. The research question was: can routine urinalysis during pregnancy be discontinued in women with normal results of dipstick urinalysis and microscopy at the first antenatal visit?

Design: A prospective observational study was undertaken.

Setting: A metropolitan public hospital and a private hospital in Sydney (NSW).

Participants: One thousand women were enrolled at their first antenatal visit (March to November 1999), and 913 completed the study.

Research Variables: The primary outcome was a diagnosis of hypertension (gestational hypertension, pre-eclampsia, or pre-eclampsia superimposed on chronic hypertension). Other variables were proteinuria, haematuria, parity, past history of pre-eclampsia, renal disease, diabetes mellitus and multiple pregnancy.

Results: Thirty-five women had dipstick proteinuria at their first antenatal visit. In 25 (25/35) of these women, further dipstick proteinuria was detected during pregnancy, and two (2/35) were diagnosed with pre-eclampsia. Of the 867 without dipstick proteinuria at the first visit, 338 (39%) had dipstick proteinuria ($\geq$1+) at some time during pregnancy. Only six women developed proteinuria before the onset of hypertension. Women who had an abnormal result of a midstream urine test at their first visit, were more likely to have a urinary tract infection diagnosed during pregnancy than women with a normal result, however, the numbers were small.

Conclusion: This study suggests that urinalysis can be omitted from the routine antenatal care of 'low risk' women, provided that urinalysis and microscopy is conducted on a carefully collected mid stream specimen of urine at the booking visit.

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CHAPTER ONE: INTRODUCTION

Routine urinalysis is common practice in many antenatal clinic settings in the developed world. Collecting urine for analysis is awkward for women, especially as pregnancy advances, expensive for the organisation in terms of the time it takes to perform the test by clinicians, the equipment required and there is no evidence to support it as a best standard practice. The commitment to ensure practice was evidence-based and cost effective was the impetus for the HULA Study (Habitual Urinalysis is a Laborious Activity).

Practice within the St. George Hospital Maternity Unit, a public hospital in Sydney, New South Wales (NSW), was inconsistent on the issue of urinalysis in pregnancy. Automated testing was used on the antenatal ward but not in the main antenatal clinic, the outreach clinics or the Birth Centre. The specimen jars used by the women were sometimes jars brought from home, which were highly likely to be unsterile before the urine sample was collected, leading to a possibility of contamination. On some occasions, the women themselves interpreted the dipstick reading and documented it on the antenatal health card. Reading the dipstick should take place 60 seconds, after it was immersed into the urine (Bayer, Victoria, Australia). The colours on the dipstick are altered if the result is read outside the 60 second timeframe, which sometimes occurred in clinical practice. Clearly, work needed to be done to standardise urinalysis in pregnancy and ensure midwives and doctors who provide antenatal care use an evidence-based approach. This research aimed to standardise the practice of urine collection and method of testing but more importantly to standardise the actions made by clinicians when faced with abnormal results. The management of abnormal urinalysis will be described later in Chapter 3.

In early 1998, a group of interested clinicians and researchers gathered to discuss possibilities for research on issues pertaining to midwifery and obstetric practice within the St George Hospital. The issue of routine antenatal urinalysis had been a contentious issue among the midwives in the unit for some time and was raised at this meeting. A literature search, to ascertain the current research findings on urinalysis in pregnancy was proposed. This revealed evidence on 'how to test' (Bachman, Heise, Naessens &

Timmerman, 1993; Saudan, Brown, Farrell, & Shaw, 1997; Tincello & Richmond, 1998; Young, Buchanan & Kinch, 1996), and 'what to test for' (Abyad, 1991; Hagay et al., 1996; Meyer, Mercer, Friedman & Sibai, 1994; Rouse, Andrews, Goldberg & Owen, 1995) but there was little evidence relating to which women would benefit from routine urinalysis in pregnancy. From this initial issue, the HULA study was conceived.

Many meetings followed these initial discussions as the HULA study was designed. There was agreement that a randomised controlled trial was not appropriate at this stage, as the outcomes for some women may have been jeopardised if routine urinalysis was omitted from their antenatal care without supportive evidence. It was felt that enough uncertainty existed as to the safety of removing routine urinalysis that a randomised controlled trial would have been unethical. Eventually, a prospective descriptive study was chosen as the design for the HULA study. The methodology is outlined in more depth in Chapter 3 of this thesis.

The main aim of the HULA study was to determine whether routine urinalysis testing in the antenatal period has benefits for pregnant women. If routine urinalysis in pregnancy for all women could not be demonstrated as necessary, then antenatal care could be revolutionised with cost saving implications for organisations providing antenatal care. The time currently spent conducting urinalysis, could be spent more judiciously on other aspects of antenatal care, for example, talking to women about health promotion issues such as, nutrition, relationship changes in pregnancy or cessation of smoking, where relevant.

This thesis will describe the research that sought to address the need for routine urine testing in pregnancy.

The primary questions were:

1. What is the prevalence of proteinuria on urinalysis using the Clinitek 50 Ames machine at the antenatal booking visit?

2. What is the prevalence of microscopic haematuria throughout pregnancy and is it a persistent phenomenon postpartum?

3. Does proteinuria, detected through routine antenatal urinalysis, predict which women will develop pre-eclampsia?

4. What is the prevalence of a subsequent abnormal urinalysis (proteinuria and /or haematuria) in women who have a normal urinalysis at their booking visit?

The secondary questions were:

1. What proportion of women, develop proteinuria prior to a significant blood pressure (BP) rise?

2. What is the timeframe between the development of proteinuria and the significant rise in BP?

3. Can routine urinalysis be safely abandoned in the antenatal clinic?

This thesis will describe the background to the study by discussing the known and unknown aspects of urine testing in contemporary antenatal care. The considerations that led to the development of the HULA study and the method in which the study was conducted will also be described. Finally, the results and recommendations will be reported. The HULA Study results will provide evidence upon which to base clinical practice. Incorporating research results into clinical practice is not without challenge and the final chapter of this thesis describes the importance and significance of pursuing evidence based practice. This study has already been published in the *Medical Journal of Australia* (Murray et al., 2002) and a copy of this paper is found at the end of this thesis (see page 88).

Organisation of this thesis

Chapter 1 sets the scene for how the HULA Study came about and its context in antenatal care. In this chapter, the main questions are described. Chapter 2 presents the literature around urinalysis in pregnancy. The research was conducted in 1998 – 1999. Other research findings have been published since that first literature review and have been included in the literature review and in the discussion chapter (Chapter 5). Two

ancillary studies were conducted prior to, and in support of, the principal research and they are also described in the second chapter. The ancillary studies were a national telephone survey and a local pilot study. Chapter 3 outlines the methodology used in the HULA Study. The results are reported in Chapter 4. In Chapter 5, the research questions are answered and then discussion of the results culminates with recommendations made for antenatal care. Chapter 6 describes evidence-based practice in relation to maternity care making specific reference to issues around antenatal urinalysis. Finally, the author presents a reflective piece on her journey of learning through undertaking the HULA study.

Summary

The impetus for the HULA Study was to standardise clinical practice around routine urinalysis in pregnancy based on available evidence and to test its value in the antenatal care of low risk women. The literature was reviewed on two separate occasions, once before the study commenced in 1998 and subsequently after the data entry was complete at the end of 2000. The next chapter presents the literature available pertinent to urinalysis in pregnancy.

CHAPTER TWO: BACKGROUND: THE LITERATURE

Introduction

Many aspects of urinalysis are controversial and inconsistent in midwifery practice. These include the method of urine collection, the method of analysis and the method of quantifying protein to assist in the diagnosis of pre-eclampsia. The literature addresses several topics pertaining to urinalysis in pregnancy, for example, the management of asymptomatic bacteruria (Abyed, 1991; Bachman et al., 1993; Hagay et al., 1996; Rouse et al., 1995; Smaill, 1997); the assessment of proteinuria in the normal and hypertensive pregnancy (Brown & Buddle, 1996; Kou, Koumantakis & Gallery, 1992; Ramos, 1999; Saudan et al., 1997; Young et al., 1996), and the inadequacy of dipstick proteinuria in hypertensive pregnancy, (Brown & Buddle, 1995; Halligan, Bell & Taylor, 1999; Meyer et al., 1994). The fundamental question of whom should be tested and when should testing occur is unclear. This chapter presents the known evidence relating to these areas.

Why test urine in pregnancy?

In many maternity units around Australia, a urine sample is obtained from every woman at each antenatal visit. Routine urinalysis in pregnancy has become an established component of antenatal screening. Urinalysis is usually conducted at each antenatal visit to detect: (i) proteinuria; which may indicate pre-eclampsia or urinary tract infection (UTI) (Brown & Buddle, 1995; Brown, Hague & Higgins, 2000); (ii) haematuria; which is a symptom of UTI or renal disease, for example, pyelonephritis or glomerulonephritis (Brown et al., 2005; Rouse et al., 1995); (iii) nitrites and leucocytes, again symptomatic of UTI (Bachman et al., 1993); and, (iv) glucose which is suggestive of pre existing or gestational diabetes mellitus (GDM) (Hoffman, Nolan, Wilson, Oats & Simmons; 1998). The most significant disorders diagnosed by these pathologies are pre-eclampsia, urinary tract infection and pyelonephritis. Each of these disorders will be discussed in the next section.

Hypertension in pregnancy

Hypertension in pregnancy is diagnosed, when the systolic blood pressure is $\geq$ 140 mmHg and /or the diastolic blood pressure, using Korotkoff V sound, is $\geq$ 90 mm Hg (Brown et al., 2000). Hypertensive disorders are a major cause of maternal and fetal

mortality and morbidity (Brown et al., 2000; Chan, Brown, Simpson & Davis, 2005; Salas, 1999).

The Australasian Society for the Study of Hypertension in Pregnancy (ASSHP) Consensus Statement (Brown et al., 2000) classifies the hypertensive disorders of pregnancy as follows:

- Gestational hypertension (GH);
- Pre-eclampsia (PE);
- Chronic hypertension, (essential (EH) or secondary); and
- Pre-eclampsia superimposed on chronic hypertension (Brown et al., 2000).

Gestational hypertension

Gestational hypertension is defined as hypertension occurring after 20 weeks gestation without other symptoms of multisystem involvement and carries a good prognosis for both mother and baby. It has a reported incidence of 10% in the nulliparous population (Brown et al., 2000).

Pre-eclampsia

Pre-eclampsia is defined as being a multi system disorder including the feto-placental unit, characterised by a significant rise in BP after 20 weeks gestation in association with one or more of the following signs:

- Proteinuria $\geq$ 300mg/24 hrs;
- Renal insufficiency, which is identified by a serum creatinine $\geq$ 0.09mmol/L or oliguria;
- Liver disease diagnosed by severe epigastric or right upper quadrant pain;
- Neurological involvement which may include hyperreflexia with clonus, severe headaches, visual disturbance and convulsions in the case of eclampsia;
- Haematological disturbances such as thrombocytopenia and disseminated intravascular coagulation;
- Intrauterine growth restriction (IUGR) (Brown et al., 2000; Chan et al., 2005).

Pre-eclampsia is the most common hypertensive diagnosis followed by gestational hypertension and essential hypertension (Brown & de Swiet, 1999) and complicates 2 –

10% of pregnancies in the industrialised world (Chan et al., 2005; Duley, 2004; Power, 1997; Rinehardt, Terrone, Larmon, Perry and Martin, 1999).

Positive predictive factors for the development of pre-eclampsia are nulliparity, pre existing hypertension and the diagnosis of pre-eclampsia in a previous pregnancy (Brown et al., 2000; Odegard, Vatten, Nilsen, Salvesen & Austgulen, 2000; Sibai et al., 1998). The ASSHP Consensus statement also alerts clinicians to other 'at risk' features to be aware of when caring for the pregnant population and include, family history of pre-eclampsia; different partner to previous pregnancies; diabetes mellitus; multiple pregnancy; autoimmune disease, particularly Systemic Lupus Erythamatosus (SLE) and the presence of antiphospholipid antibodies (Brown at al., 2000; Duckitt & Harrington, 2005).

In recent times, many studies have contributed to the increased understanding of the pathophysiology of pre-eclampsia but its specific aetiology remains obscure (Salas, 1995; Visser & Wallenburg, 1999). Genetic, immunologic, environmental and vascular-mediated factors are all thought to play an important role in the development of pre-eclampsia (Odegard et al., 2000). Dekker and Sibai (1998) describe shallow endovascular cytotrophoblast invasion in the spiral arteries and generalised maternal endothelial dysfunction as characteristics of pre-eclampsia. Another theory presented is the role of vasospasm in contributing to the rise in blood pressure and the excretion of protein (Meyer et al. 1994).

Chronic hypertension

Chronic hypertension is subdivided into two groups, essential hypertension and secondary hypertension. Almost 2% of Australian women of childbearing age have chronic hypertension, most being classified as essential hypertension (Brown at al., 2000). Essential hypertension is a blood pressure of $\geq$ 140 mmHg systolic and /or $\geq$ 90 mmHg diastolic without any apparent cause in the first trimester of pregnancy or pre conceptually. Secondary hypertension has an underlying cause, for example, renal disease, endocrine disorders or coarctation of the aorta (Brown et al., 2000). The presence of proteinuria before 20 weeks gestation in women with hypertension is consistent with the presence of known or undetected renal disease and is associated with adverse neonatal outcomes (Sibai et al., 1998).

Pre-eclampsia superimposed on chronic hypertension

Pre-eclampsia superimposed on chronic hypertension is confirmed if liver dysfunction, thrombocytopenia or neurological problems become apparent and occurs in 20% of women in this subgroup (Brown et al., 2000).

Monitoring of hypertension

The definition of elevated BP changed during the course of this research. At the outset of the research, the definitions used at St. George Hospital were in compliance, with the 1993 Australasian Society of the Study of Hypertension in Pregnancy (ASSHP) recommendations for the management of hypertension in pregnancy. Hypertension in pregnancy at that time, was diagnosed with a rise in systolic BP of ≥25mmHg and/or a rise in diastolic BP of ≥15mmHg above the pre-conceptual or first trimester booking BP (ASSHP, 1993; Brown & Buddle, 1996). The publication of the ASSHP Consensus statement in 2000 presented a change in the definition of hypertension in pregnancy to a systolic BP ≥140mmHg and /or a diastolic BP ≥90mmHg (Brown et al., 2000). This definition is easier to work with in terms of definitive diagnosis of the hypertensive states of pregnancy.

