

LAPORAN AKHIR GERAN USM JANGKA PENDEK

TAJUK GERAN :

***STUDY OF SERUM MAGNESIUM IN ACUTE
CORONARY SYNDROME PATIENTS***

NO AKAUN : 304/PPSP/6131370

PENYELIDIK UTAMA :
PROFESOR MADYA DR ZURKURNAI YUSOF

CO-RESEARCHER :
DR ALZAMANI MOHAMMAD IDROSE



SENARAI SEMAKAN UNTUK BUKU LAPORAN AKHIR GERAN USM JANGKA PENDEK

NAMA PENYELIDIK UTAMA	: Profesor Madya Dr Zurkurnai Yusof
NAMA CO-RESEARCHER	: Dr Alzamani Mohammad Idrose
TAJUK GERAN	Study of Serum Magnesium in Acute Coronary Syndrome : Patients
NO.AKAUN	: 304/PPSP/6131370

**SENARAI SEMAKAN SEMASA PENYERAHAN BUKU LAPORAN AKHIR
(Sila Tandakan (4) Pada Kotak Yang Berkenaan)**

NO.	PERKARA	ADA	TIADA
1.	Borang Laporan Akhir Projek Penyelidikan USM Jangka Pendek	/	
2.	Borang Laporan Hasil Penyelidikan, PPSP	/	
3.	Salinan Menuskrip	/	
4.	Penyata Perbelanjaan (Financial Statement)	/	
5.	Laporan Komprehensif (termasuk kertas persidangan atau seminar dan penerbitan saintifik hasil daripada projek ini)	/	
6.	Surat pemakluman penghantaran Laporan Akhir ke Bhg. Penyelidikan	/	

Nota: * No. 1-5 - Perlu dimasukkan dalam Buku Laporan Akhir
* No.6 - Hantar terus Kepada Pn. Che Merah Ismail (RCMO) hanya salinan kepada Bhg. R&D, PPSP

**BORANG LAPORAN AKHIR PROJEK
PENYELIDIKAN USM JANGKA
PENDEK**

UNIVERSITI SAINS MALAYSIA
DITERIMA
30 JUL 2007
PEJABAT DEKAN
PELANTAR PENYELIDIKAN KLINIKAL

1. **Nama Ketua Penyelidik:** Profesor Madya Dr Zurkurnai Yusof
Name of Research Leader

Profesor Madya/
Assoc. Prof.

Dr./
Dr.

Encik/Puan/Cik
Mr./Mrs/Ms

2. **Pusat Tanggungjawab (PTJ):**
School/Department

Pusat Pengajian Sains Perubatan, Kubang Kerian, Kelantan

3. **Nama Penyelidik Bersama:**
Name of Co-Researcher

Dr Alzamani Mohammad Idrose, Dr Hasenan Nordin, Dr Rashidi Ahmad

4. **Tajuk Projek:**
Title of Project

Study of Serum Magnesium in Acute Coronary Syndrome Patients

5. **Ringkasan Penilaian/Summary of Assessment:**

Tidak
Mencukupi
Inadequate

Boleh
Diterima
Acceptable

Sangat Baik
Very Good

1 2

3

4 5

i) **Pencapaian objektif projek:**
Achievement of project objectives

ii) **Kualiti output:**
Quality of outputs

iii) **Kualiti impak:**
Quality of impacts

iv) **Pemindahan teknologi/potensi pengkomersialan:**
Technology transfer/commercialization potential

v) **Kualiti dan usahasama :**
Quality and intensity of collaboration

vi) **Penilaian kepentingan secara keseluruhan:**
Overall assessment of benefits

6. Abstrak Penyelidikan

(Perlu disediakan di antara 100 - 200 perkataan di dalam **Bahasa Malaysia dan juga Bahasa Inggeris**. Abstrak ini akan dimuatkan dalam Laporan Tahunan Bahagian Penyelidikan & Inovasi sebagai satu cara untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti & masyarakat luar).

Abstract of Research

(An abstract of between 100 and 200 words must be prepared in Bahasa Malaysia and in English).

This abstract will be included in the Annual Report of the Research and Innovation Section at a later date as a means of presenting the project findings of the researcher/s to the University and the community at large)

Please refer to attachment

7. Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.

[Sila gunakan kertas berasingan]

Applicant are required to prepare a Comprehensive Technical Report explaining the project.

(This report must be appended separately)

Senaraikan kata kunci yang mencerminkan penyelidikan anda:

List the key words that reflects your research:

Bahasa Malaysia

Serum Magnesium
Acute Coronary Syndrome

Bahasa Inggeris

Serum Magnesium
Sindrom Koronari Akut

8. Output dan Faedah Projek

Output and Benefits of Project

(a) * Penerbitan Jurnal

Publication of Journals

(Sila nyatakan jenis, tajuk, pengarang/editor, tahun terbitan dan di mana telah diterbitkan/diserahkan)

(State type, title, author/editor, publication year and where it has been published/submitted)

Abstract was published in Malaysian Journal of Medical Sciences, Volume 13, Supplement 1, January 2006 (page 28)

The paper was presented at 3 conferences : 11th National Conference on Health & Medical Science (USM, Kubang Kerian) 2006, 10th National Scientific Conference & Emergency Medicine Meeting (IOI Mall, Putrajaya) and 40th Malaysia-Singapore Academy of Medicine Congress (Sunway Pyramid, Selangor). It won best 'Oral Communication', Medical-base in the first 2 conferences mentioned.

- (b) **Faedah-faedah lain seperti perkembangan produk, pengkomersialan produk/pendaftaran paten atau impak kepada dasar dan masyarakat.**
State other benefits such as product development, product commercialisation/patent registration or impact on source and society.

This study had discovered the status of Magnesium level in all groups of Acute Coronary Syndrome patients - an approach that had never been done before anywhere in the world. It sheds light, especially among NSTEMI group of patients whereby hypomagnesemia was present as high as 30% of the population. Following this a study may be recommended in terms of role of Magnesium infusion among NSTEMI patients in order to mitigate the damage to myocardial muscle during NSTEMI attack.

