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Prevalence of Pregnancy Hypertensive Disorders in Mongolia

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Abstract

Objective—To estimate the prevalence of preeclampsia in a contemporary population of Mongolian women living in urban and rural areas. We determined the sensitivity and specificity of diagnosis based on established diagnostic criteria and assessed whether local diagnostic criteria were similar to those used in the US.

Study Design—Cross-sectional study of urban and nomadic pregnant women recruited in Ulaanbaatar (n=136) and rural provinces (n=85).

Main Outcome Measures—Preeclampsia defined as hypertension new to pregnancy after 20 weeks and proteinuria (or protein creatinine ratio ≥ 0.3 and dipstick reading $\geq +1$) or in the absence of proteinuria, hypertension and onset of: renal insufficiency, impaired liver function, thrombocytopenia, pulmonary edema, cerebral/visual symptoms. Prevalence of preeclampsia based on established criteria was compared with prevalence based on local physician's diagnosis.

Results—Prevalence of local physician diagnosed preeclampsia was 9.5% (13.2% urban, 3.5% rural). Prevalence based on established diagnostic criteria was 4.1% (4.4% urban, 3.5% rural).

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Sensitivity of physician's diagnosis was 23.8%, specificity was 98.0%, false negative rate was 2.0% and false positive rate was 76.2%. While prevalence based on local physician's diagnosis was over double that based on diagnostic criteria, overdiagnosis did not result in adverse effects. Women fulfilling diagnostic criteria for preeclampsia had babies with higher birth weights than women who did not (p-value=0.006).

Conclusion—The 4.1% prevalence of preeclampsia in Mongolia was consistent with global estimates of 2–8%, suggesting the pathophysiology of preeclampsia here may be similar to that found globally. Sensitivity of physician's diagnosis was low, specificity was high.

Keywords

Preeclampsia; Mongolia

Introduction

The global prevalence of preeclampsia, pregnancy associated hypertension and proteinuria, has been estimated at between 2%–8%, and is one of the main contributors to maternal and perinatal morbidity and mortality^{1–3}. In a cross-sectional study of 24 countries using the WHO Global Survey on Maternal and Perinatal Health, the prevalence of preeclampsia (based on newly diagnosed hypertension after the 20th gestational week and proteinuria) in low and middle income countries in Africa ranged between 0.9% in Angola to 3.7% in Uganda, in Latin America between 3.2% in Argentina to 8.2% in Brazil, and in Asia between 1.2% in Vietnam to 5.6% in the Philippines.² In developing countries, preeclampsia is currently responsible for approximately 8 million pre-term births and 20 million low birth weight infants.² Gathering adequate statistics on preeclampsia has been hindered in part by lack of adequate maternal care in the developing world. Thus, the true prevalence of preeclampsia in the developing world is likely known with less precision than in more developed countries.

We present unique data on the prevalence of preeclampsia based on clinical and laboratory measures in a population of Mongolian women living in urban and rural areas. In addition, we present data on the sensitivity and specificity of the local physician's diagnosis, and the maternal and perinatal characteristics of pregnancies that were and were not diagnosed with preeclampsia.

Materials and Methods

The data derive from a cross-sectional study that was designed to assess pregnancy hormone concentrations in urban and nomadic pregnant Mongolian women. The study was conducted at two maternity hospitals in Ulaanbaatar, Mongolia's capital, and two secondary care hospitals in the Mongolian rural provinces of Selenge and Bulgan. The protocol was approved by the Ethical Review Board of the Ministry of Health and the Ethics Review Board at the National University of Mongolia, as well as the Institutional Review Boards at the Harvard T.H Chan School of Public Health and the National Cancer Institute. Eligibility criteria for the study included being at least 18 years of age, having a naturally conceived, singleton, uncomplicated (at the time of recruitment) pregnancy and receiving care at the

