

Effect of Calcium Supplementation during Pregnancy in Maternal Patient to Preterm Birth in One of Private Hospitals in Yogyakarta

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Abstract

Calcium is one of micronutrients that plays an important role in pregnancy. Insufficient consumption of calcium in pregnant women could lead to preterm birth, which is a major cause of neonatal mortality. This study aimed to determine the maternal patients' characteristics, relationship between prematurity risk factors such as age, antenatal care, history of abortion and parity as well as calcium supplementation during pregnancy on pregnant women toward preterm birth in one of private hospitals in Yogyakarta. The survey was conducted from May to August 2016. The study was an analytical observation with cross-sectional research design. In total of 199 medical records of maternal patients that had been included were analyzed using Mann-Whitney and Chi-Square test to see the relationship of calcium supplementation to preterm birth. Fisher's exact test was used if Chi-Square's requirement was not fulfilled. The pregnant women's characteristics in the hospital were expectant mothers with normal gestational age (93%); insufficient calcium supplementation (79%); age ≤ 30 years (61%); bachelor's degree (53%); private employees (40%); antenatal care ≥ 4 (98%) and parity 1 and ≥ 4 (54%). The result of this study showed there was no relationship between age, antenatal care, history of abortion and parity as well as calcium supplementation toward preterm birth on pregnant women in one of private hospitals in Yogyakarta.

Keywords: Calcium supplementation, maternal, preterm birth

Pengaruh Suplementasi Kalsium pada Pasien Maternal Selama Kehamilan terhadap Kelahiran Prematur di Salah Satu Rumah Sakit Swasta di Yogyakarta

Abstrak

Kalsium merupakan salah satu mikronutrien yang memainkan peran penting pada masa kehamilan. Pengonsumsi kalsium yang kurang pada ibu hamil dapat menyebabkan kelahiran prematur (kelahiran < 37 minggu) yakni penyebab utama kematian neonatal. Penelitian ini bertujuan untuk mengetahui karakteristik pasien maternal, hubungan faktor-faktor risiko seperti *antenatal care*, umur, riwayat abortus dan paritas serta suplementasi kalsium selama kehamilan terhadap kelahiran prematur di salah satu rumah sakit swasta di Yogyakarta. Penelitian ini dilakukan pada bulan Mei hingga Agustus 2016. Jenis penelitian ini adalah analitik observasional dengan rancangan *cross-sectional*. Sebanyak 199 rekam medis pasien maternal yang masuk dalam kriteria inklusi dianalisis menggunakan uji *Mann-Whitney* dan uji *Chi-Square*. Uji *Fisher* digunakan apabila syarat uji *Chi-Square* tidak terpenuhi. Karakteristik pasien maternal di salah satu rumah sakit swasta di Yogyakarta yaitu minggu kelahiran normal (93%), suplementasi kalsium tidak sesuai (79%), umur ≤ 30 tahun (61%), tingkat pendidikan strata satu (53%), pekerjaan pegawai swasta (40%), *antenatal care* ≥ 4 kali (98%) dan paritas 1 dan ≥ 4 kali (54%). Hasil penelitian ini mengungkapkan tidak terdapatnya hubungan antara umur, *antenatal care*, riwayat abortus dan paritas serta suplemen kalsium ($p > 0,05$) terhadap kelahiran prematur pada pasien maternal di salah satu rumah sakit swasta di Yogyakarta.

Kata kunci: Kelahiran prematur, maternal, suplementasi kalsium

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Introduction

World Health Organization (WHO) states that health and poor nutrition in pregnant women and newborns are still the significant contributors of their morbidity and mortality.¹ Calcium is one of the micronutrients that plays an important role during pregnancy. The requirement of calcium in pregnant women is showed on the case of decreased calcium serum level in pregnant women during pregnancy.² Sufficient calcium requirements during pregnancy have a potency to minimize the risk of developing high blood pressure during pregnancy which is the significant cause of maternal mortality and the risk of preterm birth.^{3,4}