The change in the definition of hypertension by the ASSHP (2000) did not complicate or impinge on the HULA Study. The recruitment phase began in March 1999 and the last birth of the women enrolled in the study (study endpoint) took place in June 2000. Although data collection was in progress from the first day of the study, the coordinators did not record the classifications of hypertensive states until the clinical notes were being checked and final data collection took place. This occurred after June 2000 and we were aware of the updated consensus statement regarding the new definition of hypertension. Therefore the 2000 Consensus Statement was used to define hypertension in pregnancy.

Proteinuria

Protein excretion is reported to increase at the end of normal pregnancy (Hooper, 1996) with 300mgs/24 hours being considered normal (Brown & Buddle, 1997; Brown et al., 2000; Kuo et al., 1992). The definition of 1+ has been accepted by the clinical profession as reflecting true proteinuria however researchers have reported an over

estimation by up to 50% in hypertensive pregnancy due to oversensitivity of the dipstick test at this level of proteinuria (Brown & Buddle, 1995; Brown & de Swiet, 1999; Kuo et al., 1992).

Proteinuria is a significant symptom of pre-eclampsia. Its connection with hypertension in pregnancy was first reported by Lever in 1843 (Meyer et al., 1994). There is a general view in the literature that the development of proteinuria is a relatively late occurrence in pre-eclampsia and often occurs after the development of hypertension (Hooper, 1996; Kuo et al., 1992). The higher levels of proteinuria are associated with more maternal and fetal complications in the hypertensive woman (Chan et al., 2005; Saudan et al., 1997). Proteinuric hypertension has more unfavourable maternal and fetal outcomes than non-proteinuric hypertensive pregnancies (Chan et al., 2005).

Measuring proteinuria

Surveillance for proteinuria is carried out by performing an automated or an eyeball dipstick urinalysis at each antenatal visit. The result is only specific for the time of the test (Brown & Buddle, 1995). If the dipstick protein level is greater than or equal to 1+, it should be quantified biochemically. Quantitation of protein excretion is an important assessment of kidney function in the diagnosis of pre-eclampsia (Brown et al., 2000; Chan et al., 2005; Ramos, 1999; Saudan et al., 1997). The 24-hour urine collection for total proteinuria is regarded as the gold standard for this assessment (Brown et al., 2000; Kuo et al., 1992; Saudan et al., 1997) and entails the collection of all urine for a 24 hour period. This process is often awkward and cumbersome for pregnant women and there is the potential that it is not a true collection as the woman may inadvertently forget to add every sample to the collection. Having to wait more than 24 hours is also not optimum in terms of diagnosis or management of a potentially dangerous medical presentation (Ramos, 1999). The signs and symptoms of pre-eclampsia can escalate very rapidly, for example, raised BP, headache, and right upper quadrant pain indicating liver involvement. These symptoms may cause the women to become critically ill and adverse outcomes, such as, abruptio placenta or an eclamptic fit will increase the likelihood of maternal or fetal morbidity or mortality (Brown & Buddle, 1996). A prompt diagnosis can facilitate the most appropriate care of mother and baby (Chan et al., 2005).

Asymptomatic bacteruria

Proteinuria in pregnancy may also be indicative of asymptomatic bacteruria and occurs in association with the presence of nitrites, blood and leucocytes (Kumar & Clarke, 2002). Asymptomatic bacteruria is the colonisation of the urinary tract in the absence of specific symptoms and is diagnosed at > 100,000 bacteria /ml on a single, voided midstream urine (Three Centre Consensus, 2001; Tincello & Richmond, 1998). Detection of asymptomatic bacteruria is important at the antenatal booking visit, as 25 - 30% will develop symptomatic UTI later in pregnancy if untreated (Morgan & McKenzie, 1993; Smaill, 1997; Tincello & Richmond, 1998). Bacteruria has a prevalence of 5 – 10% in pregnant women (Rouse et al., 1995). Other research reports a variance of 2.3 -17%, with the higher incidence reported in women from lower socio-economic groups (Bachman et al., 1993; Smaill, 1997).

Early detection of bacteruria and treatment in the first trimester of pregnancy can reduce its sequelae, which includes pyelonephritis, preterm birth and low birth weight babies (Abyad, 1991; Morgan & McKenzie, 1993; Rouse et al., 1995; Schwalb & Stiles, 1984; Smaill, 1997; Tincello & Richmond, 1998). A meta- analysis by Smaill (1997) concluded that routine urine microscopy at booking (that is, the first antenatal visit), would detect this abnormality and appropriate antibiotic therapy would help reduce unfavourable outcomes. There is controversy as to the duration of antibiotic therapy required for the treatment of asymptomatic bacteruria, (Smaill, 1997). Some research supports a single dose of antibiotics and other research supports longer treatment (Villar, Lydon-Rochelle, Gulmezoglu & Roganti, 2000).

Screening for, and treatment of, asymptomatic bacteruria at the initial booking visit is widely supported in the literature (Freeman & Poland, 1992; Gribble, Fee & Berg, 1995; Tincello & Richmond, 1998). It is deemed to be cost effective due to the prevention of pyelonephritis, small for gestational age (SGA) babies and preterm birth (Rouse et al., 1995; Smaill, 1997). Small for gestational age refers to babies whose birthweight falls below the 10^{th} percentile of the birthweight of infants for their gestational age (Scheive, Handler, Hershaw, Persky & Davis, 1994).

Haematuria

Haematuria, detected by a dipstick test, in pregnancy is common but its significance is uncertain (Brown et al., 2005). When it is associated with leucocytes and nitrites, the diagnosis of urinary tract infection is probable and should be treated with antibiotic therapy if urine microscopy shows a positive culture (Smaill, 1997).

In some women, haematuria may persist in the absence of a diagnosis of infection usually implying underlying glomerular disease and this requires investigation. Five per cent of pregnant women are reported to have mild glomerulonephritis, which requires ongoing postpartum surveillance (Brown et al., 2005).

Physiologic and anatomic changes of the urinary tract during pregnancy predispose a woman to the development of a urinary tract infection (Able, 1996; Schwalb & Stiles, 1984). Relaxation of the smooth muscle by progesterone and ureteric compression by the enlarging uterus may be the contributory factors of urinary stasis and hydronephrosis (Smaill, 1997). Leukorrhoea caused by increased secretions in the vagina during pregnancy can harbour gram negative organisms, which may inadvertently be transported from the perianal area to the urethra and lead to urinary tract infection (Schwalb & Stiles, 1984).

The medium or long term impact of haematuria in pregnancy is unknown. Haematuria in pregnancy was not the focus of this thesis but data collected were used in a parallel study, which sought to identify the relevance, if any, of haematuria to pregnancy outcome. The results showed that 20% (n=178) of 902 women had dipstick heamaturia at least on two occasions in pregnancy, mostly occurring before 32 weeks gestation. The development of pre-eclampsia, gestational hypertension or birth of a SGA baby, were similar in women with or without dipstick haematuria. Although common in pregnancy, haematuria rarely signifies a disorder likely to affect pregnancy outcome (Brown et al., 2005). This part of the research was recently published in the American Journal of Kidney Diseases (Brown et al., 2005). A copy of this publication can be found at the end of this thesis

Nitrites and leucocyte esterase

Bacteruria is detected by a positive nitrite and leucocyte esterase test on dipstick urinalysis. Nitrites are produced from the reduction of urinary nitrates by bacteria and leucocyte esterase is an enzyme specific for neutrophils (Kumar & Clark, 2002). A positive reaction of both nitrites and leucocytes has a high predictive value for urinary tract infection. Urine dipstick for nitrites detects bacteruria at relatively low cost but only identifies half of the women with a UTI (Bachman et al., 1993).

Glycosuria

Glycosuria is uncommon in pregnancy and its occurrence may vary from day to day in the same person (Hooper, 1996). The study by Hooper (1996) revealed an incidence of 2.5% in the pregnant population. Although asymptomatic, glycosuria may be indicative of gestational diabetes mellitus (GDM) or pre-existing diabetes mellitus (Hooper, 1996; Martin, 1991). Screening for diabetes by urinalysis is inaccurate and more reliable results are achieved by plasma glucose measurements (US Public Health Service, 1994).

The next section will describe gestational diabetes mellitus, its significance in pregnancy and why serum testing is a more accurate method of screening than urinalysis.

Gestational diabetes mellitus is defined as a carbohydrate intolerance of variable severity, which is first recognised during pregnancy. Longitudinal studies have shown that women who develop GDM are at higher risk (50%), of developing diabetes mellitus later in life (Crowther et al., 2005; Hoffman et al., 1998; Martin, 1991). Gestational diabetes has an incidence of between 2 - 9% in all pregnancies and has implications for both mother and baby (Crowther et al., 2005). Poorly controlled gestational diabetes is associated with maternal and neonatal problems such as shoulder dystocia and nerve palsies during birth due to macrosomia, hydramnios and pre-eclampsia. The baby may also be more susceptible to hyaline membrane disease, neonatal hypoglycaemia and jaundice (Kumar & Clark, 2002; Martin, 1991).

Physiological changes in kidney function during pregnancy need to be taken into consideration when assessing for glycosuria such as, the increase in glomerular

filtration and impaired tubular reabsorption (Hooper, 1996). The diagnosis of glycosuria by urinalysis is also unpredictable because:

- changes in urine glucose lag behind changes in blood glucose;
- the mean renal threshold is approximately 10mmol/L but the range is 7-13 mmol/L. The threshold rises with age;
- urine tests do not correlate with serum glucose below the renal threshold;
- and, renal threshold for glucose falls in pregnancy (Kumar & Clark, 2002).

Dipstick urinalysis has poor sensitivity for glycosuria and its presence only predicts 36% of those who have confirmed GDM, therefore urinalysis is not considered effective as an antenatal screening tool (Hooper, 1996).

Current research recommends universal screening in the light of results of a randomised clinical trial by Crowther et al. (2005). The results of this study demonstrated a reduction in the incidence of perinatal complications when GDM was treated, compared with routine care (1% vs 4%), (Crowther et al., 2005). McIntyre, Cheung, Oats & Simmons, (2005) argue that universal screening should be implemented as:

- " most women with gestational diabetes have no symptoms, and many have none of the classic risk factors associated with gestational diabetes.
- Screening based on risk factors adds an extra complexity to busy routine clinical practice and may lead to some women failing to undergo appropriate testing.
- ACHOIS patients were relatively "low risk", being predominantly of European background, with a mean age of around 30 years, and a mean body mass index of around 26Kg/m^2. Many would not have been tested based on risk factors" (McIntyre, 2005, p 289).

There is no evidence to support the theory that perinatal mortality increases with treated GDM but some studies report perinatal mortality increases in untreated GDM (Crowther et al., 2005; Hoffman et al., 1998).

Screening test protocol for Gestational Diabetes Mellitus

The Australian Society for Diabetes in Pregnancy recommends that a serum screening test be performed at 26–28 weeks gestation (Crowther, 2005; Hoffman, 1998; Martin, 1991, US Public Health Service, 1994). The test involves a non-fasting serum test taken one hour after the ingestion of a 50g glucose drink. A result of ≥ 7.8 mmol/L is predictive of GDM. Alternatively, a 75g glucose drink may also be given and a result of ≥ 8 mmol/L is predictive of GDM. The diagnosis is confirmed by having a 75g fasting glucose tolerance test (GTT) performed.

Routine urinalysis is not used to identify those at risk of GDM. Venous blood glucose measurement has been found to be a more sensitive method of GDM screening (Hooper, 1996) and is consistent with recommendations by the Australian Diabetes in Pregnancy Society consensus statement (Hoffman 1998). It is evident that glycosuria should not be taken as a screening or diagnostic test for gestational diabetes. This was important to consider in the research undertaken in this study.

The next section discusses the evidence in relation to the methods of urinalysis in pregnancy.

Collecting and testing the sample

Mid stream specimen of urine

The collection of a MSU involves thorough perineal cleansing with sterile cotton wool swabs and sterile water and collection of a mid stream urine into a sterile container. Some research supports the hypothesis that a MSU would yield a more accurate result due to less risk of contamination than an ordinary sample (Brown & Buddle, 1995; Brown & de Swiet, 1999). Perineal cleansing, before sampling, results in 20% fewer positive cultures due to reduced levels of contamination (Morgan & McKenzie, 1993). Contamination of a urine specimen may occur due to introital flora in women. Supra pubic aspiration or urethral catheterisation avoids such contamination but these procedures are invasive and impractical in pregnant women (Morgan & McKenzie, 1993). A study by Abel (1996) demonstrated no difference in contamination rates when perineal cleansing was used as part of the method of collecting a MSU. Research by Bachman et al. (1993), on the validity of various tests to detect bacteruria in pregnancy, employed MSU in their methodology. In clinical practice at the St. George Maternity

Unit prior to the study, women were asked to provide a midstream stream urine sample for testing. Perineal cleansing was not part of the protocol. The protocol for the HULA Study employed perineal cleansing, to reduce contamination and ensure a more accurate sample was available for testing.

Automated vs eyeball testing

There are two methods by which dipstick urinalysis is analysed in the clinical setting, the eyeball test and the automated test. Urine is tested in most antenatal settings (antenatal clinics, doctors' rooms, home) using a visual 'dip stick' test as opposed to testing with an automated urinalysis machine.

