A prevalence survey of acute self-reported infections in pregnancy

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A prevalence survey of acute self-reported infections in pregnancy

Running head: Prevalence of acute infections in pregnancy

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Abstract

Objective

The objective of this study was to estimate the weekly prevalence of the onset of self-reported infection in women at least 20 weeks pregnant.

Design

We conducted a survey of pregnant women in a hospital antenatal clinic in Sydney Australia between August 2008 and April 2009. Women were asked to report whether they had an infection in the seven days prior to completing the questionnaire, and were asked details of symptoms and medication taken.

Results

A total of 737 women at least 20 weeks pregnant completed the survey; 94% of women approached. Five per cent of the questionnaires completed reported the onset of an infection in the seven days prior to survey completion. When symptoms were analysed, 3.5% of women were classified as having a moderate or severe infection in the past seven days. The most common infection reported was a cold/upper respiratory tract infection followed by gastroenteritis. Women pregnant with their first child had a lower rate of self-reported infection than women who had other children (2.9% vs 7.2%).

Conclusions

These results can be used to inform future research examining acute infection as a trigger for pregnancy complications.

Key words: pregnancy, infection, prevalence, obstetrics, crossover studies

Article summary

Article focus

- Survey to ascertain the prevalence of the onset of infections in any seven day period during the second half of pregnancy
- Information regarding type of infection and medication taken to treat infection were also collected

Key message:

- Five per cent of women at least 20 weeks pregnant reported the onset of an infection in the prior seven days, 3.5% of these women had a moderate or severe infection
- Only 21% of women reporting an infection sought medical care while 65% took medication to treat the infection
- This information can be used to inform future research into acute infections as a possible trigger for pregnancy complications such as pre-eclampisa.

Strengths and limitations of this study:

- Strengths include the estimate of prevalence of infection in a short-term window of time rather than at any time during pregnancy to inform research into acute triggers of pregnancy complications, and the use of information regarding symptoms and medication taken to distinguish between mild and more severe infections.
- Limitations include the use of self-reported infection however this is a tool that has previously been used to report infection in a number of populations.

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Competing interests statement

The author(s) declare that they have no competing interests.

Authors' contributions and acknowledgements

SJL designed and administered the survey, analysed data and drafted manuscript. CLR and JBF developed the study and helped design survey. CLR, JBF, JVT and JW contributed to data analysis and interpretation. All authors edited the manuscript and gave final approval of the version to be published.

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Background

Acute infections during pregnancy are associated with adverse outcomes including miscarriage, preterm prelabour rupture of membranes, preterm birth and stillbirth[1-3]. Epidemiological evidence suggests that maternal infections may precipitate other complications of pregnancy including preeclampsia[4]. Early pregnancy evokes a mild and limited systemic inflammatory response with increased levels of pro-inflammatory mediators such as prostaglandin E_2 (PGE_2), tumor necrosis factor (TNF)-α[5], interleukins 1 and 6.[6,7] These inflammatory mediators promote vascular remodelling and placental invasion, necessary in early pregnancy to ensure adequate fetal growth. The placenta reaches its full size by about 20 weeks. Vascular remodelling is complete, and as expected, a concurrent decrease in circulating inflammatory markers has been observed.[8-10] In clinically normal pregnancies, maternal inflammation remains subdued until the onset of labour, when PGE_2 and proinflammatory cytokines mediate the ripening of the cervix, rupture of membranes, and myometiual contractility.[11,12] Therefore, acute infection may trigger perturbations in the temporal control of maternal inflammation, causing adverse pregnancy outcomes.[13,14] The maternal immune response to such an infection could mimic the cytokine milieu involved in the onset of labour.

Previous studies in pregnancy have centred on specific infections such as urinary tract infection and periodontal disease rather than investigating prevalence of all infections which may evoke an inflammatory response. Acute infectious episodes are known to increase the risk of cardiovascular diseases (CVD) including the risk of first-time myocardial infarction and stroke. Studies of these diseases suggest the effect of infection may be generic and not linked to specific types of infection.[15] The current

study arose out of the design phase of a similar study among pregnant women, to investigate the possible role of infection and other acute triggers in the onset of preeclampsia, an acute hypertensive disorder of pregnancy. An accurate estimate of the prevalence rate of infections during the second half of pregnancy (when women are at risk of preeclampsia) is necessary to calculate the study sample size; a simple overall infection rate will not suffice when assessing acute triggers. Few studies have assessed the prevalence of acute infections during pregnancy and none have addressed the specific issue of timing during pregnancy[4]. Use of 'infection at any time during during pregnancy' may result in systematic misclassification of exposure and dilution of the true risk of complications occurring later in pregnancy. The aim of this current study is to ascertain the prevalence of the onset of infections in any seven day period during the second half of pregnancy.

Methods

The study was conducted in the antenatal clinic of a teaching hospital with tertiary obstetric and neonatal care facilities in Sydney, Australia between August 2008 and April 2009. Methods have been described in detail previously in a separate report of recent activities during pregnancy[16]. Briefly, women who were at least 20 weeks pregnant and able to complete the questionnaire in English were eligible. Women were approached in the antenatal clinic by a trained researcher not involved in their medical care and completed a short questionnaire after giving informed consent. The questionnaire was developed from a review of literature and discussion with clinical staff and was piloted prior to study commencement.

The questionnaire asked women about demographic characteristics and whether they had an infection during their pregnancy. Other studies have similarly identified recent

infections using self-report[17-21] and concordance studies find this to be reliable[22-25]. In the questionnaire, infection was defined as "symptoms lasting more than 24 hours that you think were caused by an infection". Participants were also prompted with a list of examples such as a cold or flu, urinary tract infection, thrush, tooth abscess or an infected wound when considering if they had an infection in the past seven days. The questionnaire sought information about infection in the seven days prior to its completion, so women were eligible to complete the survey more than once, providing there was at least fourteen days between each questionnaire. If the women responded that they had an infection in the last 7 days they were asked to record perceived severity (mild, moderate or severe) of symptoms from a provided list (see Figure 1). Details were also collected regarding medical advice sought, tests received and medication taken for their infection. Details of symptoms and medication were used to analyse severity of infections. Women who had taken antibiotics or had three or more symptoms that they rated as moderate or severe were classified as having a 'moderate/severe' infection. As the timing of the onset of infection was important, women were given a calendar to help prompt them with the date of onset of infection and were also asked how confident they were of the date the infection first appeared.

Survey data were analysed using frequency tabulations and contingency table analyses. Stratified analysis, using chi square tests, examined the impact of gestational age, parity, plurality, maternal education and other medical conditions on the prevalence of infection. This study was approved by the Northern Sydney and Central Coast Human Research Ethics Committee.