* Sila berikan salinan/Kindly provide copies

- (c) **Latihan Sumber Manusia**
Training in Human Resources

i) Pelajar Sarjana:
Dr Alzamani Mohammad Idrose
Graduates Students


(Perincikan nama, ijazah dan status)
(Provide names, degrees and status)
Master of Medicine (Emergency)

ii) Lain-lain:
Others

9. **Peralatan yang Telah Dibeli:**
Equipment that has been purchased

Tiada. Kajian menggunakan mesin sedia ada di makmal.

juj


Tandatangan Penyelidik
Signature of Researcher

3

17/7/07
Tarikh
Date

**BORANG LAPORAN AKHIR HASIL
PENYELIDIKAN PPSP**

BORANG LAPORAN HASIL PENYELIDIKAN
PPSP

Tajuk geran: The Study Of Serum Magnesium Level in Acute Coronary Syndrome Patients

Penyelidik: Prof. Madya Zurkurnai Yusof, Dr Alzamani Mohd Idrose, Dr Hasenan Nordin, Dr Rashidi Ahmad

Jenis geran: Jangka pendek

Tempoh geran: 3 tahun

Jenis laporan: Laporan Kemajuan Alatan di beli Ya:nyatakan.....

Laporan Akhir*: Tidak

OBJEKTIF SPESIFIK KAJIAN (sama spt dalam proposal asal)	SECARA RINGKAS TERANGKAN PENCAPAIAN/HASIL	OBJEKTIF TERCAPAI ATAU TIDAK
<p>1. Is there significant deficiency in plasma Magnesium level among Acute Coronary Syndrome patients ?</p>	<p>Yes, there is. As a whole, the means of Serum Magnesium in ACS is significantly lower compared to the control. However upon further analysis, it was found that the subgroup NSTEMI contributed largely to the low level of the Magnesium. In individual analysis, it was found that there was no difference in terms of the means of Serum Magnesium in STEMI and UA patients.</p>	<p>achieved</p>
<p>2. Is Magnesium level investigation worthwhile taken, ie show significant results and subsequently change management?</p>	<p>Yes, it is worthwhile. The study showed that there is a significant proportion of hypomagnesemia in ACS patients and all of its subgroups. This is especially true in NSTEMI whereby almost 30% of the population present with hypomagnesemia. The presence of hypomagnesemia indicates the suggested need of Magnesium supplements in this group. Although previous large studies like the ISIS-4 and MAGIC showed routine infusion of Magnesium in MI patients were not warranted, they did not address the need of giving Magnesium in hypomagnesemic portions of the population.</p>	<p>achieved</p>
<p>3. Is there any significant difference in terms of Magnesium level in comparison between subsets of Acute Coronary Syndrome (Unstable Angina, Non ST Elevation Myocardial Infarct and ST elevation Myocardial Infarct)?</p>	<p>There is a significant difference between the subgroups of ACS. The means of NSTEMI showed significantly lower Magnesium level compared to STEMI and UA. No significant difference however was found between the means of STEMI and UA. On further analysis, it was also found that there was significant proportion of hypomagnesemia in all subgroups</p>	<p>achieved</p>

	<p>compared to the control group. In the case of STEMI, there was also a significant proportion of hypermagnesemia compared to the control healthy population. From the study, Odds Ratios were calculated for each group and it was found that the Odds Ratio of getting STEMI, UA and NSTEMI in patients presenting with classical clinical signs and symptoms and hypomagnesemic are higher compared to the control population. This may be helpful in the case of NSTEMI, whereby there is difficulty of differentiating between NSTEMI and UA. If hypomagnesemia is present, the Odds of getting NSTEMI compared to UA is higher. However, this may be only used as an adjunct and not as a diagnostic tool.</p>	
<p>4. Is there a role of Magnesium therapy in Acute Coronary Syndrome patients among local population?</p>	<p>Not as a routine. The majority of patients still present with normomagnesemia. However, Magnesium supplements should still be considered in patients with established hypomagnesemia demonstrated by the lab result. The proportion of ACS population presenting with hypomagnesemia is still significant compared to the control healthy group.</p>	<p>achieved</p>
<p>5. Can knowledge of Serum Magnesium level contribute to diagnosis-making process of Acute Coronary Syndrome patients?</p>	<p>Odds Ratio of getting STEMI, UA and NSTEMI in patients presenting with classical clinical signs and symptoms and hypomagnesemic are higher compared to the control population. This may be helpful in the case of NSTEMI, whereby there is difficulty of differentiating between NSTEMI and UA. If hypomagnesemia is present, the Odds of getting NSTEMI compared to UA is higher. However, this may be only used as an adjunct and not as a diagnostic tool.</p>	<p>achieved</p>

- *Laporan Akhir perlu disertakan salinan manuskrip dan surat yang dihantar kepada mana-mana jurnal untuk penerbitan.*

Nama Penyelidik Utama (PI): Profesor Maya Dr Zurkurnai Yusuf

t.t.:

Tarikh: 29 Julai 2007

ABSTRAK

ABSTRAK

Kajian Serum Magnesium Dalam Pesakit-pesakit Sindrom Koronari Akut Alzamani MI, Zurkurnai Y, Rashidi A, Hasenan N Hospital Universiti Sains Malaysia 2005

PENGENALAN Terdapat banyak kajian samada in-vitro atau klinikal yang menunjukkan kemungkinan peranan yang dimainkan oleh magnesium dalam sindrom koronari akut. Banyak kajian menunjukkan paras magnesium yang rendah (hipomagnesemia) dalam sindrom koronari akut. Bagaimanapun tidak ada kajian seumpamanya dijalankan di Malaysia. Terdapat keperluan untuk mengetahui samada terdapat hypomagnesemia dalam sindrom ini di kalangan populasi pesakit di Negara ini. Pengetahuan tentang status magnesium ini akan menjadi panduan bagi kajian lanjut, rawatan atau rawatan sampingan menggunakan magnesium pada pesakit sindrom ini pada masa hadapan.

OBJEKTIF

1. Untuk menentukan sama ada terdapat paras kekurangan magnesium di dalam pesakit sindrom koronari akut
2. Untuk justifikasi siasatan magnesium sebagai rutin bersama siasatan elektrolit lain seperti Na dan K
3. To determine any differences of serum Magnesium between ACS subgroups:
4. Menentukan perbezaan serum magnesium di antara subpopulasi sindrom koronari akut : STEMI, UA dan NSTEMI
5. Sebagai asas untuk kajian lanjut berkenaan rawatan menggunakan magnesium di kalangan pesakit sindrom coronary akut.