Visual dipstick test can be inaccurate as it is prone to observer error (Brown & Buddle, 1995; Halligan et al., 1999; Kuo et al., 1992; Saudan et al., 1997). Dipstick urinalysis for proteinuria has been shown to give high false positive and negative results (Brown & Buddle 1995; Meyer et al., 1994; Saudan et al., 1997), questioning its reliability as an accurate test for use in the clinical setting. High frequencies of false positives and false negatives are the main criticism of eyeball dipstick urinalysis (Brown & Buddle, 1995; Kuo et al., 1992). Brown and Buddle (1995) demonstrated a high sensitivity on dipstick urinalysis at 1+ and 2 + proteinuria, which increased the number of false positives. Kuo et al. (1992) compared dipstick diagnosis of proteinuria in 24 hour urine collections with dipstick urinalysis, in a group of hypertensive pregnant women and found poor correlation. In the prospective study by Brown and Buddle (1995), dipstick testing produced a false negative rate of 8 – 18% and a false positive rate of 67% in urine at the 1+ level. These authors reassure clinicians that 3+ or 4+ has a much higher predictive value for true proteinuria and means the test is accurate most of the time at the higher levels of proteinuria.

Poor sensitivity of the dipsticks (55%) reported by Bachman et al. (1993) suggests that 50% of women with asymptomatic bacteruria would be missed using eyeball dipstick testing alone. Dipstick haematuria has a poor sensitivity for true haematuria (Brown et al., 2005). Other researchers have postulated that the dipstick has a high sensitivity for proteinuria 1+, leading to a high frequency of false positives (Brown & Buddle, 1995). Halligan and others (1999) however insists that his study reported a false negative rate of 40-45% which he interpreted as the dipsticks being under-sensitive. In the case of

proteinuria, research conducted by Saudan et al. (1997) demonstrated that an automated urinalysis device improved the detection of true positives from 48% by visual dipstick to 74%. Urine test results are used in clinical decision making, therefore it is imperative that they are accurate and timely. The findings of Saudan et al.'s (1997) research led to the introduction of automated testing in all antenatal areas of St. George Hospital. The automated method of urine testing was therefore used in the HULA study that is reported in this thesis.

Twenty four hour urine collection vs spot urine protein/creatinine ratio

Normal excretion of protein is 300mgs per 24 hours (Brown & Buddle, 1995). This may increase in the hypertensive pregnancy to provide a diagnosis of pre-eclampsia. True proteinuria is considered to be ≥300mg/day. Proteinuria 1+ (0.3g/L) on automated dipstick urinalysis is deemed significant and requires quantitation (Brown & Buddle, 1995). Quantifying the excretion of protein is important to ascertain the severity and progression of pre-eclampsia (Halligan et al., 1999). Proteinuric hypertension has a higher incidence of negative outcomes for mother and baby (Chan et al., 2005).

Twenty four hour urine collection for protein is the gold standard for protein quantitation but there are issues with this method (Brown & Buddle, 1995). Firstly, it is not a timely test, as there is a delay of over 24 hours before obtaining a result. This is often suboptimal in terms of gaining data to make a clinical judgement prior to instigation of treatment. In some cases, pre-eclampsia may have a rapid onset therefore urgent assessment and test results are helpful in its diagnosis and management. There is also the possibility for an omission of a urine sample to the 24 hour collection which would alter the result. A study by Reinhardt et al. (1999) reported a 12 hour urine collection as accurately depicting proteinuria. The process is similar to the 24 hour urine collection and the amount of protein excreted by the kidneys over the 12 hour period is simply doubled to give the result for the 24 hour period. It is not used in clinical practice and has been superceeded by the spot protein/creatinine ratio (Saudan et al., 1997; Young et al., 1996). The spot protein/creatinine (PC) ratio may be performed on a random midstream urine sample and sent for biochemical analysis. The urine protein/creatinine ratio is obtained by dividing the urine protein concentration (mg/L) by the urine creatinine concentration (mmol/L) (Saudan et al., 1997). A ratio of ≥ 30 is considered to be significant (Brown et al., 2000).

The spot protein/creatinine ratio test correlates well with 24 hour urine protein excretion, and has been shown to be both timely and accurate thus enabling timely management of hypertensive pregnant women (Brown et al., 2000; Chan et al., 2005; Meyer et al., 1994; Saudan et al., 1997). The Australasian Society into the Study of Hypertension in Pregnancy (ASSHP) and the International Society into the Study of Hypertension in Pregnancy (ISSHP) have accepted the PC ratio as a reliable method of protein quantitation (Brown et al., 2000; Brown, Lindheimer, de Swiet, Van Assche & Montquin, 2001). The PC ratio is the method of proteinuria quantification used at the St. George Hospital and was therefore used in the HULA study.

Whom to test?

The objective of urinalysis in pregnancy is to detect substances, which may determine who is at risk of certain conditions that may adversely affect the mother or baby. The conditions and their significance have already been presented in this chapter. They are namely the hypertensive disorders of pregnancy, diabetes (gestational or pre existing), asymptomatic bacteruria or renal diseases such as glomerulonephritis and pyelonephritis. Glomerulonephritis occurs as an immunological response and effects both kidneys. Pyelonephritis is the term given to acute bacterial infection of the kidney (Kumar & Clarke, 2002).

A prospective study by Gribble et al. (1995) investigated the practice of routine urinalysis for proteinuria in a low risk group of 3014 pregnant women. This research concluded that routine testing provided no clinically important information and there was no impact on pregnancy outcomes. Women with risk factors for the development of pre-eclampsia were excluded. The study also excluded women with pre existing diabetes mellitus, pre existing renal disease, chronic hypertension, multiple pregnancy or proteinuria $\geq$ 30 mg/dl on the initial urine screen. The development of proteinuria was not predictive of those who went onto develop pre-eclampsia (Gribble et al., 1995).

The literature fails to indicate which women should be tested or if a selective testing regime is appropriate. It is plausible to suggest that once a booking microscopy is conducted, selective urinalysis could be done throughout the remainder of the pregnancy unless clinically indicated. This idea formed the hypothesis of the HULA

study. The need for routine urinalysis in pregnancy may in fact be true but validation was necessary and it was hoped, that the results of this study would add some evidence to this issue.

Summary of the evidence

The following is a summary of the evidence currently available on the aspects of urinalysis in pregnancy:

- Urinalysis and microscopy should be conducted at the antenatal booking visit of all pregnant women and will detect asymptomatic bacteruria or asymptomatic renal disease (Brown et al., 2005, Rouse et al., 1995)
- A positive culture for asymptomatic bacteruria should be treated with an appropriate antibiotic to prevent the development of a urinary tract infection or pyelonephritis during the pregnancy (Rouse et al., 1995; Smaill, 1997; Villar et al., 2000)
- Women with true haematuria may have underlying glomerular disease and require further investigation. Haematuria rarely signifies a disorder likely to impact on pregnancy outcome (Brown et al., 2005).
- A MSU yields a more accurate result due to the reduction in contamination (Abyed, 1991)
- Automated urinalysis is the recommended method of dipstick urinalysis as it reduces the observer error of eye ball testing by reporting less false positives and less false negatives (Saudan et al., 1997).
- Spot urine protein/creatinine ratio is now accepted as the recognised method of protein quantification and correlates well with the 24 hour urine collection method which was known as the 'gold standard' (Brown et al., 2000, Chan et al., 2005; Saudan et al., 1997; Young et al., 1996).
- Pre-eclampsia is defined clinically by ASSHP as a systolic BP of $\geq$ 140mmHg and/or a diastolic BP $\geq$ 90mmHg with of without the presence of proteinuria 1+ ($\geq$ 300mgs/day) (Brown et al., 2000; Chan et al., 2005)
- Routine urinalysis for proteinuria on low risk women does not yield any important clinical information in terms of pregnancy outcome (Gribble et al., 1995)

- Glycosuria is a poor predictor of who will develop GDM or who has underlying diabetes mellitus (Crowther et al., 2005).
- Serum screening for GDM between 26 – 28 weeks gestation is the recommended method of screening by the ASDIPS (Crowther et al., 2005; Hoffman et al., 1998; Martin, 1991).
- All pregnant women should be screened and those diagnosed with GDM should be treated, to reduce the possibility of unfavourable perinatal outcomes and increase the maternal sense of wellbeing (Crowther et al., 2005).

PRELIMINARY INVESTIGATIONS

During the planning process for the proposed study, it was decided that before the methodology for the HULA Study was decided upon, two small preliminary studies should be conducted. They were:

- a pilot study of high risk women attending the Day Assessment Unit (DAU) at St. George Public Hospital; and,
- a national telephone survey of antenatal services to ascertain clinical practice.

Pilot Study

A retrospective audit of the medical records of all antenatal women attending the DAU for the period of two months, who were diagnosed with hypertension and proteinuria, was undertaken. A sample of forty-one was reached. The DAU is a hospital facility where women with pregnancy related risks are managed on an outpatient basis. The majority of these women are monitored for hypertensive disorders. Hospitalisation only occurs where mother and baby need further intensive surveillance. These women are referred from the antenatal clinics, the Birth Centre and from private obstetricians. Details about parity, first trimester BP, gestation at onset of proteinuria, gestation of onset of significant BP rise, protein/creatinine ratio (if conducted) and significant medical conditions such as diabetes, essential hypertension, and previous pre-eclampsia was collected and analysed.

The following section further describes this pilot study.

Aim of the Pilot Study

The aim of the pilot study was to determine the percentage of women with hypertension in pregnancy attending the DAU who developed proteinuria prior to a significant rise in BP. This information was thought to be useful in determining the most appropriate design and sample size for the HULA study.

Pilot Study Analysis

The data from the pilot study was analysed using frequencies. Two classifications were made of this group, women who developed proteinuria before a significant rise in BP and women who did not develop proteinuria or developed it after the rise in BP.

Results of the Pilot Study

The results of this retrospective study showed that 10% (n=4) of the 41 women developed proteinuria prior to a significant elevation of BP. It was postulated therefore that this figure would be less in the general pregnant population as this sample was from a high-risk population. The HULA study sought to confirm the accuracy of this finding by using a prospective analysis and a larger sample.

Telephone Survey

Clinicians believe that the practice related to urinalysis in pregnancy varies widely. A national telephone survey was conducted in April 2001, to qualify this anecdotal theory of practice inconsistency within the antenatal setting. This is in accordance with the National Health and Medical Research Council guidelines on 'getting research into practice', which recommend that comparison be made between national/international and local situation, at the outset of a project (NHMRC, 1999)

Aim of the telephone survey

The aim of this telephone survey was to ascertain practice standards in different antenatal settings around Australia and to determine if the practice in each centre was based on the current evidence. The research coordinators felt that the information gathered would provide further credence for the need of a research such as the HULA study and would help to standardise clinical practice if inconsistency was revealed.

Method

Thirty maternity units were randomly selected from throughout Australia. Each state and territory was included and hospitals in six of the eight states and territories responded. A tertiary referral hospital in each state capital city, a maternity unit in a major town and a maternity unit in a rural setting were chosen where possible (Table 1). This was to ensure representation of the different areas of Australia. Eight of the main maternity units in Sydney were surveyed as it has the greatest population concentration nationally, as well as a large clinical workforce. The researchers believed that this assessment would yield a good cross representation of clinical practice within this country. It may also reflect the level of dissemination of research results and the integration of such recommendations into practice protocol.

Table 1: Types of hospitals who responded to the National Telephone Survey.

State	Tertiary hospital in capital city	Maternity unit in major town or metropolitan area	Maternity unit in rural setting
WA	1	1	1
NT	1	0	0
QLD	1	1	1
SA	2	1	0
NSW	5	8	4
VIC	1	1	0

The survey was carried out by one of the researchers (Noreen Murray). The antenatal clinic of each unit was contacted by telephone, and the unit manager or a clinical midwife familiar with antenatal practice within that unit was interviewed. The advantage of the telephone survey was that it was a prompt method and reduced the risk of non-compliance, which may have occurred if a written survey was used.

Answers to the following questions were sought:

1. Is a booking urinalysis performed on each pregnant woman?
2. Is the sample tested using a MSU sample?

3. Which method of urinalysis is used at your hospital/clinic - eyeball dipstick or automated dipstick?
4. What action is taken on the diagnosis of proteinuria 1+?
5. How is proteinuria quantified, (i) 24-hour urine collection, (ii) spot urine for protein/creatinine ratio?
6. Are all women tested at each visit or is there a practice of selective testing?

The results were documented on a survey sheet.

Analysis

The data from the telephone survey were analysed by frequencies. The clinical practice issues involved in urinalysis in pregnancy were reported descriptively. These issues included the use of eye-ball or automated dipstick urinalysis in pregnancy and the method of protein quantification; 24 hour urine collection or the spot protein/creatinine ratio.

Results of National Telephone Survey

Inconsistency in regard to urinalysis in pregnancy was revealed in the 29 maternity units that responded to the telephone survey. Evidence already available in the literature was not being used in many centres.

Routine urine microscopy at booking was performed in 12/29 maternity units. The urine sample tested in 6/29 units was a MSU. Eight centres only did a microscopy if the woman was symptomatic of a urinary tract infection, be that at booking or otherwise. One maternity unit reported only doing booking microscopy on teenage pregnancies.

Women in 17/29 centres received a new container for urine collection if urinalysis was required. Ten centres used the same container throughout each woman's pregnancy and women attending three centres were asked to urinate on a dipstick prior to analysis.

Automated urinalysis equipment was available in 4/29 centres surveyed but only two actively used the machines. The reason stated for non-use was the expense of the paper used to print the results.

Proteinuria 1+ was quantified by 24 hour urine collection in 23/29 centres, with 6 units using the spot protein/creatinine ratio. Some centres used a combination of both and this was determined by physician/obstetrician preference or whether the woman was being managed as an inpatient or an outpatient. Women being managed as inpatients were required to give a 24 urine collection for analysis in these instances. One centre reported not quantifying proteinuria as antenatal women who developed risk factors for example hypertension, were transferred to a tertiary referral hospital in the capital city. Some clinicians interviewed were unfamiliar with the spot urine protein/creatinine ratio test.

Twenty units routinely performed dipstick urinalysis on all women at every visit. The remainder selectively tested. The selective method varied in terms of gestation at which the urinalysis was performed and seemed to be at the discretion of the policy makers in each individual unit.

These results reveal considerable inconsistent policy within maternity units, lack of dissemination of research results to the clinical 'coal face' and ultimately women not receiving optimal evidence based health care in pregnancy.