maternity hospital in Ulaanbaatar, the Bulgan General Hospital or the Mandal soum's General Hospital, Selenge aimag. Women were excluded if they had a diagnosis of preeclampsia, or had other complications, during the time of recruitment. None of the women were excluded because of preeclampsia being diagnosed in prior pregnancies. A local study coordinator at each site, in addition to obstetricians and other health personnel collected the data. Eligible pregnant women were recruited by an obstetrician or nurse during one of their third trimester visits; 100% of the women agreed to participate. Of the 413 Mongolian women who participated in this study, 207 were from Ulaanbaatar and 205 were from either Selenge or Bulgan. During a routine third trimester visit, height and weight were measured and the women were interviewed to ascertain information on gravidity, parity, age at first pregnancy, history of pregnancy complications, age at menarche, and smoking status. The decision to investigate the prevalence of preeclampsia in the current pregnancy was made halfway through the data collection for the original study, thus pregnancy charts were reviewed for only 53.5% of the women (n=221; 136 from Ulaanbaatar, 61 from Selenge and 24 from Bulgan), regardless of their preeclampsia diagnosis status. Information was abstracted on the index pregnancy, including physician's diagnosis of preeclampsia, and the neonate, as well as routine blood chemistries.

The guidelines for the diagnosis of preeclampsia established by the American College of Obstetricians and Gynecologists (ACOG) and the International Society for the Study of Hypertension in Pregnancy (ISSHP) in 2013 were applied to calculate the prevalence of preeclampsia.^{4,5,6} The diagnostic criteria were hypertension new to pregnancy after twenty weeks defined as a systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg observed twice at least 4 hours apart, or blood pressure at any time over 160/110, and proteinuria defined as ≥ 300 mg/24 hour urine collection or protein creatinine ratio ≥ 0.3 and a dipstick reading $\geq +1$. In the absence of proteinuria, the diagnosis was made with hypertension as above and a new onset of any of the following: renal insufficiency (serum creatinine concentration > 90 $\mu\text{mol/L}$), impaired liver function (elevated liver transaminases measured at twice the normal concentration), thrombocytopenia (platelet count $< 100,000/\mu\text{L}$), pulmonary edema, or cerebral or visual symptoms. Despite existing guidelines, physician diagnosed preeclampsia may include a heterogeneous cluster of symptoms, as each woman with preeclampsia can present differently.⁷ Whether women had complications after delivery was abstracted (yes, no, bleeding).

Birthweight Z-score was calculated using the formula: $Z = \frac{bw - \overline{bw}}{SD(bw)}$ where bw is each child's birthweight, $\overline{bw}$ is the mean birthweight for gestational age, and $SD(bw)$ is the standard deviation of birthweight.⁸ Small for gestational age was defined as being born weighing less than the 10th percentile of birth weight for gestational age. This was calculated using birth weights taken in a United States cohort.⁹ Low birthweight was defined as $< 2,500$ g and pre-term birth was defined as < 37 weeks gestation.

Descriptive statistics for maternal and perinatal characteristics were generated for preeclampsia defined by physician diagnosis and by established diagnostic criteria. Differences between means were compared using t-tests or using the Wilcoxon rank sum test when $n < 30$ for either group and between proportions by using chi-square tests or using

Fisher's exact test when any cell size was less than 5. These data were presented by physician diagnosed preeclampsia, by fulfillment of established diagnostic criteria for preeclampsia, and by geographical area of residence. Data were analyzed using SAS version 9.3.

Results

The overall prevalence of preeclampsia based upon ACOG and ISSHP criteria was 4.1% (9/221), and was higher in Ulaanbaatar (4.4%, 6/136) than in the rural provinces of Selenge and Bulgan (3.5%, 3/85). The overall prevalence of preeclampsia based on the local physician's diagnosis was 9.5% (21/221), and was higher in urban Ulaanbaatar (13.2%, 18/136) than in the rural provinces combined (3.5%, 3/85).

Figure 1 presents the number of women with a physician's diagnosis of preeclampsia and the number who met clinical diagnostic criteria for preeclampsia. Of the 413 women who participated in the study, 44 were diagnosed with preeclampsia by a local physician. We were able to obtain medical data for 21 of these women, 5 of whom fulfilled the ACOG diagnostic criteria for preeclampsia. Based on ACOG criteria, the sensitivity of physician's diagnosis was 23.8% while the specificity was 98.0%. The false negative and positive rates were 2.0% and 76.2%, respectively. Overdiagnosis of preeclampsia by physicians appeared to be exclusively a phenomenon of Ulaanbaatar with nearly all women not meeting diagnostic criteria residing there. Of the 4 women meeting the diagnostic criteria who were not diagnosed by a physician, 3 resided in Ulaanbaatar and 1 in the rural areas.