METODOLOGI Paras magnesium dalam serum 420 pesakit yang datang dengan gejala sakit dada di ambil di Jabatan Kecemasan. Setelah disahkan berdasarkan kriteria WHO dan Panduan Praktis Klinikal Kementerian Kesihatan Malaysia (berdasarkan EKG, enzim kardiak atau angiogram), sebanyak 255 dipastikan sebagai kes sindrom coronary akut (64 STEMI, 155 UA dan 37 NSTEMI. Baki 165 disahkan bukan dalam kategori sindrom koronari akut. Sebanyak 95 kes control diambil sebagai bandingan (terdiri daripada sukarelawan dengan julat umur dari akhir belasan hingga 60an)Hanya satu mesin digunakan untuk mengukur serum magnesium..

KEPUTUSAN Terdapat perbezaan yang signifikan di antara purata serum magnesium sindrom koronari akut dan kontrol ($p=0.038$; <0.05) There is no significant difference between the means of Non-ACS and the Control group; $p= 0.115$ (> 0.05) .Ujian ANOVA satu hala menunjukkan perbezaan signifikan di dalam subpopulasi sindrom koronari akut secara amnya ($P < 0.05$) Terdapat perbezaan signifikan di antara STEMI dan NSTEMI ($p=0.007$) serta di antara STEMI dan kontrol ($p=0.005$).Tiada perbezaan signifikan di antara purata serum magnesium STEMI dan kontrol ; $p= 0.867$ (> 0.05). Tiada perbezaan signifikan di antara purata serum magnesium UA dan kontrol $p=$

0.089 (> 0.05). Terdapat perbezaan signifikan di antara purata NSTEMI dan kontrol ; $p=0.002$ (< 0.05) . Hypomagnesemia terdapat di dalam : 12.5% of STEMI($p<0.05$), 9.7% of UA($p>0.05$), 29.7 % of NSTEMI($p<0.05$), 10.3% dalam kumpulan bukan sindrom koronari akut (pesakit kardiak) $p<0.05$), 6.9 % pesakit bukan sindrom koronari akut (bukan pesakit kardiak) ($p>0.05$) dan 3.2% dalam pesakit kontrol. 9.4% of STEMI memiliki paras hipermagnesemia. 'Odd's Ratio' bagi mendapat sindrom koronari akut dengan kehadiran hipomagnesemia adalah 4.559 kali berbanding kontrol (95% Julat Keyakinan di antara 1.364 and 15.236). $P<0.05$. 'Odd's Ratio' untuk mendapat STEMI dengan kehadiran hipomagnesemia dalam pesakit yang simptomatik adalah 4.381 kali berbanding kontrol. (Julat keyakinan 95% di antara 1.116 and 17.204) ; $P<0.05$. 'Odd's Ratio' untuk mendapat NSTEMI dengan kehadiran hipomagnesemia dalam pesakit yang simptomatik adalah 11.795 kali berbanding kontrol (Julat Keyakinan 95% di antara 3.022 dan 46.032). $P = 0.000$ (<0.05)

RUMUSAN

Berbanding kontrol, terdapat paraturan hipomagnesemia yang signifikan di dalam kumpulan sindrom koronari akut dan setiap subpopulasi. NSTEMI memiliki paras hipomagnesemia yang tertinggi. Fakta bahawa kebanyakan pesakit STEMI dalam status normomagnesemia dan 9.4% dalam hipermagnesemia mungkin menjelaskan mengapa kajian besar seperti ISIS-4 dan MAGICA tidak menunjukkan sebarang perbezaan bagi pemberian magnesium kepada pesakit-pesakit miokardial infark. Pemberian serum magnesium boleh diberikan hanya kepada pesakit yang datang dengan hipomagnesemia. Hipomagnesemia di dalam pesakit dalam pesakit sindrom koronari akut boleh digunakan sebagai bantuan bagi membuat diagnosa. Peranan magnesium dalam sindrom koronari akut tidak harus diabaikan. Kajian lanjut diperlukan bagi pemberian magnesium untuk pesakit yang benar-benar datang dengan hipomagnesemia.

ABSTRACT

The Study Of Serum Magnesium Level in Acute Coronary Syndrome Patients

Alzamani MI, Zurkurnai Y, Rashidi A, Hasenan N
Hospital Universiti Sains Malaysia
2005

INTRODUCTION There had been many studies done in the past either in-vitro or clinically indicating the possible role that Magnesium may play in acute coronary syndrome. Many studies showed the presence of hypomagnesemia in coronary artery disease and also during the attack of myocardial infarct. However there is hardly any studies done on Magnesium done in Malaysia, none with regards to coronary artery disease or acute coronary syndrome. There is a need to know whether there is hypomagnesemia in Acute Coronary Syndrome in the local population. Knowledge on this will serve as a guide on future investigations, studies and treatment of Acute Coronary Syndrome or as an adjunct of ACS treatment.

OBJECTIVES

1. To ascertain whether there is a significant level of Mg deficiency among the Acute Coronary Syndrome patients in USM hospital
2. To justify Mg investigations as a routine investigation together with other electrolytes investigation like Na and K
3. To determine any differences of serum Magnesium between ACS subgroups: STEMI,UA and NSTEMI
4. To form a basis for further investigations regarding Magnesium treatment in ACS patients

METHODOLOGY The Serum Magnesium level of 420 patients with chest pain were taken at the Emergency Department. Upon confirmation based on WHO criteria and Malaysian Ministry of Health's Clinical Practice Guidelines(based on clinical, ECG, cardiac enzymes or angiogram). 255 were confirmed as genuine cases of Acute Coronary Syndrome(64 ST-Elevated Myocardial Infarct,155 Unstable Angina 37 were confirmed as Non-ST Elevated Myocardial Infarct). The remaining 165 were non-Acute Coronary Syndrome cases. A total of 95 control cases made up of healthy volunteers (age range from late teen to elderly) were taken for comparison Only one machine was used, utilizing the same Magnesium ion measurement method for all samples.