The incidence of preterm birth in Indonesia had reached 675,700 babies in 2010 and made Indonesia as the fifth country in the world with the biggest incidence of preterm birth.^{5,6} Special District of Yogyakarta (DIY) Health Office in 2012 reported that the maternal mortality rate in Yogyakarta province was 87.3 per 100,000 women and the infant mortality was 25 per 1,000 live births.⁷ The high prevalence of preterm birth in Indonesia and DIY in particular has made preterm birth as a national concern. Babies who were born too early are at the risk of low learning ability (low IQ) and/or they will suffer from vision and hearing problems.⁸

The incidence of preterm birth is caused by many factors. There is no definite factor that causes prematurity, so it is important to assess the risk factors which linked to preterm birth.⁹ World Health Assembly Resolution in 2012 recommended the use of calcium supplements during pregnancy to reduce the prevalence of preterm delivery.¹⁰ This study aimed to determine the characteristics of maternal patients and revealed the relationship of age, antenatal care, history of abortion, parity and calcium supplementation during pregnancy in maternal patients toward preterm birth

in a private hospital in Yogyakarta. The hypothesis was that calcium supplementation during pregnancy significantly related to preterm birth.

Methods

This study was conducted with analytical observation and cross-sectional research design in one of the private hospitals in Yogyakarta. The hospital's name in this study was not revealed due to the ethical reason. This study used maternal patients' medical records in period of June 2015–June 2016 as research material with calcium supplementation as the independent variable and the gestational age as the dependent variable. The characteristics of maternal patients were gestational age, calcium supplementation, age, education level, occupation, antenatal care, history of abortion and parity. The survey was conducted from May to August 2016.

Subjects

The subjects of the study had to meet the inclusion criteria. Therefore, the subjects were pregnant women who delivered singleton baby, in the age of 20–35 years old, was consuming calcium supplements based on doctor's prescription during trimester II–III. Meanwhile, pregnant women who were smoking and/or drinking, had certain health problems such as asthma, chronic hypertension, diabetes, preeclampsia and fetal abnormalities, underwent abortion/miscarriage, and not doing antenatal care (ANC) from I–III trimester were excluded.

Sampling method and size

The subjects in this study were selected by using consecutive sampling technique. The minimum sample size to find the effect of calcium supplementation toward preterm birth was 195 samples. The sample size was obtained through qualitative calculation for

cross-sectional study¹¹ with $Z_{1-\alpha/2}$ (normal standard variable value on the type error I was 5%) was 1.96, d-value (precision) was 0.05, and the value of P (proportion of the population based on previous studies) was 0.15.¹² The total sample in this study was 199 medical records.

Ethics committee approval

The research proposal was submitted for ethical clearance to The Medical and Health Research Ethics Committee (MHREC), Faculty of Medicine Sardjito Hospital Universitas Gadjah Mada. MHREC stated that the study had met the ethical principle outlined in the Declaration of Helsinki 2008 and therefore, it could be carried out and MHREC had a right to monitor the activities of the study. The study was initiated after the issue of EC approval.

Data collection

The sufficiency of calcium supplementation was determined from the amount of calcium supplements where the maternal patients obtained from doctor's prescription and documented in patient's medical record. The adequate calcium supplementation during pregnancy is 1500–2000 mg/day.¹ The data of health and socio-demography including age, education level, type of occupation; life-style including smoking and/or drinking (alcohol); maternity information including gestational age, history of abortion, parity and antenatal care, those data were collected from medical records. Other than that, preterm birth was defined as the gestational age less than 37 weeks. The antenatal care was defined as the patient care received from healthcare professionals during pregnancy. In addition smoking was defined as both active and passive smoker.

Data analysis

The data were entered and analyzed using

the Statistical Package for Social Sciences (SPSS) version 22.0. Based on the number of subjects >50, Kolmogorov-Smirnov test was used as the parameter analysis of normality. The result was not normally distributed ($p < 0.05$). The comparative hypothesis test was used to compare age, antenatal care, history of abortion, parity and sufficiency of calcium supplementation toward gestational age or the incidence of preterm birth. The unpaired comparative hypothesis tests used in this study were numerical and categorical comparative hypothesis tests. The data were analyzed using Mann-Whitney test to see the differences between the mean of gestational age to the prematurity risk factors. Chi-Square test was used to find out the effect between the prematurity risk factors to the preterm birth. Fisher's exact test was used when the requirement of Chi-Square test was not fulfilled. The relationship between calcium and preterm birth factors toward the preterm birth were obtained from the value odds ratio (OR). The statistical analysis were done with 95% confidence ($p < 0.05$).