All women fulfilling the diagnostic criteria for preeclampsia (n=9) were diagnosed with hypertension by a physician during pregnancy and experienced one of the following: platelet counts below $100.00 \times 1000/\mu\text{L}$ (n=4, 44.4%), or proteinuria dipstick reading $> +1$ (n=5, 55.6%) (Table 1). One of the women also experienced visual changes during her pregnancy, indicating severe preeclampsia by ACOG 2013 guidelines.⁴

Characteristics for women are compared in Table 1 by whether or not they met the ACOG diagnostic criteria for preeclampsia. Women meeting the diagnostic criteria for preeclampsia (n=9) had babies with a significantly higher birth weight (p-value=0.04) and higher birth weight Z-scores (p-value=0.006) compared to babies of women who did not fulfill the diagnostic criteria for preeclampsia (n=212), and only one of the former delivered preterm (at 36.5 weeks) while 10 of the latter delivered preterm.

Table 2 presents the characteristics of pregnancies by preeclampsia diagnosed by the local physician and preeclampsia based on ACOG diagnostic criteria. Overall, it appears that among women who were diagnosed with preeclampsia, there were no significant differences in maternal and perinatal factors between those who did or did not meet the ACOG diagnostic criteria except for higher platelet counts (p-value = 0.045) and protein values (p-value = 0.004) in the former. The women who were diagnosed with preeclampsia but did not meet the diagnostic criteria, did not experience complications after birth and none had children who were low birth weight (defined as less than 2500g), though one was small for gestational age (p-value = 0.49).

Among women who were not diagnosed with preeclampsia by a physician, those few who met the diagnostic criteria for preeclampsia (n=4) had babies with significantly higher birth weights (p-value = 0.04) and birth weight Z-scores (p-value = 0.01) than those who did not meet the diagnostic criteria, and none of the former experienced pregnancy complications or had children who were small for gestational age or low birth weight. Only 1 of the babies was born pre-term (36.5 weeks). Of the women who were not diagnosed with preeclampsia and did not meet the ACOG diagnostic criteria (n=196), 9 (4.6%) had children born at low birth weight and 11 (5.6%) had a child who was small for gestational age.

Discussion

The prevalence of preeclampsia observed in Mongolia based on physician diagnosis (9.5%) is slightly higher than the range of global estimates, which fall between 2 and 8%, and is closer to the prevalence of preeclampsia estimated in countries such as Brazil (8.2%) and Mexico (7.3%) rather than other Asian countries such as China (2.8%) or Nepal (2.2%).^{1,2} Preeclampsia prevalence in Mongolia based on established ACOG diagnostic criteria was 4.1%, slightly less than half the prevalence based on the local physician's diagnosis and falling squarely within the global prevalence range. These data are consistent with the possibility that in resource-limited settings, such as those in Mongolia, the prevalence of preeclampsia based on physician diagnosis may be overestimated, and that overdiagnosis may be more common in urban health care settings than rural ones.

Overdiagnosis of preeclampsia by physicians in developing countries may be beneficial, as has been proposed by the Cleveland Clinic Foundation, if it ensures improved care for those at higher risk, or encourages the mother to seek proper medical care for the remainder of her pregnancy.⁴ Among women who did not fulfill the ACOG diagnostic criteria, those who were diagnosed with preeclampsia by their physician had outcomes similar to or better than those who were not diagnosed with preeclampsia by their physician. While being falsely diagnosed could result in being delivered early because of lack of alternative treatment, there was no evidence of this, as gestational age was similar in women with and without a physician's diagnosis who did not meet diagnostic criteria. These data suggest that overdiagnosis in this population does not result in adverse effects and could serve to improve outcomes for both mother and child.