RESULTS There is a significant difference between the means of ACS and the Control group; $p= 0.038 (< 0.05)$.There is no significant difference between the means of Non-ACS and the Control group; $p= 0.115 (> 0.05)$.One way ANOVA test showed significant difference in the group as a general ($P< 0.05$).There are significant differences between : STEMI and NSTEMI ($p=0.007$) and STEMI and CONTROL ($p=0.005$). There is no significant difference between the means of STEMI and the Control group $p= 0.867$

(> 0.05) There is no significant difference between the means of UA and the Control group $p= 0.089$ (> 0.05). There is significant difference between the means of NSTEMI and the Control group $p= 0.002$ (< 0.05). Hypomagnesemia was present in : 12.5% of STEMI($p<0.05$), 9.7% of UA($p>0.05$), 29.7 % of NSTEMI($p<0.05$), 10.3% of Non-ACS (Cardiac Origin)($p<0.05$), 6.9 % of Non-ACS (Non-cardiac Origin)($p>0.05$) and 3.2% of control patients. 9.4% of STEMI patients had hypermagnesemia. The Odd's Ratio for getting Acute Coronary Syndrome in the presence of hypomagnesemia in symptomatic patients is 4.559 times compared to normal control. (95% Confidence Interval between 1.364 and 15.236). $P<0.05$. The Odd's Ratio for getting STEMI in the presence of hypomagnesemia in symptomatic patients is 4.381 times compared to normal control. (95% Confidence Interval between 1.116 and 17.204) ; $P<0.05$. The Odd's Ratio for getting NSTEMI in the presence of hypomagnesemia in symptomatic patients is 11.795 times compared to normal control. (95% Confidence Interval between 3.022 and 46.032). $P = 0.000$ (<0.05)

CONCLUSIONS

There is a significant difference of serum magnesium level in ACS group compared to control. Mean serum magnesium tend to be lower in ACS group. Compared to the control healthy population, there is a significant proportion of hypomagnesemia in ACS group as a whole as well as each subgroup. NSTEMI has the highest proportion of hypomagnesemia. The fact that the majority of the STEMI patients were in normomagnesemic state as well as 9.4% of them in hypermagnesemic state may explain why routine infusion of Magnesium in large studies like the ISIS-4 and MAGICA did not show any significant difference..Routine investigation for Serum Magnesium may be done since there is a significant proportion of ACS patients in hypomagnesemic state compared to control healthy population. Hypomagnesemia in patients presenting with chest pain may be used as an adjunct for diagnosis making. The role of Magnesium infusion for ACS syndrome patients should not be dismissed. Further study with regard to its role especially in patients with hypomagnesemia during ACS attack needs to be done.

SALINAN MANUSKRIP

MANUSCRIPT DRAFT

The Study Of Serum Magnesium Level in Acute Coronary Syndrome Patients Alzamani MI*, Rashidi A, Hasenan N**, Zurkurnai Y****

****Emergency Department, Hospital Kuala Lumpur
Hospital Universiti Sains Malaysia*

Introduction

Some studies in the past showed presence of hypomagnesemia in Myocardial Infarct patients ^{1,2}. Magnesium seems to be able to dilate the coronary arteries particularly in situations in which coronary vascular reactivity appears pathological. In fact magnesium improves vasospastic angina and dilates segments of human coronary arteries ^{3,4}. Moreover, magnesium suppresses angina induced by exercise by improving the regional myocardial flow ⁵. In addition, some studies provide supportive evidence that supplementation of magnesium chloride may reduce the incidence of fatal and nonfatal arrhythmias after an infarct ⁶. In fact, quality of life of Acute Coronary Syndrome(ACS) patients given magnesium infusion improved significantly ⁷.

In view of no studies regarding the level of Serum Magnesium during the attack of ACS in patients in Asia before, there is a need to at least know the level of serum Magnesium in Acute Coronary Syndrome which is made up of ST-elevated Myocardial Infarct (STEMI), Unstable Angina (UA) and Non-ST Elevated Myocardial Infarct (NSTEMI) in the population. Knowledge on this will serve as a guide on future investigations, studies and treatment of the disease.

Aims of The Study

- ▶ To determine the serum Magnesium in ACS as compared to healthy, normal control population
- ▶ To ascertain whether there is a significant level of Mg deficiency among the Acute Coronary Syndrome patients (in terms of both means and proportion of hypomagnesemia, compared to normal population)
- ▶ To justify Mg investigations as a routine investigation together with other electrolyte investigations like Na and K
- ▶ To determine any differences between subgroups of ACS
- ▶ To determine whether knowledge of Magnesium level among ACS patients can contribute to diagnosis-making process

Methodology

The serum Magnesium level of 420 patients with chest pain were taken at the Emergency Department. Upon confirmation based on WHO criteria, 255 were confirmed as genuine cases of Acute Coronary Syndrome (64 STEMI, 155 UA and 37 were confirmed as NSTEMI). 95 healthy control samples (age range from late teen to elderly) were taken from volunteers for comparison. The study was approved by the ethical committee and carried out with University short term grant. The Serum Magnesium was measured using the Calmagite method. The same machine (Hitachi 912 Automatic Analyzer) was used for all samples taken. Rigorous Quality Control was applied for the reagent testing and machine configuration in the lab

Results

The means of Serum Magnesium in Populations of Acute Coronary Syndrome patients are as tabulated in Table 1 .

Table 1

Patient Group	Population (N)	Mean of Mg Level of patients	Mean of Mg Level of Healthy Control*	P value (independent t-test)
ACS	256	0.88±0.15	0.91±0.10	0.038
STEMI	64	0.91±0.16	0.91±0.10	0.87
UA	155	0.88±0.14	0.91±0.10	0.09
NSTEMI	37	0.81±0.16	0.91±0.10	0.001

*Note : Population (N) of Healthy Control Population is 95.

Hypo, normo and hypermagnesemia state is determined by mean \pm 2 SD derived from the healthy control population of the local population :