Cost analysis of urinalysis

A hypothetical cost analysis was conducted for a hospital service with an annual birth rate of 2,000 births (Table 2). It was estimated that a urine test took a clinician a minimum of five minutes to perform. This did not include the time spent explaining the collection process, waiting for the woman and discussing the significance of the results. The costing of a midwife (5^{th} year registered nurse level) was chosen. Other costs included the specimen jar, cotton wool balls for cleansing, the Multistix and the paper used for the automated machine. Costs are reported in Australian dollars.

Two thousand women receive care through our antenatal services per annum, with an average of eight visits in pregnancy, equating to 16,000 visits per year. Additional costs include the paper used in the automated urinalysis device (A$47 for 5 rolls). An average of 30 rolls of paper would be necessary for 2,000 women.

Table 2: Cost of routine urine testing per woman per visit

Salaries and consumables	Per visit $A
Midwife (5th yr RN $20 per hour) – 5 mins per test	1.66
Multistix test strips ($15.30 for 100) – 1 per visit	0.15
Urine jars ($8.75 for 100) – 1 per visit	0.08
Cotton wool swabs (55c for bag of 40) – 2 per visit	0.01
Total per woman per visit ($A)	1.92

We calculated that the annual cost of routine urinalysis for 2,000 women is A$30,720. This was based on 2,000 women at an average of eight visits per woman ($1.92 per visit) as described earlier and outlined in Table 2.

Justification for the HULA Study

There is much interest in the significance of routine urinalysis in pregnancy from midwifery, obstetric and renal medicine perspectives. The information provided in answering the key questions will have major implications for clinical practice. This study aims to determine groups of women for whom routine urinalysis is appropriate.

Best clinical practice needs to be research based. To date, a study into the efficacy of routine antenatal urinalysis has not been conducted and the practice needs to be challenged and investigated. It was known that there would be some initial extra costs incurred due to the standardisation of routine urine collection methods. However, if the research can demonstrate that routine urinalysis in pregnancy is an unnecessary practice, there will be long term savings in equipment and time currently spent conducting routine urinalysis. Short-term expenditure in the form of a well-conducted study may lead to long-term cost savings.

Summary

In 1998, when the HULA study was conceived, there was little in the literature to support selective urinalysis during pregnancy. Much of the literature focused on the assessment for and the quantification of, proteinuria in normal and hypertensive pregnancy, management of asymptomatic bacteruria and the inadequacy of dipstick

urinalysis. The question of whom should be tested and when still needed to be answered.

This chapter also described two preliminary studies, which were undertaken to assist in determining the methodology to be used in the HULA study. Paucity of evidence and a need to standardise practice around urinalysis in pregnancy was the impetus for this study.

The next chapter describes the methods used to undertake the HULA study.

CHAPTER THREE: METHODOLOGY

The HULA study aimed to address the practice of routine urinalysis in pregnancy. This chapter describes the approach to the research and the methods used.

Design

The design chosen was a prospective observational study on a sample of antenatal women attending a metropolitan teaching hospital and an adjoining private hospital. Women were enrolled at their first antenatal visit, and observed throughout their pregnancy.

Ethics approval

Ethics approval to undertake the study was granted by the South Eastern Sydney Area Health Service Ethics Committee.

Method

From March 1999 to November 1999, all pregnant women who attended for their first antenatal visit (the booking visit) at the St. George Public Hospital in Sydney were invited to participate in this study. An additional 100 women were recruited from the adjoining private hospital. The study coordinators gave each woman a thorough verbal and written explanation of the study (See Appendix E). Each woman signed two consent forms, one was filed in her medical records and the second was given to the woman to keep. Each woman received a study number to maintain anonymity. The number was written on her data sheets (See Appendices C and D), her antenatal hospital record and her NSW Department of Health Antenatal Card. The data sheets contained such information as the woman's demographic details, medical and obstetric history, booking BP and all urinalysis results. Ten per cent of the women who were approached declined to participate in the study. They stated that they did not care to be part of the research project citing lack of time or interest as the main reasons for non-participation.

Population attending St. George Hospital

St. George Hospital provides care to a large multicultural community, many of whom do not have English as their primary language. The study sample contained women

from many culturally diverse backgrounds, which is representative of the population in this community. Interpreters were used to provide informed consent to these women.

Sample size

The sample number was deducted by means of balancing the logistics of the study process and the number needed to convey a reasonable representation of the clinical manifestations pertinent to the study. A sample size of one thousand women was chosen. Of these, 100 pregnant women were recruited from a private obstetrician at St. George Private Hospital. The remaining 900 women were from the public antenatal clinics and the Birth Centre of St. George Public Hospital. The investigators had a specific timeframe and budget to perform the HULA Study as money had been received from a National Health and Medical Research Council (NHMRC) grant for the purposes of clinical research. The annual birth rate at St. George Maternity Department is approximately 2,500 births. On these grounds it was calculated that the recruitment process would be completed in six months, taking into consideration the fact that some women would decline enrolment but on the other hand, women from the private hospital would be invited to participate.

It was felt by the investigators that 1,000 was an optimum sample size to deduce meaningful results. It was large enough to ensure external validity. It was also considered large enough to ensure accurate reporting of the incidence of the principal medical conditions affecting pregnancy, which are central to this study that is, pre-eclampsia, gestational hypertension and essential hypertension.

Since women who choose to have their babies in the private hospital system are predominantly from the higher socio-economic grouping, it was felt that the sample would be more representative of a proportion of the childbearing population in this area. Recruitment from the private hospital also meant that the target of 1,000 women would be reached sooner.

Recruitment Procedure

Due to cost constraints the information sheet and consent form for the study were not translated into different languages. Interpreters however, for the main language groups, Arabic, Mandarin and Cantonese, were booked on a permanent basis in the antenatal

clinic. This ensured accessibility for interpretation and explanation purposes for those language groups. Interpreters for other different languages were booked when necessary. The interpreters received inservice education on the design of the study, the consent form and the information sheet. They were also taught how to describe the collection of a MSU. The interpreters used were health care interpreters who have specific training and accreditation in medical terminology. The recruiting midwife was always present with the interpreter during these explanations.

Once consent was given, written and oral step-by-step instructions on the collection of a urine sample were given to each woman. The urine collection procedure included perineal cleansing, avoiding skin contact with the collection container, and collecting a mid stream specimen of urine. A copy of these instructions was attached to the inside of each toilet door in the antenatal clinic department. The coordinator asked the women to repeat verbally how they were going to collect the MSU prior to collection to ensure that each woman understood the process. This identified any misunderstandings at the outset and helped ensure standardisation in urine collection. See Appendix B for instruction on how to collect a MSU.

Urinalysis was conducted using a Clinitek 50 automated urinalysis machine. A urine microscopy was a baseline test in the study to out rule bacteruria. In approximately 50% of the women the GP had undertaken a primary MSU at the first visit of the pregnancy. A MSU was only sent for microscopy at the hospital booking visit, if this had not previously been done by the GP.

The results of the MSU were documented on the women's antenatal card, their hospital records and on their data sheets (See Appendix C). Urinary tract infection was diagnosed when greater than 10^6/L organisms were cultured, with associated pyuria in the absence of epithelial cells. A UTI was treated with an appropriate antibiotic. A repeat urine microscopy was conducted after the antibiotic therapy was completed to ensure the treatment was effective.

At each subsequent antenatal visit the women were required to collect a sample as instructed at the booking visit and it was tested using the Clinitek 50 machine. The

results were documented in the woman's second data sheet (See Appendix D) and in the medical records and antenatal health record as previously described.

Blood pressure monitoring

Blood pressure monitoring is an important part of antenatal care and occurs routinely at each antenatal visit. Blood pressure was measured with a manual sphygmomanometer on the right upper arm, the woman seated and feet resting on a firm surface and the phase five Korotkoff sound was used in the measurement of diastolic BP (Brown, Buddle, Farrell, Davis & Jones, 1998). The phase five Korotkoff sound is the term given to the disappearance of the pulse sound when recording the diastolic BP as it correlates well with intra-arterial diastolic BP (Brown, Reiter, Smith, Buddle, Morris & Whitworth, 1994). A large BP cuff was used if the woman's upper arm measured greater than 33cms in circumference (Brown et al., 2000). This method of BP monitoring is in accordance with the ASSHP Consensus statement (Brown et al., 2000) and was standard protocol at St. George Hospital.

Definitions

Pre eclampsia

The definition of a significant rise in BP at the outset of the study was an increase in systolic BP of ≥25 mmHg and/or a rise in diastolic BP of ≥15mmHg from the first trimester or pre pregnant BP (Australasian Society for the Study of Hypertension in Pregnancy (ASSHP), 1993). The definition changed in the course of the study to a systolic BP of ≥140 mmHg and a diastolic BP of ≥90 mmHg as recommended by the ASSHP (Brown et al., 2000). Proteinuria may be associated with this significant rise in BP.

Proteinuria

Proteinuria is defined as a level of protein ≥ 1+ on automated urinalysis of a clean catch (MSU) specimen of urine (Brown et al., 2000).

Haematuria

Haematuria is defined as a ≥ a trace of blood on automated urinalysis of a clean catch specimen of urine (Brown et al., 2005).

Study Protocols

Proteinuria (≥1+): If the dipstick analysis indicates proteinuria ≥ 1+, the same sample was sent to biochemistry for 'spot urine: protein/creatinine ratio'. If the ratio is elevated to ≥ 30, referral to the Obstetric registrar was made.
Part of the same sample was sent to microbiology for culture and sensitivity. A positive culture was reported to the medical officer and antibiotic therapy prescribed. A repeat MSU was conducted at the subsequent antenatal visit to ensure treatment was complete.

Haematuria (≥ trace): If the dipstick analysis indicated haematuria, the same sample was sent to microbiology for culture and sensitivity. The medical officer was informed of any positive culture of a pathogenic organism and an appropriate antibiotic prescribed.

Women who developed more than one episode of haematuria in the absence of infection were referred to the Renal Professor involved in the study. The following blood tests were also ordered; Full Blood Count; Urea & Electrolytes; Uric Acid; Liver Function Tests; and a MSU for microscopy to identify the type of red blood cell which in turn would indicate the source of microscopic haematuria. Dysmorphic haematuria originates in the kidney and isomorophic haematuria has its origins in the epithelial tissue of the bladder or urethra. A renal ultrasound was also done to out rule any renal pathology such as calculi or tumours.

Nitrites and Leucocytes: If the dipstick analysis indicated the presence of nitrites and leucocytes, the MSU was sent for culture and treatment instigated if infection was diagnosed.

Management of abnormal urine results

Abnormal urine results were defined as proteinuria ≥1+, haematuria at trace level and presence of leucocytes and nitrites on automated dipstick urinalysis. The abnormal results were managed as follows:

- Proteinuria >1+ required quantitation by sending the MSU to biochemistry for a spot protein/creatinine ratio.

- Haematuria trace – the MSU was sent to microbiology for culture and sensitivity. If a culture of pathogenic micro-organisms of 10^6 /L was diagnosed then antibiotic therapy was required.
- Leucocytes and nitrites are indicative of UTI and may occur in conjunction with proteinuria or haematuria. If leucocytes or nitrites were present the MSU was sent to microbiology for culture and sensitivity. Antibiotic therapy was prescribed if the culture was positive.

Once the antibiotic therapy was complete, the woman provided a repeat MSU for culture and sensitivity to ensure the treatment was effective.

Study sites and coordination

All antenatal settings at St. George Hospital, including antenatal clinic (ANC), the outreach antenatal clinics and the Birth Centre clinics participated in the study. The study was coordinated by two clinical midwives -Julie Curtis, Clinical Nurse Specialist in the antenatal clinic and Noreen Murray, Acting Clinical Midwifery Consultant. Julie took responsibility for the ANC while Noreen took responsibility for the outreach clinics and the Birth Centre. The booking of a hundred women from one of the private obstetricians at the adjoining private hospital helped accelerate the recruitment phase and provided a more diverse sample. The midwife who worked in conjunction with the private obstetrician received inservice training on the recruitment and data collection process and Noreen was available for technical support.

The midwife co-ordinators were responsible for the:

- Education of staff regarding the study and standard antenatal practice;
- Enrolment of women;
- Collection of data at enrolment and subsequent visits;
- Ensuring standard practice was followed in the collection and documentation of urine samples, quality assurance processes are described later in this chapter;
- Ensuring standard action was taken in the event of abnormal results; and,
- Follow up of enrolled women.

The provision of inservice education, written available protocols and practical onsite support from co-ordinators were the education methods utilised to disseminate

information about the background and rationale of the study to the midwifery and medical staff working in the antenatal service at the time of the study. (See appendix A)

The pathology laboratory administrator was also informed that there would be an increased workload for their department. The renal physician involved in the study liaised with the laboratory administrator and the temporary increase in costs incurred by increased microscopy and spot protein/creatinine ratios, were wavered. The renal physician involved in this study has conducted a great deal of urodynamics research at the hospital laboratory over the years and the extra costs incurred by the HULA study were wavered in view of the potential long term savings if routine urinalysis became obsolete.

Data collection

Demographic details, previous relevant medical and obstetric history were collected from each woman at the booking visit. Blood pressure was measured using a mercury sphygmomanometer and the results of automated dipstick urinalysis and urine microscopy were recorded. The medical conditions, which are reported to be associated with the development of pre-eclampsia or potential negative pregnancy outcomes, were recorded. These included essential hypertension, previous pre-eclampsia, renal disease, diabetes and multiple pregnancy.

Details of gestation, urinalysis, BP and relevant microbiology or biochemistry result were recorded at each subsequent visit and recorded on the second data sheet. The completed first data sheet was filed in a collection folder in numerical order and by month of expected birth.

The subsequent data sheets were filed in a separate folder in numerical order at each antenatal venue. As the women reached the study endpoint (gave birth), their data forms were collected and stored for final data collection of pregnancy outcomes. This process took place in the clinical information department. Each woman's clinical notes were viewed and the information checked with the data sheets. Information on the baby's birthweight, length, head circumference, and the woman's type of birth and final diagnosis of a hypertensive disorder was gathered. Both coordinators undertook this

task, providing additional assurance that the preliminary data was recorded correctly. Occasional omissions in the data collection were corrected at this time.