Results

Among women who were at least 20 weeks pregnant approached to complete the survey, 738 (94%) agreed to participate; 97% when approached for the first time and 87% when approached to complete the survey for a subsequent time. A total of 737 surveys were completed, including 161 women completed the survey more than once. The only significant difference between women completing the survey more than once and those who only completed one survey was increased gestational age. The majority of the women that completed the survey were over 30 years of age, had a University degree, and were having their first baby (see Table 1).

Forty per cent of women surveyed said that they had had an infection at some stage during their pregnancy. Five per cent of the surveys completed reported the onset of an infection in the seven days prior to survey completion (see Table 2) and 5.7% reported the onset of an infection 7 to 14 days before completing survey. For women who reported an infection in the seven days prior to completing the survey, the most common infection was a cold/upper respiratory tract infection with a prevalence rate of 2.6%, followed by gastroenteritis or vomiting (0.7%), influenza (0.5%), candidiasis (0.4%) and urinary tract infection (0.4%). When only 'moderate/severe' infections were examined, the weekly prevalence of the onset of any infection decreased to 3.5% and the prevalence of the onset of a cold/upper respiratory tract infection in the seven days prior to survey completion decreased to 1.2%.

Table 2 shows the weekly prevalence of the onset of infection by demographic and pregnancy variables. The prevalence of onset of infection differed significantly by parity, plurality and for women who had high blood pressure. Less women who were

pregnant for the first time reported the onset of an infection compared to women who were pregnant for a second or subsequent time (2.9% vs 7.2%, p = 0.008). Women who were pregnant with twins reported a higher prevalence of infection than women pregnant with a singleton (16.1% vs 4.5%, p = 0.004), however there was no difference between groups in the prevalence of moderate/severe infection. Women that reported having a hypertensive disorder of pregnancy reported more infection than women without a medical condition (15.3% vs 4.6%, p = 0.01).

Of those women reporting an infection in the seven days prior to survey completion, the proportion who sought medical advice or took medication are outlined in Table 3. Twenty one per cent of women with an infection saw a health care professional and 65% took some type of medication to treat the infection. Most commonly paracetamol /acetaminophen was taken, followed by antibiotics and 5% of women with an infection reported taking aspirin. Just over 50% of women reporting an infection stated that they had a fever and a third of these women reported having their temperature taken. The two women that reported having an investigative test performed had urine samples taken for urinary tract infections. The highest rates of onset of any infection in the seven days prior to the survey were in the southern hemisphere winter month of August (11.5%) while January (summer) had the lowest infection rate (0.6%). Most women (92%) were confident or very confident of the date when symptoms of infection first appeared.

Discussion

This is the first study to look at the prevalence of infection in a seven day window in pregnant women. There are a number of studies that report the prevalence of select infections at any time during pregnancy and it is necessary to estimate weekly rates

for comparison to these studies. Our study found a lower prevalence of self-reported infection during the whole pregnancy (40%) than Collier *et al*[17] (64%) however they included first trimester. Weekly rates for specific infections in pregnancy reported in other studies include: urinary tract infection 0.2% to 0.5%[17 26,27] (similar to 0.4% reported in our study), gastroenteritis 0.8%[20] (0.7% in this study), influenza 0.1%[27] (0.5% in this study), acute respiratory infectious disease 0.2%[28] and the common cold 0.4%[29] (compared to 1.2% of moderate/severe upper respiratory tract infections reported in this study). Our study has a higher prevalence rate for the common cold however a population-based cohort study in Canada found the weekly rate of acute respiratory illness severe enough to require a physician visit ranged from 1.1% to 1.9%[30], similar to the prevalence rate of severe colds observed in this study.

We found the prevalence of the onset of infection was higher for women who had previously been pregnant. Children are prone to developing infections[20] which could be easily transferred to the mother. An unexpected yet interesting finding from the survey was the increased prevalence of infection in women with a hypertensive disorder of pregnancy, although the confidence intervals around the prevalence estimate are very wide. This result is of particular interest because the estimate of prevalence of infection in pregnant women from this survey is to inform future research about infection and preeclampsia. The authors propose using the prevalence estimates of infection obtained from the current study for a case-crossover study investigating the role of acute infection and other acute triggers in the onset of preeclampsia. The current study however was not designed to examine infection rates in pregnant women with hypertension. In this cross-sectional survey it was not possible to establish whether the hypertension or the infection occurred first.

The reliance upon self-report of infection is a potential limitation of the study with only 21% of women reporting an infection seeking medical attention, however mild infections that do not come to medical attention may still be a risk for pregnancy complications[17]. Self-report of infection has been used to estimate prevalence of gastroenteritis[20], influenza and fever[19 21], and genitourinary infections[18] in pregnant women. Banhidy *et al* collected information about infection both from prospectively collected medical data and self-report from women in a post-natal questionnaire[25 28]. They found that 74% of women reporting an acute respiratory disease during pregnancy had the disease recorded in their medical records[28] and 95% of women with a medically recorded urinary tract infection self-reported the infection[25]. Our study also collected information about severity of symptoms experienced and medication taken which helped to distinguish between mild and more severe infections. This stratified analysis of reported infections increases the certainty that women who experienced a severe infection truly did have an infection.

The use of self reported data may be affected by recall bias. One study using self-report of any infection during pregnancy recommended 'future studies should emphasize the importance of interviewing women as early as possible'[17] as mother's tend to under-report infection when recalling information after birth[31]. The short window of time to recall details of infection in our study (seven days) minimises this recall bias.

A further limitation of this study is that the study population is older than the general population of pregnant women in Australia[26], is highly educated and was restricted to

English speaking participants. Although this may impact the generalisability of the results, such characteristics are representative of the women that attend this hospital. Notably age or education level did not have a significant effect on the infection rate. Strengths of this paper include the investigation of any infection rather than being limited to single infections; and the investigation of acute rather than longer-term infections which may be over-estimated if weekly prevalence rates rather than date of infection onset are used.

Conclusions

This survey is the first study to estimate the weekly prevalence of infection in a population of pregnant women. The results of this study will be used to inform future research examining the association between acute infection and pregnancy complications such as preeclampsia. This study also informs clinicians about the types of infections and medications pregnant women are exposed to.