Results

A total of 1,316 maternal patients' medical records were collected and assessed for inclusion and exclusion criteria. Five hundred and sixty four medical records were included and 365 of them were excluded due to particular reasons as shown in Figure 1 and 199 medical records were used as the analyzed sample in the study. Table 1 shows the characteristics of maternal patients at one of private hospitals in Yogyakarta. The percentage of maternal patients with normal gestational age were more dominant (93%) and insufficiency of calcium supplementation in maternal patients were found more dominant (79%). The characteristic of maternal patient ages with the greatest percentage of 60% was in the range of 20 to 30 years old. Maternal

patients who worked as private employees were higher compared to other jobs which were 80 patients (40%). The percentage of maternal patients with bachelor's degree was 53.5% and it became the most educational level held by maternal patients included in inclusion criteria. Maternal patients who were having a number of antenatal care (ANC) ≥ 4 were reaching to 196 patients (98%). Most of maternal patients did not have any history of abortion or miscarriage and the percentage of the case was 89% or 178 patients. The parity/ the number of live births owned by maternal patient at first childbirth and more than equal to four ($1 \leq \geq 4$) was 108 people (54%).

Other than that, data in Table 2 shows that the types of calcium contained in calcium supplements which were prescribed by doctors in one of private hospitals and the types of the calcium were calcium pantothenate (29.89%), ossein hydroxyapatite (23.82%), calcium lactate (22.61%), calcium carbonate (19.27%) and calcium phosphate (4.40%).

There was no significant difference (Table 3) in the average of gestational age to maternal patients' age, ANC, history of abortion and

parity ($p > 0.05$) with a p-value of 0.16; 0.86; 0.19; 0.17 respectively. The p-value of 0.21 in calcium the supplementation variables showed that there was no significant difference average of gestational age between maternal patient with sufficient and insufficient calcium supplementation. However, there was no evidence of a positive relationship (Table 4) between age, ANC, history of abortion and party to the preterm birth ($p > 0.05$). It also showed that there were no significant difference and effect between the sufficiency of calcium supplementation toward the preterm birth in maternal patients ($p > 0.05$).

Discussion

Based on the maternal patients' characteristics, we found that most of maternal patients in one of private hospitals in Yogyakarta had a normal gestational age with insufficient calcium supplementation. Prematurity could be caused by the lack of daily calcium intake during the pregnancy by increasing the risk of pregnancy-induced hypertension such as gestational hypertension, preeclampsia and