Outcome Measures - Classification

The principal question of the study centred on the development of proteinuria and a significant rise in BP. These two factors were not always associated.

The classification of the outcomes fell into five categories:

- No Proteinuria. No significant rise in BP.
- No Proteinuria. A significant rise in BP.
- Proteinuria. No significant rise in BP.
- Proteinuria before a significant rise in BP.
- Proteinuria after a significant rise in BP.

Outcomes

The primary outcome was a diagnosis of hypertension, that is, gestational hypertension pre-eclampsia, essential hypertension or pre-eclampsia superimposed on essential hypertension. The definitions of hypertensive disorders of pregnancy are consistent with the most recent consensus statement from the ASSHP. (Brown et al., 2000). These definitions were described in the previous chapter. Secondary outcomes included gestation at birth and the weight for gestational age as a measure of fetal growth. Small for gestational age (SGA) was measured using growth percentiles for an Australian population (Guaran, Wein, Sheedy & Beischer, 1994). Birthweight less than the 10th percentile was classified as SGA. A urinary tract infection was diagnosed on MSU when an organism was cultured with 10^6 /L polymorphs without epithelial cells.

Confirmation of diagnosis of hypertensive disease was also made when reviewing the clinical records by checking the physician's notes, BP recordings, and biochemistry results. If uncertainty about the diagnosis occurred, the Obstetric Staff Specialist reviewed the notes in consultation with the study coordinator ensuring accuracy in the data collection.

Data Entry

A database using a Microsoft Access programme was developed with the help of a computer support technician. Most data entry (80%) was conducted by a data entry clerk who had experience in medical data entry. As the volume of data entry became excessive for the original data entry person, the remaining 20% was conducted by one of the coordinators and a research midwife.

Quality Assurance

Quality assurance strategies were employed throughout this study to ensure precision in urine collection, knowledge of the protocols by staff, accuracy in data collection and data entry. These strategies were used to ensure accurate findings and study results that were of a high calibre.

Firstly the study proposal and procedures were explained thoroughly to all midwives working in the various antenatal settings by way of inservice education. It was essential that the midwives were fully informed of the study process. One of the coordinators was available at all times (Mon – Fri) to answer questions the staff may have had pertaining to the study.

The midwives conducting antenatal care were asked by one of the study coordinators to describe how they informed a woman to collect a MSU. This occurred informally in the first month of the study or if a new midwife joined the team subsequently. Any possibility of misinterpretation was corrected. This was to ensure accuracy of instruction. It was necessary to keep staff motivated and enthusiastic about the study as their involvement in conducting the urinalysis at the antenatal clinic visits was pivotal to the study. It was imperative that the data collection and documentation be precise.

Secondly the protocol for management of proteinuria was printed, laminated and placed near each Clinitek machine for ease of use and interpretation. The method of MSU collection was placed on brightly coloured paper on the back of each toilet door used by the women. This was further reinforcement of the verbal instruction given by the recruiting midwife.

The Clinitek 50 urinalysis machines were calibrated monthly. The machines were sent to the biomedical engineering department if discrepancies were found. This occurred once during the study. The Clinitek machine was out of service for a month, as we had to wait for a part to come from overseas to fix it. During this time both the outreach teams shared one machine. This was possible as both teams' clinics ran on different days of the week.

Ten recruited women per month were randomly approached by one of the coordinators and asked to describe the method of urine collection. In all cases the method was described according to the recommended study protocol, giving as much assurance as was possible that the specimens were indeed MSU samples.

Quality assurance of the data collection was also conducted. A research midwife crosschecked 10% of the medical records, of the recruited women with their data sheets, to ensure accuracy. Every tenth set of notes was selected for review. Comparison was made between the information in the medical notes and that recorded in the data sheets. Specific examples of such data are booking BP, urinalysis at the booking visit, medical conditions pertinent to the study such as previous pre-eclampsia. The result showed a 98% accuracy rate in data collection.

Finally, the data entry was checked by a research midwife, independent of the data entry. Ten percent of the data sheets were crosschecked with the data entry on the access data base. Ninety-eight percent accuracy was reported on the information entered.

Any doubt regarding the diagnosis of hypertensive states in pregnancy was clarified by the Obstetric Staff Specialist upon review of the medical records. This was to ensure rigor in the classification of the hypertensive states of pregnancy reported in the HULA study.

Data Analysis

Data was entered into a database using MS Access and was transferred into SPSS for the purposes of analysis. Frequencies were used to describe the results of urine tests at the first visit. The clinical outcomes of women who had normal versus abnormal urine

at the first visit and of those who developed proteinuria subsequently were compared using chi-squared testing. Fisher's exact tests were used when the observed frequency was less than 5 per cell. Sensitivity, specificity, positive and negative predictors and positive and negative likelihood ratios were also calculated. Results were deemed statistically significant at the 5% level of significance ($p<0.05$). Frequencies are presented with percentages, which do not always equal 100 due to rounding.

Summary

This chapter described the methodology used in the HULA Study. Although a randomised controlled trial is the 'gold standard' in research methodology, it was not appropriate in this instance as certain women may have been disadvantaged if they were randomised to not have their urine tested during pregnancy. A prospective observational study was selected to describe the outcomes of urinalysis and pregnancy of a thousand recruited women. The study based its protocols on research evidence already available in the literature.

The following chapter describes the results of the HULA study.

CHAPTER FOUR: RESULTS

Introduction

This chapter presents the results of the study. They will be described under the following headings; demographics, first visit urinalysis, proteinuria in relation to pre-eclampsia and microscopy and urine culture.

Results of HULA Study - Demographics

One thousand women were enrolled into the study but 87 (8.7%) were lost to follow up. Miscarriage was the main reason for this followed by relocation of the women to another maternity facility. These women were excluded, as a guarantee could not be given that the study protocols would be followed in the new facility.

The mean age of the remaining 913 women was 29 years (range 14 to 48 years) and 48 per cent (n=442) were nulliparous. Women came from a range of cultural backgrounds were representative of the cultural diversity of the population serviced by St. George Hospital.

The majority of women (62%) were from English-speaking backgrounds. Nineteen percent were from Asian countries and nine percent from Arabic speaking countries. The remaining 10 percent came from European and South American countries. Six percent (n=52) of women in the study reported previous renal disease, including recurrent urinary tract infection or pyelonephritis (n=28), renal calculi (n=15) and haematuria (n=5). Two percent (n=18) reported a history of essential hypertension. Of the 471 multiparous women, 11 percent (n=50) reported a history of pre-eclampsia or gestational hypertension.

The demographics of the HULA sample is representative of the population attending St. George hospital during the time of the study. Table 3 illustrates the comparison between the women attending the South Eastern Sydney Area Health Service and the women recruited to the HULA study.

Table 3: Demographics are reported in percentages.

	English Speaking %	Asian %	Arabic %	European and South American %
South Eastern Sydney Area Health Service*	73	17	5	6
HULA Study Sample	62	19	9	10

*Source: Public Health Division. NSW Department of Health, 2001.

Urine tests at the first visit

Eleven women did not have dipstick urinalysis performed at their first visit, although all 913 women had a urine sample collected for microscopic examination and culture (Table 4).

Table 4: Dipstick urine testing at first visit N=902

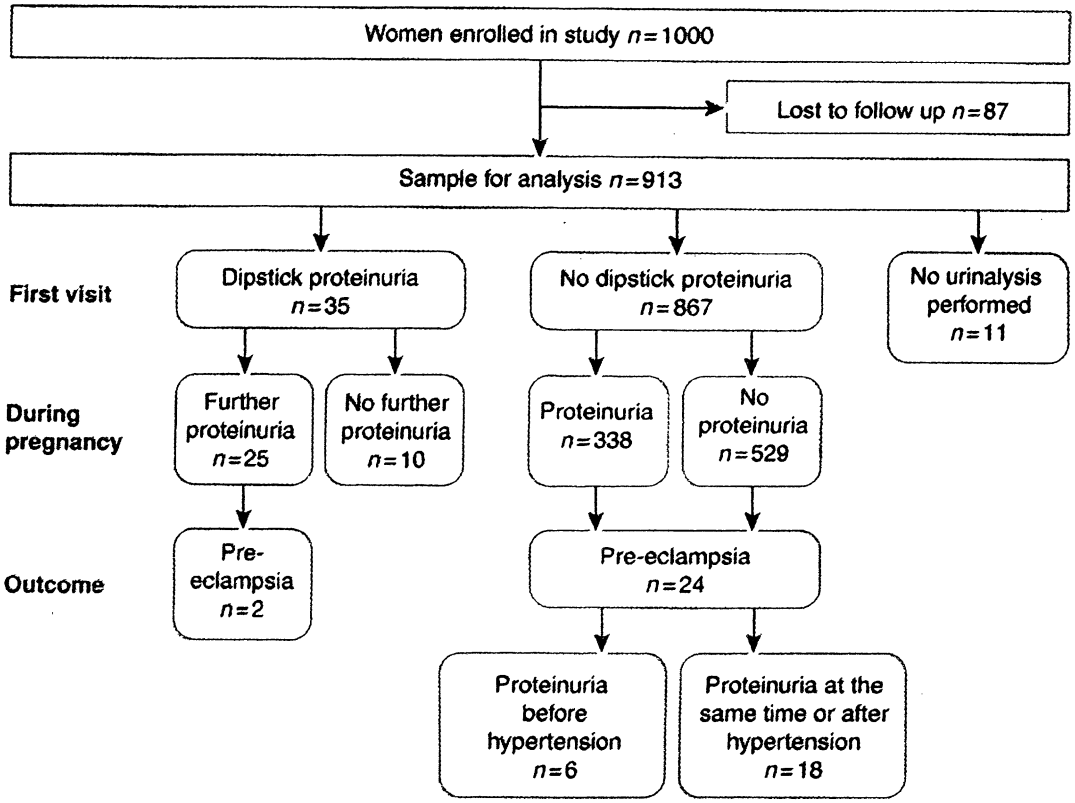
	N= 902 n (%)
Proteinuria ≥1+	35 (4)
Haematuria ≥ trace	168 (18)
Presence of white blood cells	36 (4)
Clear urine on dipstick (none of the above)	681 (75)

Thirty-five women had dipstick proteinuria at their first visit, but only 14 had a specimen sent for a spot protein/creatinine ratio. This was less than 50% compliance with study protocol in this instance and will be discussed in the next chapter. Of the 14 who had a spot urine sent for quantitation, two had true proteinuria (≥ 30mg protein/mmol creatinine). Four of the thirty-five women with first visit dipstick proteinuria had a history of renal disease. Further dipstick proteinuria was detected during pregnancy in 25 of these 35 women (71%) and two (6%) were diagnosed with pre-eclampsia.

Of the 867 women without dipstick proteinuria on the first visit, 338 (39%) had dipstick proteinuria (≥1+) at some time during pregnancy. We assumed, that the majority of these women had a specimen of urine sent for spot urine protein/creatinine ratio but this

was not part of the analysis. The study sought to identify the percentage of women with dipstick proteinuria prior to raised BP and to see if proteinuria ≥1+ at booking was indicative of women who went on to develop pre-eclampsia, (see Figure 1). There were no statistically significant differences in the proportion of women with and without first visit dipstick proteinuria at their first visit that developed hypertension during pregnancy.

Figure 1: Flow chart of proteinuria detected during pregnancy and outcomes



Proteinuria during pregnancy and pre-eclampsia

Of the 338 women (39%) who developed dipstick proteinuria during pregnancy, most (n=325; 96%) had 1+ proteinuria, with 11 having 2+, and two women 3+ proteinuria. Fifteen of the 338 women with dipstick proteinuria (4%) developed pre-eclampsia, compared with nine of the 529 women (2%) without dipstick proteinuria during pregnancy (see Table 5). Thus, 24 women, who did not have proteinuria at their first visit, developed pre-eclampsia: six had proteinuria diagnosed before the development of hypertension, six had proteinuria identified at the same time as hypertension was diagnosed, and the remaining 12 women developed proteinuria after the diagnosis of hypertension.

Of the six women who developed proteinuria (and ultimately pre-eclampsia) before the onset of hypertension, two had multiple pregnancies, one had a history of pre-eclampsia, but none had a history of renal disease. Multiple pregnancy and a history of pre-eclampsia in a previous pregnancy, are risk factors for the development of pre-eclampsia in the current pregnancy (Ramos, 1999). Consequently these women would continue to have proteinuria surveillance through routine urinalysis at each antenatal visit. Only three women without risk factors for pre-eclampsia, from this sample of 913, developed proteinuria prior to raised BP. Five of these six women gave birth at more than 36 weeks' gestation, with the remaining woman giving birth at 32 weeks gestation. There were no adverse neonatal outcomes.

Microscopic examination and culture of urine

All 913 women had a first visit midstream urine sample sent to the laboratory for microscopic examination and culture; 91% (n=833) had a 'normal' result and 8% (n=80) an 'abnormal' result. Most of the abnormal results (97%) were related to the presence of red or white blood cells or sterile pyuria. Women who had an abnormal midstream urine sample at their first visit were more likely to have a urinary tract infection diagnosed during pregnancy compared with those with a normal midstream urine sample; however, the numbers were small. Four per cent of women (n=3) with an abnormal midstream urine sample developed a urinary tract infection, compared with 1% of women (n=7) with a normal midstream urine sample ($P<0.05$; relative risk, 4.5; 95% CI, 1.2-17) (see Table 6).

Although the pathogenicity of the UTI's diagnosed in the participants of this study was not a discerning factor of the research, Escherichia. Coli (E. Coli) was the most common micro organism isolated. This correlates with findings in studies by Bachman et al. (1993) and Smaill (2002).