Table 1: The characteristics of women surveyed

	N (%)
All surveys completed	737
Women that have completed survey only once	576 (78.2)
Maternal age	
< 25 years	55 (7.5)
25 – 34 years	430 (58.3)
≥ 35 years	247 (33.5)
Gestational age	
20 – 28 weeks	241 (32.7)
29 – 34 weeks	172 (23.3)
35 – 42 weeks	324 (44.0)
Plurality	
Singleton	705 (95.7)
Twins/Triplets	31 (4.2)
Parity	
Nulliparous	376 (51.0)
Multiparous	360 (48.8)
Highest level of education completed	
Without University degree	313 (42.5)
With University degree	422 (57.3)
Medical conditions (pre-existing or pregnancy related)	

No medical conditions	564 (76.5)
Asthma	69 (9.4)
High blood pressure	25 (3.4)
Diabetes	46 (6.2)
Other	32 (4.3)
Smoking status	
Did not smoke during pregnancy	708 (96.1)
Smoked cigarettes during pregnancy	29 (3.9)

Table 2: The characteristics of women without and without a self-reported infection, and the weekly prevalence rate, per 100 surveys, of infection in the seven days prior to completing the survey

	Women with self-reported infection N	Weekly prevalence of self-reported infection % (95% CI)
All surveys completed	37	5.0 [3.4 – 6.6]
Women that have completed survey only once	28	4.8 [3.1 – 6.6]
Maternal age		
< 25 years	3	5.5 [0.0 – 10.7]
25 – 34 years	18	4.2 [2.3 – 6.1]
≥ 35 years	16	6.5 [3.4 – 9.6]
Gestational age		
20 – 28 weeks	10	4.2 [1.6 – 6.7]
29 – 34 weeks	9	5.2 [1.9 – 8.6]
35 – 42 weeks	18	5.6 [3.0 – 8.1]
Plurality		
Singleton	32	4.5 [3.0 – 6.1]
Twins/Triplets	5	16.1 [2.4 – 29.8]
Parity		
Nulliparous	11	2.9 [1.2 – 4.6]
Multiparous	26	7.2 [4.5 – 9.9]
Highest level of education completed		

Without University degree	14	4.5 [2.2 – 6.8]
With University degree	23	5.5 [3.3 – 7.6]
Medical conditions (pre-existing or pregnancy related)		
No medical conditions	26	4.6 [2.9 – 6.3]
Asthma	4	5.8 [0.1 – 11.5]
High blood pressure	4	15.3 [0.5 – 30.2]
Diabetes	3	6.5 [0.0 – 13.9]
Other	0	0.0
Smoking status		
Did not smoke during pregnancy	36	5.1, [3.5 – 6.7]
Smoked cigarettes during pregnancy	1	3., [0.0 – 10.5]

Table 3. Medication taken or health advice sought by women with self-reported infection

	N	%
	37	
Medication taken		
Paracetamol /acetaminophen	12	32.4%
Aspirin	2	5.4%
Antibiotics	7	18.9%
None	3	8.1%
Other*	13	35.1%
Medical Care		
Advice sought from doctor	8	21.6%
Medical test/investigation performed	2	5.4%
Temperature taken	7	18.9%

*Includes antifungal cream, antibacterial throat lozenges and gargle

Figure 1. List of symptoms that participants who reported having an infection were asked about details of severity (none, mild, moderate or severe)

See attached file

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General symptoms for infection
- Fever
- Night sweats / chills
- Fatigue / weakness

Upper respiratory tract infection (e.g. A cold, influenza, tonsillitis)
- Runny nose or blocked nose
- Sneezing
- Sore throat
- Headache, sinus/face pain
- Swollen glands

Lower respiratory tract infection (e.g. Pneumonia, bronchitis)
- Dry cough
- Productive cough (coughing up phlegm or mucous)
- Shortness of breath
- Chest pain
- Pain when breathing

Urinary tract infection (e.g. Bladder or kidney infections)
- Burning sensation when urinating
- Cloudy or foul-smelling urine
- Pus or blood in urine
- Frequent urination
- Urgency, pressure or pain in bladder

Genital tract infection (e.g. Thrush)
- Abnormal vaginal discharge with an unpleasant smell
- Intense itching, swelling and irritation

Gastro-intestinal infection (e.g. Food poisoning)
- Nausea, vomiting (other than morning sickness)
- Diarrhea
- Stomach pain

Other infections
- Tooth abscess
- Infected cut or scratch / Wound infection
- Skin infection / boils

207x218mm (96 x 96 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5, 6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	14
Outcome data	15*	Report numbers of outcome events or summary measures	16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	16, 17
		(*b*) Report category boundaries when continuous variables were categorized	14, 16
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Subject Heading:	Obstetrics & gynaecology
Keywords:	Maternal medicine < OBSTETRICS, Prenatal diagnosis < OBSTETRICS, PERINATOLOGY, QUALITATIVE RESEARCH

A survey of acute self-reported infections in pregnancy

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Abstract

Objective

The objective of this study was to estimate the weekly incidence of self-reported infections in women at least 20 weeks pregnant.

Design

We conducted a cross-sectional survey of pregnant women in a hospital antenatal clinic in Sydney Australia between August 2008 and April 2009. Women were asked to report whether they had the onset of a new infection in the seven days prior to completing the questionnaire, and were asked details of symptoms and medication taken.

Results

A total of 737 women at least 20 weeks pregnant completed the survey; 94% of women approached. Five per cent of the questionnaires completed reported the onset of an infection in the seven days prior to survey completion. When symptoms were analysed, 3.5% of women were classified as having a moderate or severe infection in the past seven days. The most common infection reported was a cold/upper respiratory tract infection followed by gastroenteritis. Women pregnant with their first child had a lower rate of self-reported infection than women who had other children (2.9% vs 7.2%).

Conclusions

These results can be used to inform future research examining acute infection as a trigger for pregnancy complications.

Key words: pregnancy, infection, incidence, obstetrics, crossover studies

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Article summary

Article focus

- Survey to ascertain the incidence of new infections in any seven day period during the second half of pregnancy
- Information regarding type of infection and medication taken to treat infection were also collected

Key message:

- Five per cent of women at least 20 weeks pregnant reported the onset of a new infection in the prior seven days, 3.5% of these women had a moderate or severe infection
- Only 21% of women reporting an infection sought medical care while 65% took medication to treat the infection
- This information can be used to inform future research into acute infections as a possible trigger for pregnancy complications such as pre-eclampisa.

Strengths and limitations of this study:

- Strengths include the estimate of incidence of infection in a short-term window of time rather than at any time during pregnancy to inform research into acute triggers of pregnancy complications, and the use of information regarding symptoms and medication taken to distinguish between mild and more severe infections.
- Limitations include the use of self-reported infection however this is a tool that has previously been used to report infection in a number of populations.

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Competing interests statement

The author(s) declare that they have no competing interests.

Authors' contributions and acknowledgements

SJL designed and administered the survey, analysed data and drafted manuscript. CLR and JBF developed the study and helped design survey. CLR, JBF, JVT and JW contributed to data analysis and interpretation. All authors edited the manuscript and gave final approval of the version to be published.

We wish to acknowledge the help of research midwives Kristen Rickard, Jill Milligan and Jocelyn Segley with administering surveys in the antenatal clinic.