Although the etiology of preeclampsia remains elusive, there are several established risk factors including having a higher BMI (26 kg/m^2), anemia, nulliparity, chronic hypertension prior to pregnancy and a lack of sufficient prenatal care.^{1,10} BMI tended to be slightly higher among women who met the established diagnostic criteria for preeclampsia compared with those who did not, and among the 413 women initially enrolled in the study, BMI was positively associated with physician diagnosed preeclampsia. A recent systematic review and meta-analysis of 22 studies performed in low and middle income countries by the WHO found that women who were overweight pre-pregnancy or in early pregnancy were nearly twice as likely to develop preeclampsia (OR = 1.98, 95% CI = 1.64, 2.40), and those who were obese were at nearly four times the risk (OR = 3.87, 95% CI = 3.48, 4.29).¹⁰ Thus, in agreement with the suggestion of these authors, the importance of addressing rising maternal overweight and obesity in low and middle income countries will be crucial in

reducing the prevalence of preeclampsia.¹⁰ It would be of interest to further explore additional risk factors for preeclampsia, particularly extent of prenatal care. We found a higher proportion of women were diagnosed with preeclampsia in urban than in rural settings, which may be consistent with WHO findings that show an increase in preeclampsia prevalence with increasing gross national income.²

Women fulfilling the ACOG diagnostic criteria for preeclampsia had children born with birth weights and birth weight Z-scores that were significantly higher than women who did not fulfill the diagnostic criteria. While there were very few women who fulfilled ACOG diagnostic criteria but were not diagnosed with preeclampsia, they also had children with both a higher birth weight and birth weight Z-score when compared to the women who did not fulfill diagnostic criteria. They also were more likely to have platelet counts and protein levels indicative of preeclampsia, however they did not exhibit any severe features (headache, upper edema, visual changes, etc.) nor did they appear to have elevated transaminase levels, which might have contributed to a lack of diagnosis. While severe, early-onset preeclampsia is associated with small for gestational age births,^{11,12} birth weight has generally not been shown to be lower in preeclampsia at term,¹³ and in some studies babies of preeclamptic pregnancies were larger than those of uncomplicated pregnancies.^{11,14} Most of the cases (8 of 9) in the current study were born at 37+ weeks, while the remaining case was born at 36.5 weeks. In the US, 15% of preeclampsia cases are delivered between 34 and 36 weeks.¹⁵ While one of the women had visual changes consistent with severe preeclampsia, the sample size of the current study may have been too small to include additional severe cases.

A strength of this study was the availability of clinical and laboratory data to provide for validation of the physician's diagnosis. This allowed us to investigate potential factors, such as having a higher BMI and living in an urban setting that might lead to overdiagnosis of preeclampsia in a developing country such as Mongolia. But there are several issues to consider when interpreting the present findings. We attempted to choose a representative sample of Mongolian women by recruiting women in urban and rural settings. Some of the differences we observed by urban/rural setting may have been due to the maternity hospital in Ulaanbaatar serving as a tertiary care center for women throughout Mongolia. To lessen this possibility we restricted recruitment at the maternity hospital to women who resided in Ulaanbaatar, and who would therefore have had received routine prenatal care there. Women were excluded if they had been diagnosed with preeclampsia before recruitment. While none of the women were excluded for this reason, it is possible that severe cases of preeclampsia delivered or were transferred to the tertiary care hospital in Ulaanbaatar before the third trimester recruitment. Further, with only 413 participants in total and 221 with abstracted medical data, power may have been limited to demonstrate statistically significant differences in some of the pregnancy factors between groups. Thus our findings should be considered preliminary in nature and require follow-up with a larger cohort, either in other areas of Mongolia or in surrounding countries.

In summary, while the prevalence of preeclampsia in Mongolia when based on ACOG diagnostic criteria appears consistent with those of other countries, the presence of over-

diagnosis by the local physician may be a function of the resource-limited setting, being beneficial in ensuring satisfactory outcomes for mother and child.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- The prevalence of preeclampsia in Mongolia based on ACOG and ISSHP diagnostic criteria (4.1%) was consistent with global estimates of between 2 and 8%.
- The proportion of Mongolian women diagnosed with preeclampsia was more than twice the actual prevalence (9.5%) based on strict ACOG and ISSHP diagnostic criteria. Women who were diagnosed without meeting diagnostic criteria subsequently had babies of normal gestational age and birth weight, suggesting no adverse consequences from their diagnosis.
- Women who met the diagnostic criteria for preeclampsia had babies with higher birth weights than women who did not.