Table 5: Development of hypertension and pre-eclampsia

A: According to the result of dipstick urinalysis at the first antenatal visit (n = 902)*

	No proteinuria	Proteinuria†	P‡	Relative risk (95% CI)
	n = 867	n = 35		
No hypertension	809 (93%)	31 (89%)	0.2	1.8 (0.6–4.8)
Pre-eclampsia	24 (3%)	2 (6%)		
Hypertension, other§	34 (4%)	2 (6%)		
B: In women with no proteinuria at the first antenatal visit (n = 867) who subsequently developed dipstick proteinuria during pregnancy				
	n = 529	n = 338		
No hypertension	503 (95%)	306 (91%)	0.01	1.5 (1.1–1.9)
Pre-eclampsia	9 (2%)	15 (4%)		
Hypertension, other§	17 (3%)	16 (5%)		

*Eleven women did not have dipstick urinalysis performed at their first visit. †Protein >1+ on dipstick urinalysis. ‡χ^2 test for differences between groups. §Includes gestational hypertension, chronic hypertension, and pre-eclampsia superimposed on chronic hypertension.

Table 6: Development of hypertension and subsequent urinary tract infection according to the results of midstream urine tests at the first antenatal visit (n=913)

	"Normal" urine (n=833)	"Abnormal" urine* (n=80)	P†	Relative risk (95% CI)
No hypertension	778 (93%)	73 (91%)	0.5	1.3 (0.6–2.8)
Hypertension				
Pre-eclampsia	22 (3%)	4 (5%)		
Gestational hypertension	21 (2%)	2 (2%)		
Chronic hypertension	5 (1%)	1 (1%		
Pre-eclampsia superimposed on chronic hypertension	7 (1%)	0		
Urinary tract infection during pregnancy	7 (1%)	3 (4%)	0.05	4.5 (1.2–17)

*Infection and/or haematuria. †χ^2 tests for differences between groups; where number of observations <5, Fisher's exact test was used.

Summary

This chapter presented the detailed results of the HULA study. The development and severity of proteinuria during pregnancy was the principal focus of the analysis. The prevalence of proteinuria 1+ at booking, the incidence of true proteinuria when these samples were quantified biochemically, and the incidence at which proteinuria occurred in subsequent automated urinalysis were reported. The diagnosis of the hypertensive states of pregnancy, were also presented in relation to the development of proteinuria.

In Chapter Five the results will be discussed in terms of their relevance to clinical practice, whether they are consistent with previous research and whether evidence has been obtained to help answer the fundamental questions posed at the beginning of this piece of research. The question central to this study, *'Can routine urinalysis be eliminated from the antenatal care of low risk women once initial urinalysis and microscopy is complete?'* will be addressed.

CHAPTER FIVE: DISCUSSION AND RECOMMENDATIONS

Introduction

This chapter discusses the results of the data of the HULA study. Reference to existing evidence from the literature in the context of best midwifery practice in the conduct of urinalysis in pregnancy is highlighted. This study sought to answer seven questions pertaining to aspects of urinalysis in pregnancy. Two studies from the recruited sample of pregnant women ran parallel, to answer these questions (i) the HULA study and (ii) the haematuria study. The latter was not the subject of this thesis but the results are referred to in this discussion chapter as they are now published, are of interest to clinicians and add further evidence to the argument of the relevance of urinalysis in pregnancy. The initial questions and the answers deduced from the results of both studies are presented and their relevance discussed.

Primary questions

1. *What is the prevalence of proteinuria on urinalysis using the Clinitek 50 Ames machine at the antenatal booking visit?*

Thirty-five women of the 902 women who had automated dipstick urinalysis performed had proteinuria at the booking visit. Only two of these 35 women developed pre-eclampsia, which suggests that proteinuria at booking is a poor predictor of who will develop pre-eclampsia in the pregnancy.

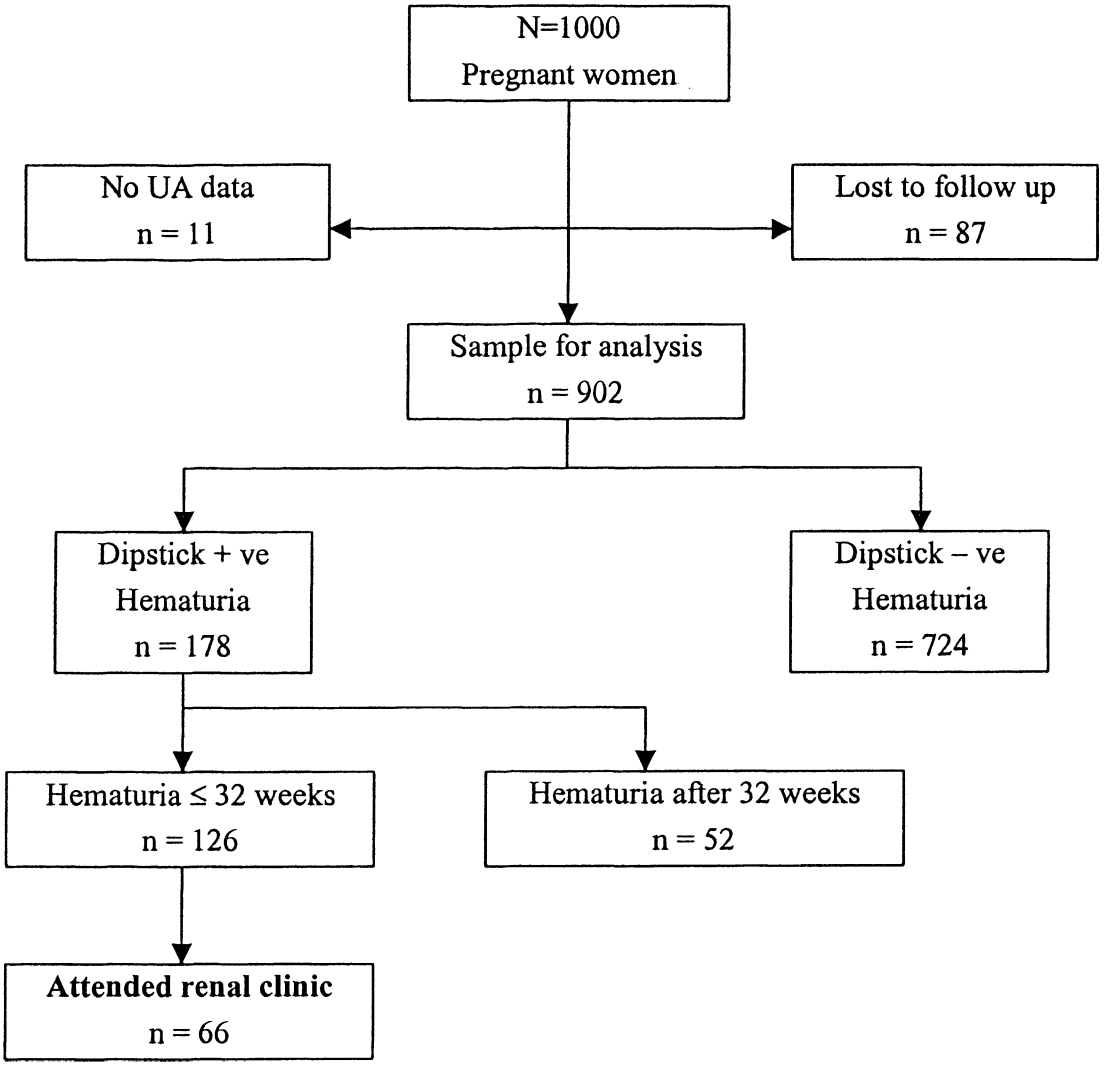
2. *What is the prevalence of microscopic haematuria throughout pregnancy and is it a persistent phenomenon post partum?*

One hundred and seventy eight of the 902 women (20%) had microscopic haematuria on at least two occasions in pregnancy (Figure 2). A study by Stehman-Breen, Miller, Fink, and Schwartz (2000) reported a similar incidence of 16% in the pregnant population.

Microscopic haematuria persisted in half (n=15) of the women who attended a follow-up, three months postpartum. This translates to approximately 5% of the pregnant population to have subsequent, possible mild glomerulonephritis (Brown et al., 2005). This figure correlates with the incidence of glomerulonephritis found in the general Australian population (Chadban, 2003).

The implications of these findings are further support for performing a booking urinalysis and microscopy to identify these women with haematuria, and to ensure long term surveillance for potential kidney disease. Pregnancy outcomes of women with haematuria in pregnancy are unlikely to be different from women without haematuria in pregnancy (Brown et al., 2005).

Figure 2: Detection of dip-stick haematuria in a cohort of 1,000 pregnant women



3. *Does proteinuria, detected through routine antenatal urinalysis, predict women who will develop pre-eclampsia?*

Only two of the thirty-five women, who had dipstick proteinuria at booking, developed pre-eclampsia. Eight hundred and sixty seven did not have dipstick proteinuria at their booking visit however 338 had dipstick proteinuria at some time during the pregnancy.

Of these 338 women, 24 developed pre-eclampsia. There is no statistically significant difference in the proportion of women with and without dipstick proteinuria at their booking visit and the development of hypertension in pregnancy. There is no statistically significant difference in the percentage of women who develop pre-eclampsia, in women without dipstick proteinuria (2%) or in women with dipstick proteinuria at booking (4%) or subsequent visits (6%). Bigger numbers may be needed to demonstrate statistical difference.

4. *What is the prevalence of a subsequent abnormal urinalysis (proteinuria and/or haematuria) in women who have a normal urinalysis at their booking visit?*

Of the 867 women without proteinuria at booking, 338 (39%) developed dipstick proteinuria at some time during the pregnancy. One hundred and two (57%) women with haematuria had associated proteinuria of > 1+.

Secondary questions

1. *What proportion of women, develop proteinuria prior to a significant rise in BP?*

Of the 867 women who did not have dipstick proteinuria at the booking visit, 24 went on to develop pre-eclampsia. Only six of these women had proteinuria prior to the development of hypertension. Three of these six women had risk factors for the development of pre-eclampsia; two had multiple pregnancies and one had a history of pre-eclampsia. There is no treatment for proteinuria except 'expectant observation'. This result questions the logic of testing such a large number of women to identify so few.

2. *What is the timeframe between the development of proteinuria and the significant rise in BP?*

Only six women developed proteinuria prior to a significant rise in BP. This number is too small to deduce a significant conclusion.

3. *Can routine urinalysis be safely abandoned, from antenatal care once urinalysis and microscopy is conducted at the first antenatal visit?*

From the results of this research, it would seem reasonable to withdraw routine urinalysis from antenatal care of 'low risk' women, once a booking microscopy is

completed. Urinalysis may be performed again if symptoms such as hypertension or dysuria arise.

Discussion

Proteinuria

The presence of proteinuria during initial urinalysis in pregnancy is a poor predictor of the women who proceed to develop pre-eclampsia (Brown & Buddle, 1995; Sibai et al., 1998). In this study, 35 women had proteinuria at their first antenatal visit but only two went on to develop pre-eclampsia. Of the 338 women who had proteinuria at some time during their pregnancy, 24 women developed pre-eclampsia. The timing of the development of proteinuria bears great relevance to this study. One of the reasons routine urinalysis is conducted is to detect proteinuria in conjunction with raised BP. Six women developed proteinuria before the elevation of BP whereas 18 developed it at the same time or after the significant rise in BP.

In clinical practice, proteinuria during pregnancy alone does not warrant any specific intervention, except a heightened awareness of the potential of a significant rise in BP. Hypertension is the *sine que non* of pre-eclampsia (Brown et al., 2000; Hooper, 1996). Even after signs of hypertension and proteinuria develop, the disease in each individual woman follows a largely unpredictable course (Power, 1997). On further examination of the six women who developed proteinuria before hypertension, 50% had preexisting risk factors that would have classified them as risk associated pregnancies; two had multiple pregnancies and one had a previous history of pre-eclampsia. That leaves only three women classified with proteinuria prior to a raised BP. The overall benefit of testing so many to identify so few does not seem to be a practical or efficient use of resources. This is particularly so as there were no adverse maternal or neonatal outcomes in this group.

The minimal levels of proteinuria prior to raised BP correlates with a study by Hooper (1996), which investigated, the association of proteinuria and pre-eclampsia. Six hundred and ten antenatal records were reviewed. These records identified 17 women (2.8%) developed pre-eclampsia but only three had proteinuria that proceeded the finding of hypertension (Hooper, 1996). Proteinuria is thought to be a late occurrence in

the development of pre-eclampsia (Kuo et al 1992; MacLennan, 1986) and this was demonstrated in the HULA study.

Previous research by Gribble et al. (1995) found that, in 'low risk' women with no objective signs of hypertensive disorder, routine urinalysis throughout pregnancy provided no clinically important information in terms of outcome. Although a large sample size was used in this study (n=3217), the author excluded women who had pre existing hypertension, diabetes mellitus, renal disease, collagen-vascular disease, multiple pregnancy and proteinuria of $\geq$ 30mg/dl at the first antenatal visit. The HULA study described in this thesis included all women who presented to our unit for antenatal care during the study period in order to provide a representative sample of the women in this area. By not restricting the criteria of the women who enrolled it the study it was thought to provide a more realistic representation of women presenting for antenatal care and the results achieved may give a more accurate picture of what actually happens with routine urinalysis and pregnancy outcomes.

Nitrites, blood and leucocyte esterase

Current research recommends first visit urine microscopy to detect asymptomatic bacteruria in pregnancy (Bachman et al., 1993; Brown et al., 2005; Rouse et al., 1995; Schieve et al., 1994; Smaill, 2002) Proteinuria alone is not indicative of bacteruria. In Gribble's research (1995), only two of 56 women with a positive urine culture at the first obstetric visit also had true proteinuria of 300mg/L at that same visit. The Three Centre Consensus Guidelines on Antenatal Care in Australia (2001) recommend a MSU be tested by dipstick for blood, leukocyte esterase, nitrites and protein at the booking visit. If the sample is positive for any of the four categories a MSU is sent for microscopy and culture. Only 1.8% of the participants in the HULA study developed a UTI. The literature reports a wide variation in the occurrence of UTI within pregnant women (2 – 8%) and it is proportionate to the socio economic status of the women (Rouse et al., 1995; Schieve et al., 1994; Smaill, 2002).