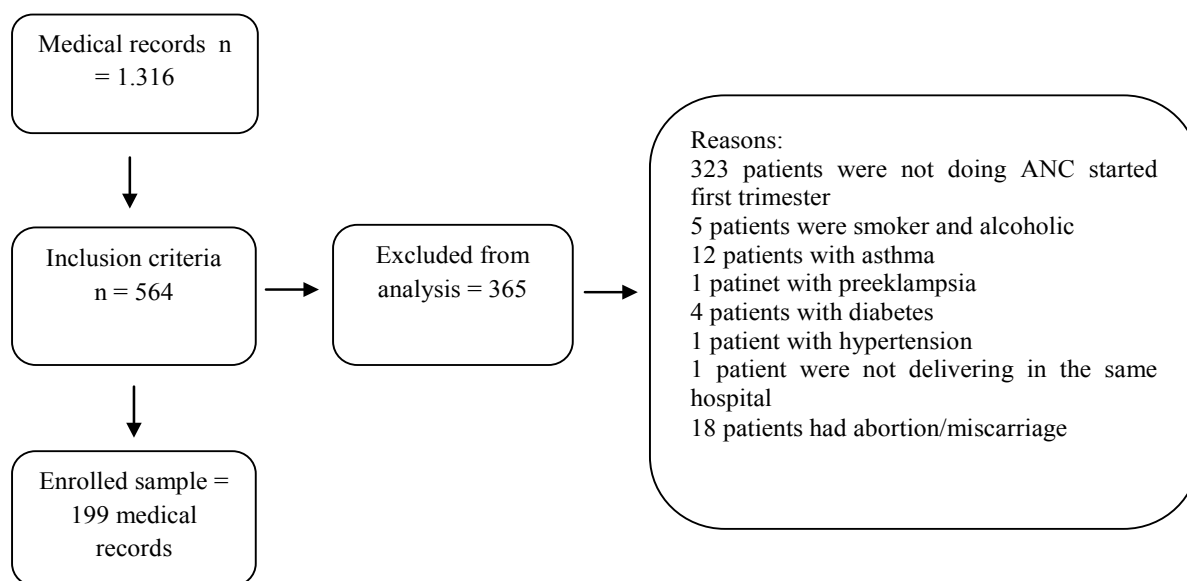


Figure 1 Flow of Enrolled Maternal Patients' Medical Records in Period of June 2015–June 2016 in One of Private Hospitals in Yogyakarta

eclampsia.¹³

The age of maternal patients in the study with range of 20–30 years old (61%) were high. The basic reason of these restricted ages in the study was suggested by Weng *et al.*¹⁴ that the optimal maternal age to reduce adverse events during childbirth was in the range from 26–30 years old. Kozuki *et al.*¹⁵ added the determination of range of safe maternal age was at the age of >18 and <35 years. Pregnant women with younger age (<18 years) had the possibility of immaturity while pregnant women over the age of 35 years were also at risk of preterm delivery because of the declining process in organ

function due to aging.¹⁵ We found that there is no relationship between age and preterm birth, this finding was possibly caused by the age limitation in inclusion criteria. The finding of this study might be explained as women younger than 20 years old did not have adequate blood circulation toward the cervix and uterus to provide the nutrition for the fetus.¹⁶ Pregnant women with age over 35 years old were at risk of diminished flexibility and elasticity of birth canal which were required on the birth process.¹⁷

Maternal patients' occupations were related to maternal physical activity which performed during the pregnancy. In this study the

Table 1 The Characteristics of Maternal Patients

	Characteristics	Total (n)	Percentage (%)
Gestational Age	Normal (≥ 37 weeks)	186	93
	Premature (< 37 weeks)	13	7
Calcium Supplementation	Sufficient	41	21
	Insufficient	158	79
Age (Year)	20–30	121	61
	31–35	78	39
Education Level	High school	30	15
	D1 (one year associate degree)	2	1
	D2 (two years associate degree)	1	0.5
	D3 (three years associate degree)	46	23
	Bachelor's degree	107	53.5
	Master's degree	13	7
Occupation	Private employee	80	40
	Civil servant	12	6
	Housewife	67	34
	Business woman	19	10
	Nurse	9	5
	Dentist	1	1
	Physician	1	1
	Police	2	1
	College student	3	2
	Lecturer	2	1
	Pharmacist	1	1
	Teacher	2	1
Antenatal Care	≥ 4	196	98
	< 4	3	2
History of Abortion	0	178	89
	≥ 1	21	11
Parity	2–3	91	46
	1 & ≥ 4	108	54

Table 2 The Type of Calcium in Prescribed Calcium Supplements

Type of Calcium	Patients (n)*	Percentage (%)
Calcium Pantothenate	197	29.89
Ossein Hydroxyapatite	157	23.82
Calcium Lactate	149	22.61
Calcium Carbonate	127	19.27
Calcium Phosphate	29	4.40

*: One patient was possible to get more than one kind of calcium in a prescription

highest occupation held by the patients was private employee (40%). However, Kartum revealed that there was no relationship of physical activity of women before pregnancy to preterm birth but women who were not active during pregnancy had a higher risk of the preterm birth (22.2%) compared with women with lower and high level of physical activity (4.8% and 4.9%).¹⁸ The percentage of patients who had bachelor's degree (S1) as their education level was 53.5%. This characteristic was supported by Shin *et al.* which explained mothers education below high school level had a high possibility of preterm birth compared with mothers with bachelor's degree (S1) education level or above (OR 1.16; 95% CI 1.05–1.28).¹⁹ High and low maternal education was closely related to the understanding level of health care, hygiene, and the need for antenatal care.