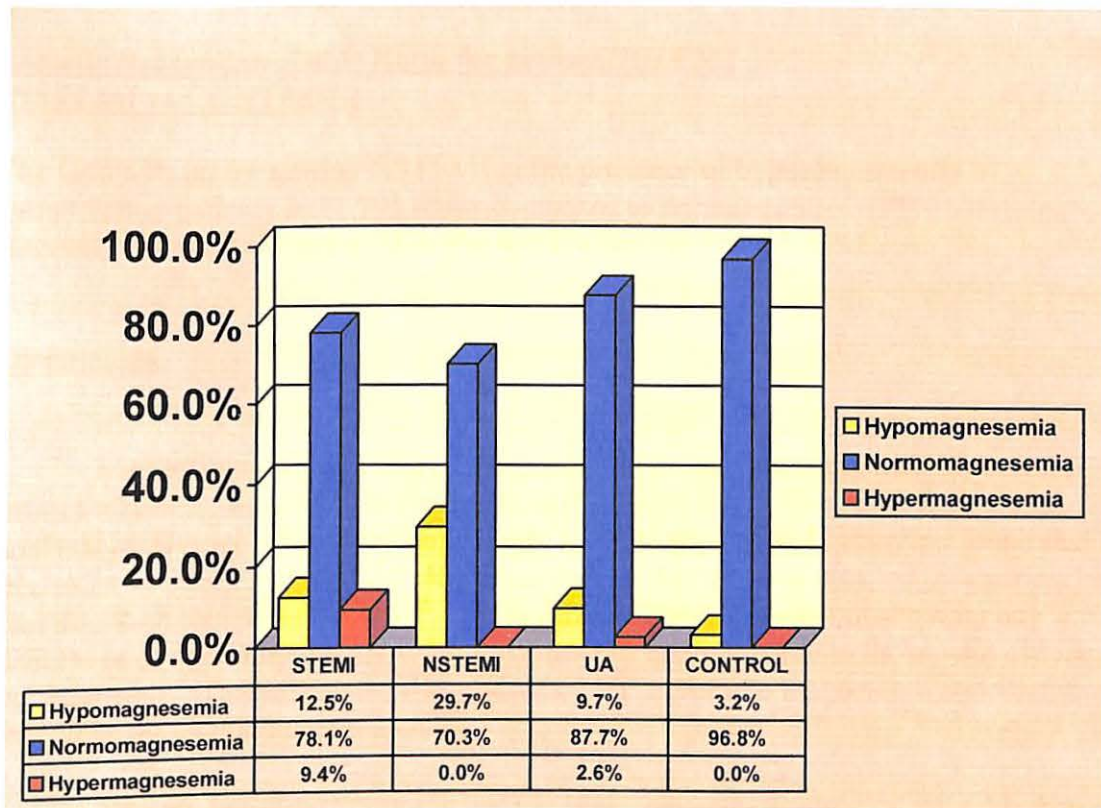
Hypomagnesemia : Serum Magnesium \leq 0.70 mmol/L

Normomagneseia : Serum Magnesium \geq 0.71 and \leq 1.12 mmol/L

Hypermagnesemia : Serum Magnesium \geq 1.13

**** Significant difference when compared to normal population noted in ACS and NSTEMI groups ($p < 0.05$)**

Graph 1 : Proportion of Magnesium Level



Logistic Regression : Odds Ratio For Getting ACS

The Odd's Ratio for getting Acute Coronary Syndrome in the presence of hypomagnesemia in symptomatic patients is 4.559 times compared to normal control. (95% Confidence Interval between 1.36 and 15.24). P= 0.014

Logistic Regression : Odds Ratio for getting STEMI (STEMI VS CONTROL)

The Odd's Ratio for getting STEMI in the presence of hypomagnesemia in symptomatic patients is 4.381 times compared to normal control. (95% Confidence Interval between 1.12 and 17.20). The lower border is > 1.0 with P=0.034 (<0.05) and therefore significant.

Logistic Regression : Odds Ratio for getting UA (UA VS CONTROL)

The Odd's Ratio for getting UA in the presence of hypomagnesemia in symptomatic patients is 3.286 times compared to normal control. (95% Confidence Interval between 0.93 and 15.24). Nevertheless this OR is not significant since the lower interval is less than 1.0. $P=0.66(>0.05)$

Logistic Regression :Odds Ratio for getting NSTEMI (NSTEMI vs CONTROL)

The Odd's Ratio for getting NSTEMI in the presence of hypomagnesemia in symptomatic patients is 11.795 times compared to normal control. (95% Confidence Interval between 3.02 and 46.03). $P = 0.000 (<0.05)$.

Discussions

Magnesium infusion was even considered in some patients with Myocardial Infarct who were not eligible for thrombolytics with favourable results. A global analysis by Horner of magnesium therapy in acute myocardial infarction found that this treatment was safe and useful⁸. However two double-blind controlled mega-trials had cast doubt on this point of view^{9,10}. The MAGIC trial, despite not showing any difference of mortality did show improvement of quality of life in those who did receive the treatment⁷. Cassells stated that patients with subnormal magnesium concentrations should be given magnesium in AMI¹¹.

Two studies concerning the use of magnesium and mortality after AMI predated the introduction of thrombolysis. Horner reported that i.v. administration of magnesium was associated with a 49% reduction in the incidence of ventricular tachycardia (VT) and ventricular fibrillation (VF) and that there was a smaller non-significant reduction in the incidence of asystole and electromechanical dissociation (EMD) in the treatment groups. Overall, there was a 54% reduction in mortality associated with administration of magnesium⁸. Teo and colleagues also demonstrated that administration of magnesium was a safe and effective method of reducing arrhythmias and mortality in AMI¹². Horner suggested that the anti-arrhythmic effect of magnesium was the main mechanism by which it reduced mortality.

In this study, there was a significant deficiency of the means of plasma Magnesium level among Acute Coronary Syndrome patients (Table 1). As a whole, the means of Serum Magnesium in ACS is significantly lower compared to the control. However upon further analysis, it was found that the subgroup NSTEMI contributed largely to the low level of the Magnesium. In individual analysis, it was found that there was no difference in terms of the means of Serum Magnesium in STEMI and UA patients. By itself, the Magnesium level of ACS lies in the normal range but tends to be on the lower range.

The mean of Serum Magnesium in ACS group (0.88 ± 0.15) was still within the normal range but there was a significant difference when compared to the control group; $p=0.038$ (Table 1). The lower mean of serum Magnesium was found in NSTEMI patients. Hypomagnesemia was present in : 12.5% of STEMI($p=0.00$), 9.7% of UA($p=0.039$), 29.7 % of NSTEMI($p=0.00$) and 3.2% of control patients. 9.4% of STEMI patients actually had hypermagnesemia (Graph 1).