Background

Acute infections during pregnancy are associated with adverse outcomes including miscarriage, preterm prelabour rupture of membranes, preterm birth and stillbirth[1-3]. Epidemiological evidence suggests that maternal infections may precipitate other complications of pregnancy including preeclampsia[4]. Early pregnancy evokes a mild and limited systemic inflammatory response with increased levels of pro-inflammatory mediators such as prostaglandin E_2 (PGE_2), tumor necrosis factor (TNF)-α[5], interleukins 1 and 6.[6,7] These inflammatory mediators promote vascular remodelling and placental invasion, necessary in early pregnancy to ensure adequate fetal growth. The placenta reaches its full size by about 20 weeks, by which time, vascular remodelling is complete and a concurrent decrease in circulating inflammatory markers has been observed.[8-10] In clinically normal pregnancies, maternal inflammation remains subdued until the onset of labour, when PGE_2 and proinflammatory cytokines mediate the ripening of the cervix, rupture of membranes, and myometrial contractility.[11,12] Therefore, acute infection may trigger perturbations in the temporal control of maternal inflammation, causing adverse pregnancy outcomes.[13,14] The maternal immune response to such an infection could mimic the cytokine milieu involved in the onset of labour.

Previous studies in pregnancy have centred on specific infections such as urinary tract infection and periodontal disease rather than investigating incidence of all acute infections which may evoke an inflammatory response. Acute infectious episodes are known to increase the risk of cardiovascular diseases (CVD) including the risk of first-time myocardial infarction and stroke. Studies of these diseases suggest the effect of infection may be generic and not linked to specific types of infection.[15] The current

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study arose out of the design phase of a similar study among pregnant women, to investigate the possible role of infection and other acute triggers in the onset of preeclampsia, an acute hypertensive disorder of pregnancy. An accurate estimate of the incidence rate of infections during the second half of pregnancy (when women are at risk of preeclampsia) is necessary to calculate the study sample size; a simple overall infection rate will not suffice when assessing acute triggers. Few studies have assessed the incidence of acute infections during pregnancy and none have addressed the specific issue of timing during pregnancy[4]. Use of 'infection at any time during during pregnancy' may result in systematic misclassification of exposure and dilution of the true risk of complications occurring later in pregnancy. The aim of this current study is to ascertain the incidence of acute infections in any seven day period during the second half of pregnancy.

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Methods

This cross-sectional study was conducted in the antenatal clinic of a teaching hospital with tertiary obstetric and neonatal care facilities in Sydney, Australia between August 2008 and April 2009. Methods have been described in detail previously in a separate report of recent activities during pregnancy[16]. Briefly, women who were at least 20 weeks pregnant and able to complete the questionnaire in English were eligible. Women were approached in the antenatal clinic by a trained researcher not involved in their medical care and completed a short questionnaire after giving informed consent. The questionnaire was developed from a review of literature and discussion with clinical staff and was piloted prior to study commencement.

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The questionnaire asked women about demographic characteristics and whether they had an infection during their pregnancy. Other studies have similarly identified recent

infections using self-report[17-21] and concordance studies find this to be reliable[22-25]. In the questionnaire, infection was defined as "symptoms lasting more than 24 hours that you think were caused by an infection" and onset of the most recent infection was identified as in the last 7, 8-14 or >14 days. Detailed information was only asked for the new infections in the last 7 days. Participants were also prompted with a list of examples such as a cold or flu, urinary tract infection, thrush, tooth abscess or an infected wound when considering if they had an infection in the past seven days. The questionnaire sought information about infection in the seven days prior to its completion, so women were eligible to complete the survey more than once, providing there was at least fourteen days between each questionnaire. If the women responded that they had an infection in the last 7 days they were asked to record perceived severity (mild, moderate or severe) of symptoms from a provided list (see Figure 1). Details were also collected regarding medical advice sought, tests received and medication taken for their infection. Details of symptoms and medication were used to analyse severity of infections. Women who had taken antibiotics or had three or more symptoms that they rated as moderate or severe were classified as having a 'moderate/severe' infection. As the timing of the onset of infection was important, women were given a calendar to help prompt them with the date of onset of infection and were also asked how confident they were of the date the infection first appeared.

Survey data were analysed using frequency tabulations and contingency table analyses. Stratified analysis, using chi square tests, examined the impact of gestational age, parity, plurality, maternal education and other medical conditions on the incidence of infection. This study was approved by the Northern Sydney and Central Coast Human Research Ethics Committee.

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Results

Among women who were at least 20 weeks pregnant approached to complete the survey, 738 (94%) agreed to participate; 97% when approached for the first time and 87% when approached to complete the survey for a subsequent time. A total of 737 surveys were completed, including 161 women completed the survey more than once. The significant differences between women completing the survey more than once and those who only completed one survey were increased gestational age, women with multiple pregnancies and women with university degrees[16]. The majority of the women that completed the survey were over 30 years of age, had a University degree, and were having their first baby (see Table 1).

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Forty per cent of women surveyed said that they had had an infection at some stage during their pregnancy. Five per cent of the surveys completed reported the onset of an infection in the seven days prior to survey completion (see Table 2) and 5.7% reported the onset of an infection 7 to 14 days before completing survey. For women who reported an infection in the seven days prior to completing the survey, the most common infection was a cold/upper respiratory tract infection with an incidence rate of 2.6%, followed by gastroenteritis or vomiting (0.7%), influenza (0.5%), candidiasis (0.4%) and urinary tract infection (0.4%). When only 'moderate/severe' infections were examined, the weekly incidence ofany new infection decreased to 3.5% and the incidence of a cold/upper respiratory tract infection in the seven days prior to survey completion decreased to 1.2%.

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Table 2 shows the weekly incidence of infections by demographic and pregnancy variables. The incidence of infection differed significantly by parity, plurality and for

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women who had high blood pressure. Less women who were pregnant for the first time reported the onset of an infection compared to women who were pregnant for a second or subsequent time (2.9% vs 7.2%, p = 0.008). Women who were pregnant with twins reported a higher incidence of infection than women pregnant with a singleton (16.1% vs 4.5%, p = 0.004), however there was no difference between groups in the incidence of moderate/severe infection. Women that reported having a hypertensive disorder of pregnancy reported more infection than women without a medical condition (15.3% vs 4.6%, p = 0.01).

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Of those women reporting an infection in the seven days prior to survey completion, the proportion who sought medical advice or took medication are outlined in Table 3. Twenty one per cent of women with an infection saw a health care professional and 65% took some type of medication to treat the infection. Most commonly paracetamol /acetaminophen was taken, followed by antibiotics and 5% of women with an infection reported taking aspirin. Just over 50% of women reporting an infection stated that they had a fever and a third of these women reported having their temperature taken. The two women that reported having an investigative test performed had urine samples taken for urinary tract infections. The highest incidence of infection in the seven days prior to the survey was in the southern hemisphere winter month of August (11.5%) while January (summer) had the lowest infection rate (0.6%). Most women (92%) were confident or very confident of the date when symptoms of infection first appeared.