Most of the patients had come for antenatal care to examine their fetus development to healthcare professional (98%). Complete ANC consists of one examination in the first trimester, one examination in the second

trimester and twice in the last trimester.²⁰ According to Sulistiarini and Berliana, mothers who did not perform pregnancy tests completely were at the risk of 1.534 times more likely to experience preterm birth than mothers with complete ANC.²⁰ ANC with p-value of 1 indicated that there was no significant relationship between the ANC and preterm birth. This finding was consistent with Utami *et al.* which revealed that statistically the frequency of ANC visit was not associated with preterm birth (p-value of 0.837) as caused by the quality of ANC was less than optimal.²¹ Bantul District Health Office stated that the most important antenatal visit was its own quality not the quantity.²² This statement was contrast with another study which stated that prenatal care was a risk factor of preterm delivery with OR 0.16 (95% CI 0.06–0.44) and $p < 0.001$.²³

Abortion was known to have an effect on future pregnancy, either at the onset of difficult pregnancy or on the result of the pregnancy itself.^{24,25} The history of abortion in this study did not prove any effect on preterm

Table 3 The Differences of Gestational Age in Prematurity Risk Factors

Risk Factors	Gestational Age	p-value
Age (Year)	20–30	39.0 (34–41)
	31–35	39.0 (31–42)
Antenatal Care	≥ 4	39.0 (37–40)
	< 4	39.0 (31–42)
History of Abortion	0	39.0 (31–42)
	≥ 1	39.0 (35–41)
Parity	1 & ≥ 4	39.0 (35–42)
	2–3	39.0 (31–41)
Calcium Supplementation	Sufficient	39.0 (31–41)
	Insufficient	39.0 (34–42)

birth with a p-value of 0.63. This result was supported by Agustiana based on data analysis of RISKESDAS 2010.²⁶ Mother who had a history of abortion was not statistically significant associated preterm birth. Yet, theoretically abortion could damage the wall of the uterus which was the place for fetus to grow and develop.²⁶

We found out that the dominant parity among the patients were 1 and ≥ 4 (54%) and there was no relationship between parity and preterm birth (OR 1.37; 95% CI 0.43–4.36). This study had the same conclusion as Paembonan *et al.*²⁷ but an interesting finding was showed by birth order affected the likelihood of preterm birth as found in Sulistiarini and Berliana.²⁰ The greater risk of childbirth was found at the first childbirth, then decreased at the second child, and then again increased on third, fourth or more. The first pregnancy and childbirth increased the mother's health risk because the mother had never had a previous pregnancy and the fetus would try to open a new way in birth canal.²⁰ Conversely, if childbirth was too frequent, the uterus would weak by scarring the uterus

due to repeating pregnancy.²⁸ The finding was contrast with another study which described the results of the incidence of preterm parturition parity was 50.6% in women who have parity risk (1 & >3) and 49.4% in women who have no parity risk (2–3).²⁹

There were five types of calcium that was found in the study. Calcium pantothenate known as vitamin B5 absorbed by active transport in the small intestine and transferred to the placenta but slower than vitamin B complex.³⁰ Ossein hydroxyapatite is a form of microcrystalline calcium which provides a variety of minerals and proteins associated with bone metabolism.³¹ The absorption of calcium lactate is not affected by the acid environment in the stomach and has a similar bioavailability to calcium in milk.³² Calcium carbonate is composed of 40% elemental calcium but has a low absorption level which is 7–8%. This kind of calcium is recommended to be taken with food. Calcium phosphate is a calcium which containing the second highest elemental calcium level after calcium carbonate but has a lower solubility than calcium carbonate.³³

Table 4 The Effect of Prematurity Risk Factors Toward Preterm Birth by Gestational Age

	Gestational Age				p-value	OR (95% CI)
	<37 weeks		≥37 weeks			
	n	%	n	%		
Age						
20–30	8	6.6	113	93.4	1*	1.03 (0.326–3.282)
>30	5	6.4	73	93.6		
Antenatal Care						
≥4	13	6.6	183	93.4	1	NA†
<4	0	0.0	3	100.0		
History of Abortion						
0	11	6.2	167	93.8	0.63	0.62 (0.12–3.03)
≥1	2	9.5	19	90.5		
Parity						
2–3	5	5.5	86	94.5	0.77	1.37 (0.43–4.36)
1 & ≥4	8	7.4	100	92.6		
Calcium Supplementation						
Sufficient	1	2.4	40	97.6	0.31	3.28 (0.41–26.04)
Insufficient	12	7.6	146	92.4		