Figure 1.
Numbers of women with a physician's diagnosis of preeclampsia by whether they met ACOG diagnostic criteria

Table 1

Characteristics of women by preeclampsia defined by ACOG diagnostic criteria

	Met diagnostic criteria for preeclampsia (n=9)	Did not meet diagnostic criteria for preeclampsia (n=212)	p-value*
Urban area	6	130	
Rural areas	3	81	
BMI (kg/m ²)	29.4 ± 5.1	27.3 ± 3.8	0.20
Height (cm)	156.7 ± 6.1	159.3 ± 6.3	0.16
Weight (kg)	72.8 ± 16.7	69.2 ± 10.5	0.99
Pregnancies	2.9 ± 2.6	1.8 ± 1.6	0.31
Gestational age	38.7 ± 1.1	39.4 ± 1.2	0.07
Pre-term (<37 weeks)	1 (11.1)	10 (4.7)	0.37
Baby's birthweight (g)	3838.9 ± 365.5	3525.9 ± 483.6	0.04
Baby's birthweight Z-score	1.8 ± 0.8	0.8 ± 1.0	0.006
Low birthweight (<2500 g)	0 (0)	9 (4.3)	1.00
Small for gestational age	0 (0)	12 (5.7)	1.00
Maternal birthweight (g)	3230.0 ± 366.7	3273.2 ± 570.1	0.77
Sex			
Male	5 (55.6)	108 (52.7)	0.87
Female	4 (44.4)	97 (47.3)	
Upper edema	0 (0)	6 (4.7)	
Headache	0 (0)	4 (4.8)	
Visual change	1 (33.3)	1 (1.2)	
Pain (right upper quad.)	0 (0)	1 (1.2)	
Lower chest pain	0 (0)	1 (0.8)	
Proteinuria	0.6 ± 0.7	0.01 ± 0.1	<0.0001
Platelets/μL (× 1000)	293.3 ± 52.6	222.8 ± 59.2	0.02
Creatinine μmol/L	76.6 ± 0.0	66.5 ± 59.9	0.39
Transaminases			
ALT IU/L	10.0 ± 10.3	20.0 ± 12.5	0.15
AST IU/L	17.9 ± 5.3	25.5 ± 38.5	0.60

	Met diagnostic criteria for preeclampsia (n=9)	Did not meet diagnostic criteria for preeclampsia (n=212)	p-value *
New high SBP **			
140	3 (33.3)	6 (2.8)	0.004
New high DBP **			
90	1 (11.1)	6 (2.8)	0.26
Chronic hypertension before pregnancy	0 (0)	0 (0)	
Diagnosed pregnancy hypertension	9 (100)	5 (2.4)	<0.0001
Diagnostic criteria for preeclampsia: new hypertension in pregnancy and one of the following			
Proteinuria			
1+	4 (44.4)	2 (0.94)	<0.0001
Platelets			
< 100.00/μL (× 1000)	5 (55.6)	111 (52.4)	0.85
Creatinine			
> 90 μmol/L	0 (0)	1 (0.5)	1.00
Transaminases			
ALT 42 IU/L	0 (0)	8 (3.8)	1.00
AST 40 IU/L	0 (0)	5 (2.4)	1.00

* Unadjusted

** New high SBP and DBP based on blood pressure taken after 20 weeks gestation compared with those taken before 20 weeks.

Characteristics of women by diagnostic criteria for preeclampsia and physician diagnosis of preeclampsia.