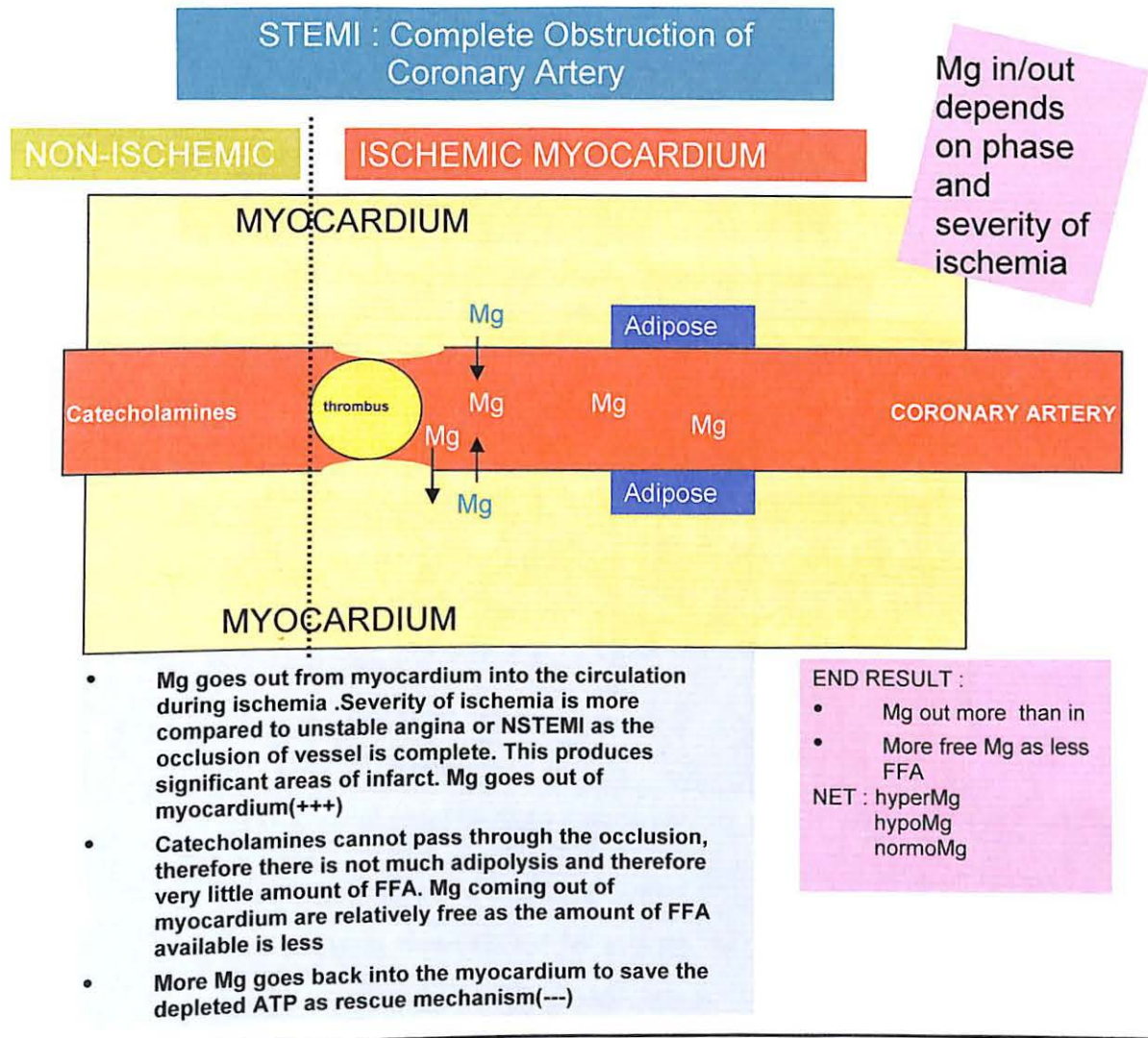
There was significant difference in terms of Magnesium level in comparison between subsets of Acute Coronary Syndrome (Unstable Angina, Non ST Elevation Myocardial Infarct and ST elevation Myocardial Infarct) . The means of NSTEMI showed significantly lower Magnesium level compared to STEMI and UA. No significant difference however was found between the means of STEMI and UA. In further analysis, it was also found that there was significant proportion of hypomagnesemia in all subgroups compared to the control group. In the case of STEMI, there was also a significant proportion of hypermagnesemia compared to the control healthy population.

Postulation That Explains the Result of This Study

Based on the findings of this study, postulation as regards why such results were obtained is made based on these principles :

1. Ischemic areas causes Magnesium to go out of intracellular area into the circulation
2. Ischemia produces stress to the body which triggers production of catecholamines from the adrenal gland
3. Catecholamines will be brought by blood circulation to ischemic area and there, causes adipolysis which produces free fatty acid (FFA) in the circulation
4. FFA binds to Magnesium and produces less available free Magnesium detectable by lab investigation.
5. Results of normo, hypo and hypermagnesemia in ACS patients depends on the type of ACS and the duration and severity of ischemia. The net result depends on the variable of Magnesium going out of cell into circulation during ischemia, the amount of catecholamines