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Discussion

This is the first study to look at the incidence of infection in a seven day window in pregnant women. There are a number of studies that report the rate of selected

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infections at any time during pregnancy and it is necessary to estimate weekly rates for comparison to these studies, assuming a constant rate of infection by week of gestation. Our study found a lower rate of self-reported infection during the whole pregnancy (40%) than Collier *et al*[17] (64%) however they included first trimester. Weekly rates for specific infections in pregnancy reported in other studies include: urinary tract infection 0.2% to 0.5%[17 26,27] (similar to 0.4% reported in our study), gastroenteritis 0.8%[20] (0.7% in this study), influenza 0.1%[27] (0.5% in this study), acute respiratory infectious disease 0.2%[28] and the common cold 0.4%[29] (compared to 1.2% of moderate/severe upper respiratory tract infections reported in this study). Our study has a higher incidence rate for the common cold however a population-based cohort study in Canada found the weekly rate of acute respiratory illness severe enough to require a physician visit ranged from 1.1% to 1.9%[30], similar to the incidence rate of severe colds observed in this study. As each completed questionnaire was anonymous, we could not determine whether any of the infections were recurrent and it is possible that some of the reported infections were chronic rather than acute.

We found the incidence of acute infections was higher for women who had previously been pregnant and, for mild infections, women with twin pregnancies. Children are prone to developing infections[20] which could be easily transferred to the mother. Women pregnant with multi-fetal pregnancies may have increased antenatal visits and surveillance by clinicians, and this may lead to an increase in the reporting of infections. An unexpected yet interesting finding from the survey was the increased incidence of infection in women with a hypertensive disorder of pregnancy, although this rate is based on small numbers and the confidence intervals around the incidence

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estimate are very wide. This result is of particular interest because the estimate of incidence of infection in pregnant women from this survey is to inform future research about infection and preeclampsia. The authors propose using the incidence estimates of infection obtained from the current study for a case-crossover study investigating the role of acute infection and other acute triggers in the onset of preeclampsia. The current study however was not designed to examine infection rates in pregnant women with hypertension. In this cross-sectional survey it was not possible to establish whether the hypertension or the infection occurred first.

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The reliance upon self-report of infection is a potential limitation of the study with only 21% of women reporting an infection seeking medical attention, however mild infections that do not come to medical attention may still be a risk for pregnancy complications[17]. Self-report of infection has been used to estimate the rates of gastroenteritis[20], influenza and fever[19 21], and genitourinary infections[18] in pregnant women. Banhidy *et al* collected information about infection both from prospectively collected medical data and self-report from women in a post-natal questionnaire[25 28]. They found that 74% of women reporting an acute respiratory disease during pregnancy had the disease recorded in their medical records[28] and 95% of women with a medically recorded urinary tract infection self-reported the infection[25]. Our study also collected information about severity of symptoms experienced and medication taken which helped to distinguish between mild and more severe infections. This stratified analysis of reported infections increases the certainty that women who experienced a severe infection truly did have an infection.

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The use of self reported data may be affected by recall bias. One study using self-report of any infection during pregnancy recommended 'future studies should emphasize the importance of interviewing women as early as possible'[17] as mother's tend to under-report infection when recalling information after birth[31]. The short window of time to recall details of infection in our study (seven days) minimises this recall bias.

A further limitation of this study is that the study population is older than the general population of pregnant women in Australia[26], is highly educated and was restricted to English speaking participants. Although this may impact the generalisability of the results, such characteristics are representative of the women that attend this hospital. Notably age or education level did not have a significant effect on the total infection rate, although a larger sample size may show an association between these factors and sexually transmitted infections. Strengths of this paper include the investigation of any infection rather than being limited to single infections; and the investigation of acute rather than chronic infections which may be over-estimated if weekly incidence rates rather than date of infection onset are used.

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Conclusions

This survey is the first study to estimate the weekly incidence of acute infections in a population of pregnant women. The results of this study will be used to inform future research examining the association between acute infection and pregnancy complications such as preeclampsia. This study also informs clinicians about the types of infections and medications pregnant women are exposed to.

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Table 1: The characteristics of women surveyed

	N (%)
All surveys completed	737
Women that have completed survey only once	576 (78.2)
Maternal age	
< 25 years	55 (7.5)
25 – 34 years	430 (58.3)
≥ 35 years	247 (33.5)
Gestational age	
20 – 28 weeks	241 (32.7)
29 – 34 weeks	172 (23.3)
35 – 42 weeks	324 (44.0)
Plurality	
Singleton	705 (95.7)
Twins/Triplets	31 (4.2)
Parity	
Nulliparous	376 (51.0)
Multiparous	360 (48.8)
Highest level of education completed	
Without University degree	313 (42.5)
With University degree	422 (57.3)
Medical conditions (pre-existing or pregnancy related)	

No medical conditions	564 (76.5)
Asthma	69 (9.4)
High blood pressure	25 (3.4)
Diabetes	46 (6.2)
Other	32 (4.3)
Smoking status	
Did not smoke during pregnancy	708 (96.1)
Smoked cigarettes during pregnancy	29 (3.9)

Table 2: The characteristics of women without and without a self-reported infection, and the weekly incidence rate, per 100 surveys, of infection in the seven days prior to completing the survey

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	Women with self-reported infection N	Weekly incidence of self-reported infection % (95% CI)
All surveys completed	37	5.0 [3.4 – 6.6]
Women that have completed survey only once	28	4.8 [3.1 – 6.6]
Maternal age		
< 25 years	3	5.5 [0.0 – 10.7]
25 – 34 years	18	4.2 [2.3 – 6.1]
≥ 35 years	16	6.5 [3.4 – 9.6]
Gestational age		
20 – 28 weeks	10	4.2 [1.6 – 6.7]
29 – 34 weeks	9	5.2 [1.9 – 8.6]
35 – 42 weeks	18	5.6 [3.0 – 8.1]
Plurality		
Singleton	32	4.5 [3.0 – 6.1]
Twins/Triplets	5	16.1 [2.4 – 29.8]
Parity		
Nulliparous	11	2.9 [1.2 – 4.6]
Multiparous	26	7.2 [4.5 – 9.9]
Highest level of education completed		

Without University degree	14	4.5 [2.2 – 6.8]
With University degree	23	5.5 [3.3 – 7.6]
Medical conditions (pre-existing or pregnancy related)		
No medical conditions	26	4.6 [2.9 – 6.3]
Asthma	4	5.8 [0.1 – 11.5]
High blood pressure	4	15.3 [0.5 – 30.2]
Diabetes	3	6.5 [0.0 – 13.9]
Other	0	0.0
Smoking status		
Did not smoke during pregnancy	36	5.1, [3.5 – 6.7]
Smoked cigarettes during pregnancy	1	3., [0.0 – 10.5]