We did not identify a strong positive relationship between calcium supplementation in maternal patients and preterm birth neither in its difference (3.28; 95% CI 0.41–26.04). A study by Hofmeyr *et al.* stated that a decrease in the risk of preterm birth of 0.76 (95% CI 0.60–0.97) in women who were taking calcium supplements sufficiently (1000 mg/day) compared with women who were taking calcium supplements insufficiently.¹³ World Health Organization recommended the consumption of calcium supplements as much as 1.5 to 2.0 g of elemental calcium/day with duration of gestational age 20 weeks (second trimester) until the childbirth.¹ Calcium supplement had shown its effectiveness in reducing the risk of preterm birth in women with low calcium intake. Pregnant women who regularly consumed less than 600 mg of calcium per day and were equipped with additional supplementation of calcium (1,500 mg/day) showed a reduced risk of preterm birth, maternal morbidity and neonatal mortality index.³⁴ A longitudinal test of calcium metabolism during pregnancy revealed that calcium absorption in maternal patients increased significantly during the second and the third trimester. The peak of the calcium deposit in the fetus occurred in the third trimester with 350 mg/day and maternal calcium absorption was increased to meet its needs, a greater increase was occurred in women with low calcium intake.¹³ Women with an average of 1,171 mg of calcium intake during pregnancy underwent calcium absorption by 57% in the second trimester and 72% in the third trimester.³⁴ Calcium played a very important role in the development of bones, nerves and muscles of the fetus. When women were lack of calcium during pregnancy, then it was possible to cause disturbed fetal development and causing the preterm birth.²

Supported by Buppasiri *et al.*, which revealed the absence of statistically significant differences between women who

took calcium supplementation before week 20 (second trimester) or after week 20 or more.³⁵ The absorption of calcium during pregnancy was mediated by changes of calcitropic hormones.³⁴ Yet, unlike the Imdad and Bhutta's research in maternal patients with calcium consumption <900 mg/day, the risk was 0.76 times greater than the maternal patients with calcium consumption >900 mg/day in the week 20–32 of pregnancy.³⁶ During the first trimester, the level of parathyroid hormone (PTH) in women who consumed sufficient calcium would decrease to low level and increase again to the highest level at the third trimester.³⁶ This situation was reflecting the increasing calcium transfer from mother to fetus.

Prematurity is a multifactorial problem. Various studies have been performed to find out the risk factors of preterm birth. However, the presence of these risk factors do not necessarily lead to preterm birth. Most of the preterm births that occur spontaneously have no clear risk factors. there is no definite factors that cause prematurity, so a prevention through one or several factors may not be successful. Therefore, if we want to reduce the number of preterm birth, the initial step to prevent preterm birth is to reduce the risk factors associated with the preterm birth.

However, the weakness of this research was the calcium supplement which was consumed by the maternal patients had different kinds of calcium salt and could affect the availability of each calcium profile in the body. Besides, the confounding factors such as calcium intake outside doctor prescription could not be controlled by the researcher and the number of subject who participated in the study was less enough.

Limitation of study

In this study, the cut-off value was made to determine the sufficiency of calcium supplementation since the dose of calcium

supplements which was consumed by maternal patients in a private hospital in Yogyakarta was under the normal dosage that had been recommended by WHO which was 1500–2000 mg/day. The cut-off value was 258 mg/day. The dose of calcium below the cut-off value would be categorized as insufficient, while above the cut-off value categorized as sufficient.

Conclusion

Maternal patients' characteristics in one of private hospitals in Yogyakarta with the highest percentage based on the study were normal gestational age 93%, insufficient calcium supplementation 79%, maternal patients' age at 20–30 years old 61%. Moreover, the occupation of maternal patients who worked as private employees 40%, education level of maternal patients on bachelor degree was 53%, with the number of patients maternal antenatal care ≥ 4 was 98% and the parity 1 & ≥ 4 was 54%. The characteristics of age, antenatal care, history of abortion, parity, and calcium supplementation of maternal patients were lightly not associated with preterm birth in a private hospital in Yogyakarta.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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