Preterm labour and SGA are the negative outcomes of persistent UTI in pregnancy (Abyed, 1991; Three Centre Consensus Guidelines, 2001; Rouse et al., 1995; Shieve et al., 1994). The HULA study reported only one baby born at less than 36 weeks gestation (32 weeks) and this woman did not have a UTI during the pregnancy. On

diagnosis of a UTI, an appropriate antibiotic can be prescribed thus reduce the possibility of negative maternal and perinatal outcomes (Brown et al., 2005; Smaill, 2002; Tincello & Richmond, 1998; Villar et al., 2000).

Quantification of Protein

The gold standard for proteinuria quantification is the 24 hour urine collection test (ASSHP, 1993; Chan et al., 2005; Saudan et al., 1997; Young et al., 1996). If automated dipstick urinalysis shows ≥ 1+ proteinuria, further testing is necessary to quantify true proteinuria (Brown et al., 2000; Saudan et al., 1997). The ASSHP has advocated the 'spot' protein/creatinine ratio as a rapid and accurate method of protein quantification (Brown et al., 2000; Chan et al., 2005; Saudan et al., 1997). The protocol for this study stipulated that if any dipstick urinalysis had a ≥ 1+ result, then the sample was to be sent for biochemical analysis by way of the spot protein/creatinine ratio.

Unfortunately, the protocol for the management of 1+ proteinuria at booking was not followed consistently in this study. Thirty-five women had dipstick proteinuria at their first antenatal visit. Only 14 of these had a MSU sent for a spot protein/creatinine ratio and only two of these women were reported to have had 'true' proteinuria (≥30mg protein/mmol creatinine). Although 21 women did not have proteinuria at booking quantified, it would not impact greatly on the study results. Only two of these thirty-five women developed pre-eclampsia. It is not known if they are the women who did have a spot urine completed at booking.

Midwifery staff providing antenatal care had received information on the study and its protocols. The protocol was printed and displayed near the automated urinalysis machine. It is assumed however that the large numbers of midwives involved in many different antenatal settings, the busy throughput at these clinics and human error contributed to this level of non compliance. The coordinators of the study endeavoured to be present at all antenatal clinics especially during the recruitment process but some of the clinics ran simultaneously and this was not always possible.

Changing practice, or incorporating research into routine practice, occurs with difficulty and resistance from some clinicians. Such challenges were also identified by the coordinators of this study, and encouragement was given to the staff. Group meetings

were held for the antenatal midwives and facilitated by the coordinators of the research. The aim of these meetings was to answer any questions regarding the background or the ongoing process of the study, even though extensive information was given to all midwifery and medical staff working at St. George Hospital before the commencement of the study. New midwifery staff commencing employment at the hospital received one-on-one inservice education about the HULA study. The importance and necessity for accuracy in the execution of the research protocol was highlighted to the midwifery staff. The potential long-term benefits of not having to do routine urinalysis on 'low risk women was of interest to both clinicians and pregnant women. These were cited as a positive reason to actively participate in this study. A monthly progress report on the HULA study was available to all staff via the Midwifery Practice and Research Centre's newsletter. One of the coordinators worked full time regular hours and was contactable by page if any problems arose for the midwives in the antenatal setting regarding the study.

Limitations

Whilst this study set out to be a rigorous piece of research, certain limitations are acknowledged by the author.

Study Design

Randomised controlled trials (RCT) are the 'gold standard' in terms of research to test effectiveness of interventions (Sackett, Richardson, Rosenberg & Haynes, 1998). A RCT however, was not feasible in this study. It was unknown if withholding routine urinalysis would have caused harm. In a RCT, women randomised to no testing may have been disadvantaged in terms of clinical diagnosis and outcomes. Consequently, a prospective observational study was the design chosen.

A prospective observational study was selected as the most suitable design. The sample size of 1000 was chosen mostly from a feasibility perspective. The sample size was discussed at length by all of the stakeholders, as there would be the potential of a Type II error. This means that while our study reported no statistical difference when there may have been a difference if the sample size was larger. Given the result and the sample size the power has been calculated as 40%, which suggests that twice the sample size is required to reach statistical significance.

The time frame for the study had to be taken into consideration, as the human and financial resources available, were finite. From the eventual sample of 913 women, the incidence of certain clinical conditions, seem to be under-reported. Pre-eclampsia has a reported incidence of 2 – 10% in industrialised nations (Chan et al., 2005; Duley, 2004). The HULA Study reported a 3% incidence of pre-eclampsia in its sample. Urinary tract infection has an incidence of 2-8% in the pregnant population (Rouse et al., 1995; Schieve et al., 1994; Smaill, 2002) but is relative to the socioeconomic status of the population studied. The HULA study reported an incidence of 1.8% (n=10) in its cohort. A bigger sample would address the possibility of Type II error.

Compliance with the ASSHP Consensus Statement

There is a further consideration to be taken into account, when describing the incidence of pre-eclampsia in the clinical setting. Wide variation in the assessment and management of pre-eclampsia has been reported in a study of practising obstetricians in Australia and New Zealand (Davis, Homer & Brown, 2002). The ASSHP guidelines (1993) were poorly adhered to in that study, which raises the question about accuracy in the clinical diagnosis of pre-eclampsia. Davis et al. (2002) reported that although most obstetricians correctly diagnosed significant BP as systolic ≥140mmHg and diastolic ≥ 90mmHg (74%) and (86%) respectively, the level of abnormal proteinuria was grossly inconsistent. The range at which the respondents deemed proteinuria as abnormal ranged from 0.0003g to 70.5g per 24 hours. The consensus statement states that ≥ 300mg /24 hours is abnormal (ASSHP, 1993). Given that a specific level of BP and proteinuria are essential for the diagnosis of pre-eclampsia and these obstetricians demonstrated variation in the criteria used for management, perhaps attention needs to address the true incidence of pre-eclampsia in relation to appropriate definitions.

Pre-eclampsia complicates between 2 - 10% of pregnancies (Duley, 2004). The number of women who developed pre-eclampsia in this study is at the lower end of this range at 3%. It is likely that there is variation in the management of hypertensive diseases of pregnancy within obstetric practice nationally (Davis et al., 2002). Within the St. George Maternity facility, both public and private hospitals, the accuracy in determining hypertensive diagnosis is high due to the adherence to evidence based protocol by physicians, obstetricians and midwifery team.

We certainly acknowledge the limitations of this study but suggest that given the wide variation in practice of urinalysis in pregnancy throughout Australia, the results and recommendations presented from this study form guidelines for health care providers. The following are recommendations from the results of this study and from the current literature pertinent to best practice on the practice of urinalysis in pregnancy.

Practice changes made as a result of the study

The main practice change attributed to the findings of this research is,

- 'low risk' women, with a negative urinalysis and microscopy at antenatal booking visit do not need further testing unless signs of hypertension or UTI present (Murray et al., 2002).
- all women have a booking microscopy to detect haematuria, as 5% of all women may have mild glomerulonephritis and need ongoing surveillance in the postpartum period (Brown et al., 2005).

Other changes were also implemented as part of the study protocol and continue to be used in the practice of urinalysis in pregnancy. These changes are based on the evidence and recommendations of previous research pertinent to issues of sample collection, automated urinalysis and protein quantitation in pregnancy. Clinicians need to be aware that:

- All women need to have an automated urinalysis and microscopy at their antenatal booking visit (Brown et al, 2005; Rouse et al., 1995; Shieve et al. 1994);
- The sample tested should be a MSU (Abyed, 1992);
- Proteinuria is defined as $\geq$1+ on dipstick urinalysis (Brown et al., 2000);
- Proteinuria 1+ should be quantified by spot protein/creatinine ratio (Brown et al., 2005; Chan et al., 2005; Saudan et al., 1997; Young et al., 1996); and,
- A spot urine protein/creatinine result of > 30 is considered significant (Brown et al., 2000; Chan et al., 2005).

Recommendations based on the evidence

1. All women presenting for antenatal care should provide a carefully collected midstream specimen of urine for automated dipstick testing.
2. If urinalysis on automated dipstick testing is negative at the booking visit, no further testing is necessary unless the woman develops hypertension or symptoms of urinary tract infection.
3. Women with abnormal results of a dipstick urine test (including the presence of leukocytes, nitrites or blood) should have a MSU sent for microscopy, culture and sensitivity. A result showing asymptomatic bacteruria should be treated with appropriate antibiotic therapy. If the results are normal, no further testing is required unless the woman develops hypertension or signs of urinary tract infection.
4. Women found to have 'true' proteinuria and/or haematuria at their first antenatal visit may have underlying renal disease and should have further investigation (Brown et al., 2005).
5. Routine urinalysis for 'at risk' women should continue as the detection of pre-eclampsia is important. This group has a predisposition to pre-eclampsia and includes women with any of the following: essential hypertension, previous history of pre-eclampsia, diabetes mellitus, renal disease, or multiple pregnancy (Brown et al., 2000).
6. Proteinuria quantitation can be conducted by the use of a spot urine protein/creatinine ratio as this test correlates well with the 24 hour urine collection (Brown et al., 2000; Chan et al., 2005; Saudan et al., 1997; Young et al., 1996).
7. There are cost saving implications for maternity units who utilise the results of this research. Reallocation of funding can be used in other, more useful, service provision.

Need for further research

Women who have recognised risk factors continue to have a urinalysis performed at each antenatal visit. It is plausible that selective testing may be a reasonable proposition for the care of these women. Further research is necessary however to determine which women can have selective testing.

To address the possibility of Type II error in this study a similar research project could be carried out using a bigger sample size.

Conclusion

The HULA study set out to answer a series of questions to gain clarity about issues relating to urinalysis in pregnancy. The research demonstrated that it is both safe and judicious to withdraw routine urinalysis from the care of 'low risk' women however testing of women with risk factors for pre-eclampsia is advocated.

Midwifery practice needs to be research based. New evidence from clinical research both invalidates previously accepted diagnostic tests and treatments and replaces them with new ones that are more powerful, more accurate, more efficacious and safe. Health care providers have a responsibility to ensure their practice is effective, safe and evidence based. To achieve this it is important to remain abreast of clinical guidelines and recommendations based on rigorous scientific research. Research aims to make a difference. This study has made an appreciable difference to routine antenatal care.

This study also revealed inconsistency in clinical practice and poor use of the already available evidence. The reasons for this are multifactorial, from poor dissemination of research findings, lack of implementation of research recommendations and/or resistance to change by clinicians or managers. Evidence based practice should be an integral part of clinical practice. The next chapter discusses evidence based practice, presents the implementation of the results of the HULA study and outlines the difficulties encountered when bridging the research-practice divide.

CHAPTER SIX: EVIDENCE-BASED PRACTICE

Introduction

This chapter provides an overview of evidence based practice in the context of midwifery practice. The importance of applying research findings to practice has already been stated in Chapter One. The national telephone survey described in Chapter Five revealed inconsistency in the practice of urinalysis in pregnancy and a failing of many hospitals to implement recommendations endorsed by research. This Chapter explores the issues surrounding evidence and practice with particular reference to the challenge of getting evidence into practice. The challenge of dissemination and implementation is illustrated by an audit conducted at St. George Hospital subsequent to the HULA study.

Evidence Based Practice

The UK Department of Health policy document *Changing Childbirth* 1993 stated that "clinical practice should be based on sound evidence" (Page, 2000). Evidence based midwifery has been significantly influenced using the principles outlined in Changing Childbirth (Page, 2000), Effective Care in Pregnancy and Childbirth (Enkin et al., 2000), and evidence based medicine (Sackett et al., 1998; Muir Gray, 2001; Page, 2000):

> *Evidence Based Medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. The practice of EBM means integrating individual clinical expertise with the best available external clinical evidence from systematic research* (Sackett et al., 1998).

For the purposes of this thesis, evidence based medicine, evidence based practice and evidence based midwifery are synonymous and will be referred to as evidence based practice.

Evidence based practice has certainly been the buzzword of the 1990s and into the new millennium. Midwifery has made great strides in investigating many aspects of care to insure practice is indeed evidence based (Walsh, 2001). The phenomenon of change, can be confronting and challenging for midwives, when faced with the implementation of research findings. When an aspect of care is withdrawn, as in the case of the HULA

study findings, women may perceive that they are getting a substandard level of care. Dissemination of research findings to women and their families is vital as an assurance of optimal health care delivery.

Resistance to change was discovered through an audit undertaken in the St. George Maternity unit on completion of the HULA research and the implementation of its recommendations.

Audit – feedback loop

Once the study was complete and its recommendations implemented, an audit was performed to ascertain compliance to the reformed protocol. Audit and feedback is a cyclical process where clinical performance is analysed and fed back to the clinician. This is a very effective method of bringing about change once the clinician acknowledges the need for change and is willing to be an active participant in the process (Bero et al. 1998).

The audit process consists of four stages:

1. The setting of practice standards based on evidence.
2. The measuring of practice against the standards in a specific pre-chosen area.
3. The implementation of strategies to address the gap between standards and practice if the standards are not being achieved.
4. The revaluation of practice, to ascertain improvement (Walsh, 2001).

The result of an audit will demonstrate if dissemination and implementation of a particular change has been effective (NHMRC, 1999).

Getting Evidence Into Practice

The HULA Study revealed it safe to omit routine urinalysis from the antenatal care of 'low risk' women once their urinalysis at the booking visit, and a urine microscopy were clear. A new protocol was drafted and implemented in all of the antenatal clinic settings, which included hospital antenatal clinic, the Birth Centre and the outreach clinics. The revised protocol mandated that an automated dipstick urine test be performed at the booking visit of all women presenting for antenatal care. If the test was normal no further testing need occur during the pregnancy unless the woman developed a significant rise in her BP or had signs of a UTI.

The Audit Result

An audit of the clinical notes of all women who attended antenatal services in one week was undertaken, to investigate the compliance to the reformed urinalysis guidelines. The audit revealed a non -compliance to the protocol in 25% of cases, for example, no spot urine sent to quantify proteinuria 1+, or the booking urinalysis was not performed. This was both surprising and disappointing considering the amount of inservice education that the staff had received during the time of the research study at this facility and the discussions about changes in practice. This non-compliance demonstrates how difficult it can be to implement research into clinical practice.