Table 3. Medication taken or health advice sought by women with self-reported infection

	N	%
	37	
Medication taken		
Paracetamol /acetaminophen	12	32.4%
Aspirin	2	5.4%
Antibiotics	7	18.9%
None	3	8.1%
Other*	13	35.1%
Medical Care		
Advice sought from doctor	8	21.6%
Medical test/investigation performed	2	5.4%
Temperature taken	7	18.9%

*Includes antifungal cream, antibacterial throat lozenges and gargle

Figure 1. List of symptoms that participants who reported having an infection were asked about details of severity (none, mild, moderate or severe)

See attached file

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General symptoms for infection
- Fever
- Night sweats / chills
- Fatigue / weakness

Upper respiratory tract infection (e.g. A cold, influenza, tonsillitis)
- Runny nose or blocked nose
- Sneezing
- Sore throat
- Headache, sinus/face pain
- Swollen glands

Lower respiratory tract infection (e.g. Pneumonia, bronchitis)
- Dry cough
- Productive cough (coughing up phlegm or mucous)
- Shortness of breath
- Chest pain
- Pain when breathing

Urinary tract infection (e.g. Bladder or kidney infections)
- Burning sensation when urinating
- Cloudy or foul-smelling urine
- Pus or blood in urine
- Frequent urination
- Urgency, pressure or pain in bladder

Genital tract infection (e.g. Thrush)
- Abnormal vaginal discharge with an unpleasant smell
- Intense itching, swelling and irritation

Gastro-intestinal infection (e.g. Food poisoning)
- Nausea, vomiting (other than morning sickness)
- Diarrhea
- Stomach pain

Other infections
- Tooth abscess
- Infected cut or scratch / Wound infection
- Skin infection / boils

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5, 6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	14
Outcome data	15*	Report numbers of outcome events or summary measures	16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	16, 17
		(*b*) Report category boundaries when continuous variables were categorized	14, 16
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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A survey of acute self-reported infections in pregnancy

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A survey of acute self-reported infections in pregnancy

Running head: Prevalence of acute infections in pregnancy

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Abstract

Objective

The objective of this study was to estimate the weekly prevalence of self-reported recently-acquired infections in women at least 20 weeks pregnant.

Design

We conducted a cross-sectional survey of pregnant women in a hospital antenatal clinic in Sydney Australia between August 2008 and April 2009. Women were asked to report whether they had the onset of a new infection in the seven days prior to completing the questionnaire, and were asked details of symptoms and medication taken.

Results

A total of 737 women at least 20 weeks pregnant completed the survey; 94% of women approached. Five per cent of the questionnaires completed reported the onset of an infection in the seven days prior to survey completion. When symptoms were analysed, 3.5% of women were classified as having a moderate or severe infection in the past seven days. The most common infection reported was a cold/upper respiratory tract infection followed by gastroenteritis. Women pregnant with their first child had a lower rate of self-reported infection than women who had other children (2.9% vs 7.2%).

Conclusions

These results can be used to inform future research examining acute infection as a trigger for pregnancy complications.

Key words: pregnancy, infection, prevalence, obstetrics, crossover studies

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Article summary

Article focus

- Survey to ascertain the period prevalence of self-reported new infections in any seven day period during the second half of pregnancy
- Information regarding type of infection and medication taken to treat infection were also collected

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Key message:

- Five per cent of women at least 20 weeks pregnant reported the onset of a new infection in the prior seven days, 3.5% of these women had a moderate or severe infection
- Only 21% of women reporting an infection sought medical care while 65% took medication to treat the infection
- This information can be used to inform future research into acute infections as a possible trigger for pregnancy complications such as pre-eclampisa.

Strengths and limitations of this study:

- Strengths include the estimate of prevalence of infection in a short-term window of time rather than at any time during pregnancy to inform research into acute triggers of pregnancy complications, and the use of information regarding symptoms and medication taken to distinguish between mild and more severe infections.
- Limitations include the use of self-reported infection however this is a tool that has previously been used to report infection in a number of populations.

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Competing interests statement

The author(s) declare that they have no competing interests.

Authors' contributions and acknowledgements

SJL designed and administered the survey, analysed data and drafted manuscript. CLR and JBF developed the study and helped design survey. CLR, JBF, JVT and JW contributed to data analysis and interpretation. All authors edited the manuscript and gave final approval of the version to be published.

We wish to acknowledge the help of research midwives Kristen Rickard, Jill Milligan and Jocelyn Segley with administering surveys in the antenatal clinic.

Background

Acute infections during pregnancy are associated with adverse outcomes including miscarriage, preterm prelabour rupture of membranes, preterm birth and stillbirth[1-3]. Epidemiological evidence suggests that maternal infections may precipitate other complications of pregnancy including preeclampsia[4]. Early pregnancy evokes a mild and limited systemic inflammatory response with increased levels of pro-inflammatory mediators such as prostaglandin E_2 (PGE_2), tumor necrosis factor (TNF)-α[5], interleukins 1 and 6.[6,7] These inflammatory mediators promote vascular remodelling and placental invasion, necessary in early pregnancy to ensure adequate fetal growth. The placenta reaches its full size by about 20 weeks, by which time, vascular remodelling is complete and a concurrent decrease in circulating inflammatory markers has been observed.[8-10] In clinically normal pregnancies, maternal inflammation remains subdued until the onset of labour, when PGE_2 and proinflammatory cytokines mediate the ripening of the cervix, rupture of membranes, and myometrial contractility.[11,12] Therefore, acute infection may trigger perturbations in the temporal control of maternal inflammation, causing adverse pregnancy outcomes.[13,14] The maternal immune response to such an infection could mimic the cytokine milieu involved in the onset of labour.

Previous studies in pregnancy have centred on specific infections such as urinary tract infection and periodontal disease rather than investigating prevalence of all acute infections which may evoke an inflammatory response. Acute infectious episodes are known to increase the risk of cardiovascular diseases (CVD) including the risk of first-time myocardial infarction and stroke. Studies of these diseases suggest the effect of infection may be generic and not linked to specific types of infection.[15] The current

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study arose out of the design phase of a similar study among pregnant women, to investigate the possible role of infection and other acute triggers in the onset of preeclampsia, an acute hypertensive disorder of pregnancy. An accurate estimate of the prevalence rate of infections during the second half of pregnancy (when women are at risk of preeclampsia) is necessary to calculate the study sample size; a simple overall infection rate will not suffice when assessing acute triggers. Few studies have assessed the prevalence of acute infections during pregnancy and none have addressed the specific issue of timing during pregnancy[4]. Use of 'infection at any time during during pregnancy' may result in systematic misclassification of exposure and dilution of the true risk of complications occurring later in pregnancy. The aim of this current study is to ascertain the period prevalence of self-reported new acute infections in any seven day period during the second half of pregnancy.