DIAGRAM 1 : POSTULATED MODEL FOR STEMI

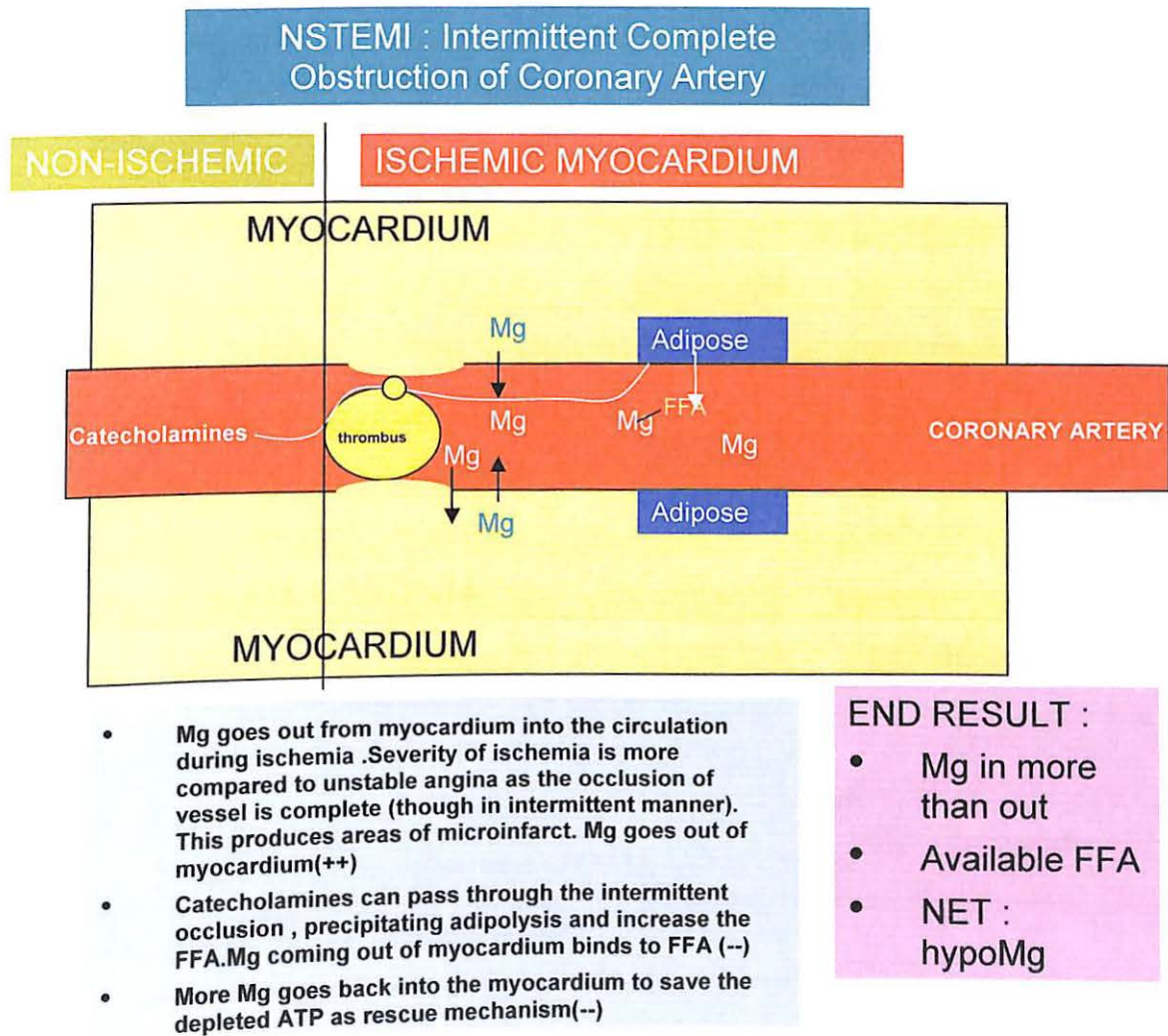


Magnesium 'fate' in STEMI: postulation (Diagram 1)

During ischemia, Mg goes out from myocardium into the circulation. Compared to Unstable angina or NSTEMI, severity of ischemia is more as the occlusion of vessel is complete. This produces significant areas of infarct. The amount of Mg going out of myocardium is therefore expected to be much more than both UA and NSTEMI. Nevertheless, at the same time, catecholamines (produced as a result of stress caused by ischemia) cannot pass through the occlusion. Therefore there is not much adipolysis at the area beyond the occluded area. This results in little amount of free fatty acid (FFA)

produced into circulation. Therefore, less FFA is available and therefore, less Mg would bind with the FFA. As a result, Mg coming out of myocardium are relatively free as the amount of FFA available is less. On top of that, more Mg goes back into the myocardium to save the depleted ATP as rescue mechanism. As the end result, the net result of Serum Magnesium in circulation is either same with normal population or slightly higher (as shown in this study)

DIAGRAM 2 : POSTULATED MODEL FOR NSTEMI

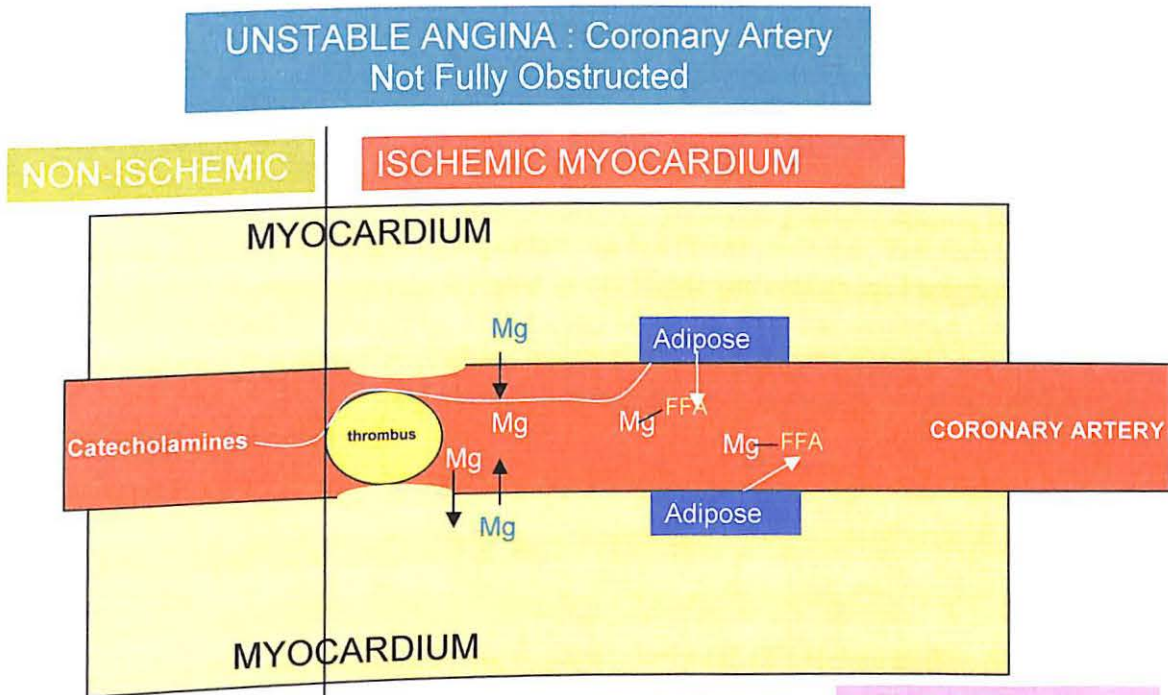


Magnesium ‘fate’ in NSTEMI : postulation (Diagram 2)

During ischemia, Magnesium goes out from myocardium into the circulation. Severity of ischemia in NSTEMI is expected to be more compared to unstable angina as the occlusion of vessel is complete (though in intermittent manner or at area of microcirculation) producing areas of microinfarct. At the same time, catecholamines produced by ischemic stress to patients can pass through the intermittent occlusion , precipitating adipolysis and increase the FFA.Mg coming out of myocardium binds to

FFA. At the same time too, more Magnesium goes back into the myocardium to save the depleted ATP as rescue mechanism. As an end-result, less Magnesium is in circulation. Therefore, the serum level of Mg in NSTEMI appear significantly lower than normal population

DIAGRAM 3 : POSTULATED MODEL FOR UNSTBLE ANGINA



- Mg goes out from myocardium into the circulation during ischemia .Nevertheless, the severity of ischemia is less compared to infarct as the occlusion of vessel is not complete. Minimal Mg goes out of myocardium(+)
- Catecholamines can pass through the occlusion , precipitating adipolysis and increase the FFA.Mg coming out of myocardium binds to FFA (-)
- Some Mg goes back into the myocardium to save the depleted ATP as rescue mechanism(-)

END RESULT :

- Mg out more than in equal
- Plenty of FFA

NET : normoMg

Magnesium 'fate' in UA : postulation (Diagram 3)

During ischemia, Mg goes out from myocardium into the circulation. Nevertheless, the severity of ischemia is less compared to infarct as the occlusion of vessel is not complete. Minimal Mg goes out of myocardium. Catecholamines can pass through the occlusion , precipitating adipolysis and increase the FFA. Magnesium coming out of myocardium binds to FFA. Some Mg goes back into the myocardium to save the depleted ATP as rescue mechanism. As the end result : Magnesium goes out of the cell more.