Why get evidence?

Midwives need to develop a body of knowledge to underpin practice and in doing so gain greater recognition as a profession (Page, 2000). An impetus for this study was to ensure care was effective and practice relevant in the antenatal setting.

The question that prompted this piece of research came from observing and reflecting on a practice issue. Curiosity led to the next step, which was a literature search on Medline and the Cochrane Library. This revealed no clear guidelines about which women should have urinalysis in pregnancy performed and when. Therefore it was evident that research was needed.

Finding evidence

Sackett et al. (1998) recommend that the first step in finding evidence-based information to inform decisions is to frame a clear question that will help in a literature search (Page, 2000; Rosenberg & Donald, 1995). The question that we sought to answer in the HULA study was "could routine urinalysis be safely omitted from antenatal care?" The literature to that date did not provide clear evidence upon which to make a decision in the context at St. George Hospital.

In providing safe and effective care, there are two, fundamental questions that every midwife should ask:

1. Is what I intend to do likely to do more good than harm?
2. Am I spending my time doing the right thing (Page, 2000)?

The essence of midwifery is the provision of safe and effective care to women and their families during pregnancy, birth and the puerperium. A failure to keep abreast of research findings may result in inadvertent harm or discomfort (Page, 2000).

Before the protocol for the HULA study was implemented, urinalysis in pregnancy was inconsistent in the St. George unit and nationally. Although the intention of testing was good, misdiagnosis probably occurred due to the widely used eyeball dipstick method of urinalysis. Eye-ball dipstick was used in all but two of the units surveyed in the national telephone survey. Studies have documented inaccuracies with eyeball dipstick urinalysis giving high false positive and negative results (Brown & Buddle, 1995; Kuo et al., 1992; Saudan et al., 1997). The use of automated urinalysis improves the percentage of true positives from 48% with visual dipstick urinalysis to 74% (Saudan et al., 1997). In some cases, inaccurate urinalysis results would potentially have led to further unnecessary laboratory testing, incurring expense for the health facility and causing worry and anxiety for women.

Further to Question 1, "is what I intend to do likely to do more good that harm?" a decision to omit routine urinalysis in pregnancy could not be made ethically without supporting evidence. Harm could have been caused by omission. Proteinuria, which is detected on urinalysis, is one of the signs of pre-eclampsia, which in turn may lead to adverse outcomes for mother and baby (Enkin et al., 2000). Haematuria and leucocytes are indicative of urinary tract infection, which may lead to SGA or preterm labour (Rouse et al., 1995). Withdrawal of urinalysis from routine antenatal care may have led to a reduction in the diagnosis of pre-eclampsia or UTI, and could have led to adverse pregnancy outcomes. During review of the literature, evidence was gathered on the best method of performing urinalysis in pregnancy, namely using a 'clean catch' specimen and using an automated device for urinalysis. There was no evidence to support that clinicians were spending their time performing a useful test, which was of any clinical benefit or significance.

In answer to Question 2, "am I doing the right thing?" if the HULA study reported routine urinalysis on 'low risk' women, of no benefit and could be safely omitted then the time spent performing this test could be spent more productively. Before the results

of the HULA study were available, it was assumed that performing routine urinalysis in pregnancy was a judicious use of time and human resource. However, the results demonstrate that the test is of no clinical benefit in low risk women once a negative MSU on booking, was identified. Exclusion of routine urinalysis in pregnancy for 'low risk' women could lead to an annual cost saving of $30,720 based on 2,000 births per year. With continually increasing demand on human and financial resources within the health care system, care needs to be effective and cost efficient.

Why put evidence into practice?

Midwives need to move beyond practice that is tradition influenced and not evidence based. Evidence based practice is a process of life-long self-directed learning in which caring for women and their families creates the need for clinically important information about diagnosis, prognosis, therapy and other clinical and health care issues. As practitioners, we need to unpick the unanswered questions of clinical practice; seek out the best evidence to answer these questions; critically appraise the evidence in terms of its validity and usefulness; apply research results to clinical practice and evaluate our performance (Sackett & Rosenberg, 1995). Rosenberg and Donald (1995) attest that evidence based practice facilitates improved communication with clients on the rationale behind management decisions of their care. This will enhance the confidence of the clinical midwives and the satisfaction of women in their care.

In the HULA study, we have illustrated the potential cost saving in relation to better use of human and financial resources. The money saved on performing a test, which is of little clinical value, could be more appropriately allocated for service provision. For example, additional midwife hours in antenatal services could be used, to accommodate the increased workload due to mandated mental health and domestic violence screening. This is now undertaken (South East Health, Annual Report, 2004-5).

Various challenges may be met, when trying to implement change in policy and practice. The existence of entrenched hierarchies, both midwifery and medical, can be an overwhelming obstacle. Authoritarian clinicians may see evidence based practice as a threat as it may reveal their current practice to be obsolete (Rosenberg, 1995).

Practical strategies, which may aid change acceptance and implementation, are assessing the attitudes and values of staff, identifying barriers to implementation, strategic planning and a SWOT analysis (strengths, weaknesses, opportunities and threats). Barriers to change need to be addressed, if change is to be effective (Walsh, 2001). Further challenges include the perceived divide between research and clinical practice. Researchers are thought to be removed from the 'coal-face' of clinical practice and clinicians and often fail to embrace research recommendations. A useful tool to help bridge this theory practice gap is the clinical audit and it is reputed to be one of the most effective methods of influencing clinicians to change practice. As we have seen from our study, although a urinalysis protocol had been established and highly promoted in our department, adherence to its recommendations was lacking. This issue may not have been discovered, had we not conducted the post research audit. The intervention of further clinical instruction and clarification of the protocol resulted in an improved uptake of the policy. Further regular audits are necessary to insure adherence to the policy continues.

Conclusion

Evidence based practice requires attitudinal change, change in work practices and a commitment to life long self-directed learning. Remaining ignorant of valid research findings has serious consequences. For example, omission of the spot protein/creatinine ratio for the quantification of proteinuria can delay the diagnosis of pre-eclampsia and its management intervention. Women and their families deserve care that is equitable, effective and evidence based.

EPILOGUE: Personal Reflection

In 1998, the *Midwifery Practice and Research Centre* at St George Hospital was successful in securing a NHMRC grant that enabled clinical midwives to participate in research.

Clinical midwives were canvassed for research proposals relevant to midwifery practice. These ideas were presented to an expert panel for adjudication and a research fellowship was awarded to the successful candidates.

Our project proposal questioned the validity of urinalysis in pregnancy and was successful in securing funding. I embarked on my maiden journey into the world of research. It was to be a huge learning curve for me but I was excited and eager for a new challenge. With great enthusiasm, I conducted the first literature search of the project.

Since the early days of the project I can honestly say I have learned so much and have gained professional confidence and personal growth. Before the study, my computer skills were limited; in fact I was almost phobic. Literature searches took me forever and giving a presentation would leave me dry in the mouth and stammering. As I reflect now with amusement on some of those steep learning moments, my introduction to Excel comes to mind. I really had little idea of the various computer programmes and their efficiency at making sense of multitudes of data. About two months into the study, Professor Brown called me and asked to see the data to that date. I proceeded to his office with pages of hand written data. After giving my opinion on its content, he paused, dipped his head and stared at me over the top of his glasses and said, "Have you got this on Excel?" "No", I replied, in a small defeated voice. He then kindly proceeded to draw up a template with information columns and study numbers and thus began my introduction to Excel and data entry.

Public speaking was not something I had much experience of either, so presenting this research at professional conferences was daunting at first. What if I had a mental block?! What if I received a difficult question from the audience?! It was nerve racking. I quickly realised that I was very *au fait* with the literature and the study design, method and that I was part of this work. As one immerses oneself in ones research, the

familiarity with its detail increases. At the last midwives conference where the results and recommendations were presented, I was quite relaxed.

Because of my work undertaking this research I am considered an authority on urinalysis in pregnancy and colleagues now contact me from other midwifery units to discuss the research findings or to congratulate me, and my co researchers on our work. As a result of withdrawing routine urinalysis from the antenatal care of 'low risk' women, there is more time for meaningful and beneficial pursuits for both the midwife and the woman in terms of time for education, mental health screening and health promotion.

Some time has elapsed since the completion of the project and its publication in a professional journal but I have not yet managed to complete my thesis. I have made many attempts but personal life events have prevented any success, namely the birth of our two children Anna Maria aged 4yrs and Andres 20 months. The lack of time for my studies was compounded by the fact, that my son was diagnosed with a rare chromosomal defect and has multiple medical problems, which at the time of writing are improving. The physical, psychological and emotional demands of motherhood can never be underestimated. When I was not able to get to my writing, I had to keep perspective on life and realise that even if I never completed my thesis, the physical and emotional welfare of my two little children was paramount. I would survive without a Masters but they would not survive without a Mum!

Conducting research gives one insight into how difficult research can be, for example, the recruitment process, the monitoring of data collection, finding the right test for analysis. My appreciation of other researchers has increased both in what I read and in the clinical setting, such as the importance of following the research protocol.

The many skills I have gained will enhance my professional ability and I would like to think that I would participate in further research in the future.

I feel privileged and proud to have been part of a research project that has contributed to existing evidence and has enabled positive change to occur in the clinical midwifery setting.

APPENDICES

Appendix A: Instructions for the midwives about the process of the study

Booking visit

1. Each woman is given HULA information sheet and MSU collection instructions.
2. A 'sticky label' will be added to the master list and a study number allocated. The study number will be recorded on the woman's hospital antenatal record. The enrolment data sheet will be completed.
3. A 'clean catch' urine sample (MSU) will be collected.
4. Urinalysis (using Clinitek machine) taken from specimen using sterile dipstick method.
5. Record result on antenatal record.
6. Record results on data sheet. Data sheet to be kept in the womans' notes.
7. MSU sent to pathology with accompanying request for microscopy and culture.
8. Signed consent form will be kept in woman's notes.

Subsequent visits

1. A 'clean catch' MSU sample will be collected, as above.
2. Urinalysis (using Clinitek machine) taken from specimen using sterile dipstick method.
3. Record results on antenatal record.
4. Record results on data sheet.
5. Management of abnormal results: See protocols

Appendix B: Instructions for collection of urine sample (MSU)

The antenatal clinics at St George Hospital have recently standardised their method of urine collection. Please follow these instructions EACH time you come to the antenatal clinic at the hospital or to STOMP clinics. This will allow us to detect any abnormalities in your urine more reliably.

You will be given: 1 yellow top jar (a new one at each visit)
1 packet of cotton balls
1 sachet of normal saline.

Collection procedure

1. Wash your hands
2. Open cotton ball packet
3. Pour cleaning solution over cotton balls
4. Wipe perineum from front to back with the cotton balls
5. Start urinating in the toilet
6. Catch a sample of urine midstream (try not to push the jar against your skin)
7. Finish urinating in the toilet
8. Wash hands
9. Return to the clinic and give specimen to the staff.

Thank you for collecting your sample in this way.

Appendix C: HULA Primary Data Sheet

Enrolment data

MRN	Study number
Enrolment date	
Gestation at enrolment	

Demographic data

Age	
Language at home (use NSW Health codes)	
Parity (circle option)	Nulliparous Multiparous
Number of previous viable births:	

Past history

Essential HT (circle option)	Yes No
Previous PE or GH (circle option)	Yes No
History of renal disease (circle option)	Yes No
If yes, specify:	
Diabetes (circle option)	Yes No
Other (circle option)	Yes No

If yes, specify:	
First trimester BP (from GP referral)	
Gestation at this BP	

Booking visit data

Results of primary MSU	
Booking BP	
Booking UA: • Proteinuria (≥+) • Spot urine prot/creat ratio	Yes No If ≥ 30 was she referred to OMC? Yes No
• Haematuria (trace • Confirmed on urine microscopy in the absence of UTI	Yes No If yes, was she referred to Obstetric Medical Clinic? Yes No
• Other (specify)	

Is this a multiple pregnancy? Yes No

Appendix D: HULA Subsequent Data Sheet

MRN Study number

Visit to SGH clinics	Date	Gestation In weeks	Proteinuria on UA (Y/N)	Glycos-uria on UA (Y/N)	Haem-aturia on UA (Y/N)	Pyuria on UA (Y/N)	Nitrites on UA (Y/N)	Spot urine P/C ratio	Blood pressure	Is this a significant rise (Y/N)
1										
2										
3										
4										
5										
6										
7										
8										
9										
10										

Was the woman diagnosed with HT? Yes No

Was this PE? Yes No

Gestational HT? Yes No

Cause of Haematuria ?

Appendix E: Information Statement: The HULA Study

The St George Hospital

INFORMATION STATEMENT

The HULA Study

The St George Hospital is currently conducting the HULA study, which is looking at the value of routine testing of urine in the antenatal clinics at the hospital and at the community outreach clinics at Rockdale and Hurstville. In this study we are testing all women's urine in a standard way and are collecting information from their records on the results of their urine tests and their blood pressure readings. We hope this information will help us decide whether it is beneficial to test urine in the clinics as we currently do.

All women who come to this hospital for antenatal care between February and July 1999 will be part of this study. Nothing different will happen to you in the clinic except from now on you will be given a clean urine jar at each visit and will be asked to collect the specimen in a standard way. The midwives will explain the standard method to you. You will not be inconvenienced by this study in any other way

This is a study observing the standard way of collecting and testing urine. There will be no difference to your care. We are simply interested in observing what happens when women collect urine, and we test urine, in standard ways.

Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or except as required by law. At the end of the year, we plan to publish the results of our observations in a report. In any publication, information will be provided in such a way that you cannot be identified. If your require further information, please contact Noreen Murray, one of the midwives coordinating the study on 9350 1111 page 212.

Complaints may be directed to the Ethics Secretariat, South Eastern Sydney Area Health Service Research

Ethics Committee (Southern Section). St. George Hospital. Gray St., Kogarah 2217. Tel: 9350 2986 Fax: 9350 2988. Email: nhcn@ozemail.com.au

Thank you for helping us with the HULA study.

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