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Methods

This cross-sectional study was conducted in the antenatal clinic of a teaching hospital with tertiary obstetric and neonatal care facilities in Sydney, Australia between August 2008 and April 2009. Methods have been described in detail previously in a separate report of recent activities during pregnancy[16]. Briefly, women who were at least 20 weeks pregnant and able to complete the questionnaire in English were eligible. Women were approached in the antenatal clinic by a trained researcher not involved in their medical care and completed a short questionnaire after giving informed consent. The questionnaire was developed from a review of literature and discussion with clinical staff and was piloted prior to study commencement.

The questionnaire asked women about demographic characteristics and whether they had an infection during their pregnancy. Other studies have similarly identified recent

infections using self-report[17-21] and concordance studies find this to be reliable[22-25]. In the questionnaire, infection was defined as "symptoms lasting more than 24 hours that you think were caused by an infection" and onset of the most recent infection was identified as in the last 7, 8-14 or >14 days. Detailed information was only asked for the new infections in the last 7 days. Participants were also prompted with a list of examples such as a cold or flu, urinary tract infection, thrush, tooth abscess or an infected wound when considering if they had an infection in the past seven days. The questionnaire sought information about infection in the seven days prior to its completion, so women were eligible to complete the survey more than once, providing there was at least fourteen days between each questionnaire. If the women responded that they had an infection in the last 7 days they were asked to record perceived severity (mild, moderate or severe) of symptoms from a provided list (see Figure 1). Details were also collected regarding medical advice sought, tests received and medication taken for their infection. Details of symptoms and medication were used to analyse severity of infections. Women who had taken antibiotics or had three or more symptoms that they rated as moderate or severe were classified as having a 'moderate/severe' infection. As the timing of the onset of infection was important, women were given a calendar to help prompt them with the date of onset of infection and were also asked how confident they were of the date the infection first appeared.

Survey data were analysed using frequency tabulations and contingency table analyses. Stratified analysis, using chi square tests, examined the impact of gestational age, parity, plurality, maternal education and other medical conditions on the prevalence of infection. This study was approved by the Northern Sydney and Central Coast Human Research Ethics Committee.

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Results

Among women who were at least 20 weeks pregnant approached to complete the survey, 738 (94%) agreed to participate; 97% when approached for the first time and 87% when approached to complete the survey for a subsequent time. A total of 737 surveys were completed, including 161 women completed the survey more than once. The significant differences between women completing the survey more than once and those who only completed one survey were increased gestational age, women with multiple pregnancies and women with university degrees[16]. The majority of the women that completed the survey were over 30 years of age, had a University degree, and were having their first baby (see Table 1).

Forty per cent of women surveyed said that they had had an infection at some stage during their pregnancy. Five per cent of the surveys completed reported the onset of an infection in the seven days prior to survey completion (see Table 2) and 5.7% reported the onset of an infection 7 to 14 days before completing survey. For women who reported an infection in the seven days prior to completing the survey, the most common infection was a cold/upper respiratory tract infection with an prevalence rate of 2.6%, followed by gastroenteritis or vomiting (0.7%), influenza (0.5%), candidiasis (0.4%) and urinary tract infection (0.4%). When only 'moderate/severe' infections were examined, the weekly prevalence ofany new infection decreased to 3.5% and the prevalence of a cold/upper respiratory tract infection in the seven days prior to survey completion decreased to 1.2%.

Table 2 shows the weekly prevalence of infections by demographic and pregnancy variables. The prevalence of infection differed significantly by parity, plurality and

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for women who had high blood pressure. Less women who were pregnant for the first time reported the onset of an infection compared to women who were pregnant for a second or subsequent time (2.9% vs 7.2%, p = 0.008). Women who were pregnant with twins reported a higher prevalence of infection than women pregnant with a singleton (16.1% vs 4.5%, p = 0.004), however there was no difference between groups in the prevalence of moderate/severe infection. Women that reported having a hypertensive disorder of pregnancy reported more infection than women without a medical condition (15.3% vs 4.6%, p = 0.01).

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Of those women reporting an infection in the seven days prior to survey completion, the proportion who sought medical advice or took medication are outlined in Table 3. Twenty one per cent of women with an infection saw a health care professional and 65% took some type of medication to treat the infection. Most commonly paracetamol /acetaminophen was taken, followed by antibiotics and 5% of women with an infection reported taking aspirin. Just over 50% of women reporting an infection stated that they had a fever and a third of these women reported having their temperature taken. The two women that reported having an investigative test performed had urine samples taken for urinary tract infections. The highest prevalence of infection in the seven days prior to the survey was in the southern hemisphere winter month of August (11.5%) while January (summer) had the lowest infection rate (0.6%). Most women (92%) were confident or very confident of the date when symptoms of infection first appeared.

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Discussion

This is the first study to look at the prevalence of infection in a seven day window in pregnant women. There are a number of studies that report the rate of selected

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infections at any time during pregnancy and it is necessary to estimate weekly rates for comparison to these studies, assuming a constant rate of infection by week of gestation. Our study found a lower rate of self-reported infection during the whole pregnancy (40%) than Collier *et al*[17] (64%) however they included first trimester. Weekly rates for specific infections in pregnancy reported in other studies include: urinary tract infection 0.2% to 0.5%[17 26,27] (similar to 0.4% reported in our study), gastroenteritis 0.8%[20] (0.7% in this study), influenza 0.1%[27] (0.5% in this study), acute respiratory infectious disease 0.2%[28] and the common cold 0.4%[29] (compared to 1.2% of moderate/severe upper respiratory tract infections reported in this study). Our study has a higher prevalence rate for the common cold however a population-based cohort study in Canada found the weekly rate of acute respiratory illness severe enough to require a physician visit ranged from 1.1% to 1.9%[30], similar to the prevalence rate of severe colds observed in this study. As each completed questionnaire was anonymous, we could not determine whether any of the infections were recurrent and it is possible that some of the reported infections were chronic rather than acute.

We found the prevalence of acute infections was higher for women who had previously been pregnant and, for mild infections, women with twin pregnancies. Children are prone to developing infections[20] which could be easily transferred to the mother. Women pregnant with multi-fetal pregnancies may have increased antenatal visits and surveillance by clinicians, and this may lead to an increase in the reporting of infections. An unexpected yet interesting finding from the survey was the increased prevalence of infection in women with a hypertensive disorder of pregnancy, although this rate is based on small numbers and the confidence intervals

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around the prevalence estimate are very wide. This result is of particular interest because the estimate of prevalence of infection in pregnant women from this survey is to inform future research about infection and preeclampsia. The authors propose using the prevalence estimates of infection obtained from the current study for a case-crossover study investigating the role of acute infection and other acute triggers in the onset of preeclampsia. The current study however was not designed to examine infection rates in pregnant women with hypertension. In this cross-sectional survey it was not possible to establish whether the hypertension or the infection occurred first.