Table 2

	Women diagnosed with preeclampsia by physician (n=21)		Women with no physician diagnosis of preeclampsia (n=200)	
	Met diagnostic criteria for preeclampsia (n=5)	Did not meet diagnostic criteria for preeclampsia (n=16)	Met diagnostic criteria for preeclampsia (n=4)	Did not meet diagnostic criteria for preeclampsia (n=196)
Urban area	3	15	3	115
Rural areas	2	1	1	81
BMI (kg/m ²)	29.1 ± 5.7	28.0 ± 3.4	29.8 ± 5.0	27.2 ± 3.8
Height (cm)	158.2 ± 7.6	160.0 ± 7.5	154.9 ± 3.7	159.3 ± 6.3
Weight (kg)	73.6 ± 20.6	71.7 ± 10.9	71.7 ± 13.2	69.0 ± 10.5
Pregnancies	3.8 ± 2.7	1.4 ± 1.0	1.8 ± 2.4	1.9 ± 1.7
Gestational age	38.8 ± 0.8	39.1 ± 1.0	38.5 ± 1.4	39.4 ± 1.2
Preterm (<37 weeks)	0 (0)	1 (6.3)	1 (25.0)	9 (4.6)
Baby's birthweight (g)	3700 ± 257.4	3621.9 ± 471.2	4012.5 ± 442.3	3517.8 ± 484.9
Baby's birthweight Z-score	1.4 ± 0.5	1.2 ± 1.1	2.2 ± 0.9	0.8 ± 1.0
Low birthweight (<2500g)	0 (0)	0 (0)	0 (0)	9 (4.6)
Small for gestational age	0 (0)	1 (6.3)	0 (0)	11 (5.61)
Maternal birthweight (g)	3150 ± 350.0	3163.6 ± 583.6	3350.0 ± 495.0	3283.9 ± 570.3
Sex				
Male	4 (80.0)	6 (37.5)	1 (25.0)	102 (54.0)
Female	1 (20.0)	10 (62.5)	3 (75.0)	87 (46.0)
Upper edema	0 (0)	0 (0)	0 (0)	6 (5.2)

*

*

	Women diagnosed with preeclampsia by physician (n=21)		Women with no physician diagnosis of preeclampsia (n=200)	
	Met diagnostic criteria for preeclampsia (n=5)	Did not meet diagnostic criteria for preeclampsia (n=16)	Met diagnostic criteria for preeclampsia (n=4)	Did not meet diagnostic criteria for preeclampsia (n=196)
Headache	0 (0)	0 (0)	0 (0)	4 (4.9)
Visual change	1 (50.0)	0 (0)	0 (0)	1 (1.2)
Pain (right upper quad.)	0 (0)	0 (0)	0 (0)	1 (1.2)
Lower chest pain	0 (0)	0 (0)	0 (0)	1 (0.9)
Proteinuria	1.0 ± 0.7	0.1 ± 0.3	0 ± 0	0 ± 0
Platelets/μL (× 1000)	293.3 ± 52.6	221.3 ± 51.6	n/a	223.0 ± 60.3
Creatinine μmol/L	76.6 ± 0.0	34.9 ± 0.0	n/a	68.7 ± 61.4
Transaminases				
ALT IU/L	12.0 ± 13.6	19.3 ± 15.2	6.0 ± 0.0	20.1 ± 12.1
AST IU/L	17.7 ± 6.5	22.1 ± 15.6	18.8 ± 0.0	26.1 ± 41.5
New high SBP *				
140	2 (40.0)	1 (6.3)	1 (25.0)	5 (2.6)
New high DBP *				
90	0 (0)	0 (0)	1 (25.0)	6 (3.1)
Chronic hypertension before pregnancy	0 (0)	0 (0)	0 (0)	0 (0)
Diagnosed pregnancy hypertension	5 (100.00)	3 (18.8)	4 (100.00)	2 (1.1)
* *				
Diagnostic criteria for preeclampsia: new hypertension in pregnancy and one of the following				
Proteinuria				
1+	4 (80.0)	2 (12.5)	0 (0)	0 (0)
* *				

	Women diagnosed with preeclampsia by physician (n=21)		Women with no physician diagnosis of preeclampsia (n=200)	
	Met diagnostic criteria for preeclampsia (n=5)	Did not meet diagnostic criteria for preeclampsia (n=16)	Met diagnostic criteria for preeclampsia (n=4)	Did not meet diagnostic criteria for preeclampsia (n=196)
Platelets				
< 100.00/ μ L ($\times$ 1000)	1 (20.0)	4 (25.0)	4 (100.0)	107 (54.6)
Creatinine				
> 90 μ mol/L	0 (0)	0 (0)	0 (0)	1 (0.5)
Transaminases				
ALT 42 IU/L	0 (0)	2 (12.5)	0 (0)	6 (3.1)
AST 40 IU/L	0 (0)	1 (6.3)	0 (0)	4 (2.0)

*
p-value < 0.05