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The reliance upon self-report of infection is a potential limitation of the study with only 21% of women reporting an infection seeking medical attention, however mild infections that do not come to medical attention may still be a risk for pregnancy complications[17]. Self-report of infection has been used to estimate the rates of gastroenteritis[20], influenza and fever[19 21], and genitourinary infections[18] in pregnant women. Banhidy *et al* collected information about infection both from prospectively collected medical data and self-report from women in a post-natal questionnaire[25 28]. They found that 74% of women reporting an acute respiratory disease during pregnancy had the disease recorded in their medical records[28] and 95% of women with a medically recorded urinary tract infection self-reported the infection[25]. Our study also collected information about severity of symptoms experienced and medication taken which helped to distinguish between mild and more severe infections. This stratified analysis of reported infections increases the certainty that women who experienced a severe infection truly did have an infection.

The use of self reported data may be affected by recall bias. One study using self-report of any infection during pregnancy recommended 'future studies should emphasize the importance of interviewing women as early as possible'[17] as mother's tend to under-report infection when recalling information after birth[31]. The short window of time to recall details of infection in our study (seven days) minimises this recall bias.

A further limitation of this study is that the study population is older than the general population of pregnant women in Australia[26], is highly educated and was restricted to English speaking participants. Although this may impact the generalisability of the results, such characteristics are representative of the women that attend this hospital. Notably age or education level did not have a significant effect on the total infection rate, although a larger sample size may show an association between these factors and sexually transmitted infections. Strengths of this paper include the investigation of any infection rather than being limited to single infections; and the investigation of acute rather than chronic infections which may be over-estimated if weekly prevalence rates rather than date of infection onset are used.

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Conclusions

This survey is the first study to estimate the weekly prevalence of recently acquired acute infections in a population of pregnant women. The results of this study will be used to inform future research examining the association between acute infection and pregnancy complications such as preeclampsia. This study also informs clinicians about the types of infections and medications pregnant women are exposed to.

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Table 1: The characteristics of women surveyed

	N (%)
All surveys completed	737
Women that have completed survey only once	576 (78.2)
Maternal age	
< 25 years	55 (7.5)
25 – 34 years	430 (58.3)
≥ 35 years	247 (33.5)
Gestational age	
20 – 28 weeks	241 (32.7)
29 – 34 weeks	172 (23.3)
35 – 42 weeks	324 (44.0)
Plurality	
Singleton	705 (95.7)
Twins/Triplets	31 (4.2)
Parity	
Nulliparous	376 (51.0)
Multiparous	360 (48.8)
Highest level of education completed	
Without University degree	313 (42.5)
With University degree	422 (57.3)
Medical conditions (pre-existing or pregnancy related)	

No medical conditions	564 (76.5)
Asthma	69 (9.4)
High blood pressure	25 (3.4)
Diabetes	46 (6.2)
Other	32 (4.3)
Smoking status	
Did not smoke during pregnancy	708 (96.1)
Smoked cigarettes during pregnancy	29 (3.9)

Table 2: The characteristics of women without and without a self-reported infection, and the weekly prevalence rate, per 100 surveys, of infection in the seven days prior to completing the survey

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	Women with self-reported infection N	Weekly prevalence of self-reported infection % (95% CI)
All surveys completed	37	5.0 [3.4 – 6.6]
Women that have completed survey only once	28	4.8 [3.1 – 6.6]
Maternal age		
< 25 years	3	5.5 [0.0 – 10.7]
25 – 34 years	18	4.2 [2.3 – 6.1]
≥ 35 years	16	6.5 [3.4 – 9.6]
Gestational age		
20 – 28 weeks	10	4.2 [1.6 – 6.7]
29 – 34 weeks	9	5.2 [1.9 – 8.6]
35 – 42 weeks	18	5.6 [3.0 – 8.1]
Plurality		
Singleton	32	4.5 [3.0 – 6.1]
Twins/Triplets	5	16.1 [2.4 – 29.8]
Parity		
Nulliparous	11	2.9 [1.2 – 4.6]
Multiparous	26	7.2 [4.5 – 9.9]
Highest level of education completed		

Without University degree	14	4.5 [2.2 – 6.8]
With University degree	23	5.5 [3.3 – 7.6]
Medical conditions (pre-existing or pregnancy related)		
No medical conditions	26	4.6 [2.9 – 6.3]
Asthma	4	5.8 [0.1 – 11.5]
High blood pressure	4	15.3 [0.5 – 30.2]
Diabetes	3	6.5 [0.0 – 13.9]
Other	0	0.0
Smoking status		
Did not smoke during pregnancy	36	5.1, [3.5 – 6.7]
Smoked cigarettes during pregnancy	1	3., [0.0 – 10.5]

Table 3. Medication taken or health advice sought by women with self-reported infection

	N	%
	37	
Medication taken		
Paracetamol /acetaminophen	12	32.4%
Aspirin	2	5.4%
Antibiotics	7	18.9%
None	3	8.1%
Other*	13	35.1%
Medical Care		
Advice sought from doctor	8	21.6%
Medical test/investigation performed	2	5.4%
Temperature taken	7	18.9%

*Includes antifungal cream, antibacterial throat lozenges and gargle

Figure 1. List of symptoms that participants who reported having an infection were asked about details of severity (none, mild, moderate or severe)

See attached file

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General symptoms for infection
- Fever
- Night sweats / chills
- Fatigue / weakness

Upper respiratory tract infection (e.g. A cold, influenza, tonsillitis)
- Runny nose or blocked nose
- Sneezing
- Sore throat
- Headache, sinus/face pain
- Swollen glands

Lower respiratory tract infection (e.g. Pneumonia, bronchitis)
- Dry cough
- Productive cough (coughing up phlegm or mucous)
- Shortness of breath
- Chest pain
- Pain when breathing

Urinary tract infection (e.g. Bladder or kidney infections)
- Burning sensation when urinating
- Cloudy or foul-smelling urine
- Pus or blood in urine
- Frequent urination
- Urgency, pressure or pain in bladder

Genital tract infection (e.g. Thrush)
- Abnormal vaginal discharge with an unpleasant smell
- Intense itching, swelling and irritation

Gastro-intestinal infection (e.g. Food poisoning)
- Nausea, vomiting (other than morning sickness)
- Diarrhea
- Stomach pain

Other infections
- Tooth abscess
- Infected cut or scratch / Wound infection
- Skin infection / boils

207x218mm (96 x 96 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5, 6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	14
Outcome data	15*	Report numbers of outcome events or summary measures	16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	16, 17
		(*b*) Report category boundaries when continuous variables were categorized	14, 16
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	16
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11, 12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	4

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.