Nevertheless, plenty of available FFA binds the free Magnesium resulting in the net normal range of Magnesium level.

Serum Magnesium can be used as an adjunct to diagnosis-making process of Acute Coronary Syndrome patients – especially if all other causes of hypomagnesemia is ruled out eg diarrhea etc. From the study, Odds Ratios were calculated for each group and it was found that the Odds Ratio of getting STEMI, UA and NSTEMI in patients presenting with classical clinical signs and symptoms and hypomagnesemic are higher compared to the control population. This is especially helpful in the case of NSTEMI, whereby there is difficulty of differentiating between NSTEMI and UA. If hypomagnesemia is present, the Odds of getting NSTEMI compared to UA is higher. However, this is only used as an adjunct and not the sole diagnostic tool.

Magnesium therapy in Acute Coronary Syndrome patients among local population should be considered especially in NSTEMI patients . The fact that significant proportion of hypomagnesemia is noted in NSTEMI patients should reignite interest of magnesium therapy in this group of patients. Moreover with the evidence that quality of life is improved among patients given magnesium as treatment in trial like that of MAGIC 2000. (MAGIC 2000). Further study regarding giving magnesium infusion in NSTEMI patients is needed.

Conclusions

The Serum Magnesium of ACS, particularly NSTEMI was within the normal range but tend to be at the lower range. Compared to the control healthy population, there was a significant proportion of hypomagnesemia in ACS group as a whole as well as each subgroup. NSTEMI group had the highest proportion of hypomagnesemia – a fact not documented in previous literature at the time this study was conducted . Hypomagnesemia in patients presenting with chest pain may be used as an adjunct for diagnosis of ACS as well as differentiating between UA and NSTEMI. Further study should be considered especially in terms of magnesium supplement for NSTEMI patients since this group of patients had a significantly high proportion of hypomagnesemia.

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**PENYATA PERBELANJAAN
(FINANCIAL STATEMENT)**

UNIVERSITI SAINS MALAYSIA
 JABATAN BENDAHARI
 KUMPULAN WANG PENYELIDIKAN GERAN USM(304)
 PENYATA PERBELANJAAN SEHINGGA 31 MEI 2007

Jumlah Geran:	RM	Tiada Rekod	Ketua Projek: PROF(M) ZULKURNAI YUSUF
Peruntukan 2005 (Tahun 1)	RM	5,214.00	Tajuk Projek: Study of Serum Magnesium Level in Acute Coronary Syndrome Patients
Peruntukan 2006 (Tahun 2)	RM	0.00	
Peruntukan 2007 (Tahun 3)	RM	0.00	Tempoh: 1 Apr 05-31 Mac 07 No.Akaun: 304/PPSP/6131370

Kwg	Akaun	PTJ	Projek	Donor	Peruntukan Projek	Perbelanjaan T'kumpul Hingga Tahun Lalu	Peruntukan Semasa	Tanggung Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
304	11000	PPSP	6131370		-	-	-	-	-	-	-
304	14000	PPSP	6131370		-	-	-	-	-	-	-
304	15000	PPSP	6131370		-	-	-	-	-	-	-
304	21000	PPSP	6131370		350.00	-	350.00	-	-	-	350.00
304	22000	PPSP	6131370		-	-	-	-	-	-	-
304	23000	PPSP	6131370		114.00	-	114.00	-	-	-	114.00
304	24000	PPSP	6131370		-	-	-	-	-	-	-
304	25000	PPSP	6131370		-	-	-	-	-	-	-
304	26000	PPSP	6131370		-	-	-	-	-	-	-
304	27000	PPSP	6131370		250.00	-	250.00	300.00	-	300.00	(50.00)
304	28000	PPSP	6131370		-	-	-	-	-	-	-
304	29000	PPSP	6131370		4,500.00	2,600.00	1,900.00	-	-	2,600.00	1,900.00
304	32000	PPSP	6131370		-	-	-	-	-	-	-
304	35000	PPSP	6131370		-	-	-	-	-	-	-
					5,214.00	2,600.00	2,614.00	300.00	-	2,900.00	2,314.00

**LAPORAN KOMPREHENSIF
/COMPREHENSIVE REPORT**

LAPORAN AKHIR / FINAL REPORT

Title :

**“Study of Serum Magnesium in Acute Coronary Syndrome Patients”
Account Number : 304/PPSP/6131370**

1.0 Introduction

This study was approved by the ethical committee and carried out since April 2004. This study was done utilizing short-term grant under Associate Professor Dr Zurkurnai Yusuf. The data collection was completed about 1 year later (April 2005). The write-up was completed in November 2005. It was reviewed extensively by internal and external examiner and was accepted by the as a partial fulfilment of the Master in Medicine (Emergency). This study also is the first in the world that included population of Non-ST Elevated Myocardial Infarction Acute Coronary Syndrome patients.

The abstract of the study is attached in this letter. 2 copies of the full thesis are in the keeping of the Graduate's Office.

2.0 Achievements

The paper was presented twice at national level and at both times, it was chosen as best paper. The author was actually offered to do a PhD by one of the examiners following him being impressed with the quality of the paper

Presentations	Location	Achievement
1. 11 th National Conference of Health and Medical Sciences. (Oral Presentation)	Universiti Sains Malaysia Kubang Kerian	Best Paper (1 st place) in Medical Category
2. 40 th Malaysia-Singapore Congress of Medicine (organized by the Academy of Medicine, Malaysia)	Sunway Pyramid, Petaling Jaya, Selangor	Accepted for presentation
3. 10 th National Conference and Scientific Meeting of Emergency Medicine (Oral Presentation)	IOI Mall, Putrajaya	Best Paper (1 st place) in Medical Category

3.0 International Level

The paper was accepted and presented at the 40th Singapore-Malaysia Congress of Medicine held at Sunway Hotel, Malaysia.

4.0 Future Plans Regarding the Study

Plans are underway for presentation at International level (4th Mediterranean Conference on Emergency and Disaster Medicine) in Sorrento, Italy in September 2007. The paper is already accepted for presentation in the conference.

Works are underway to have it published in journal.

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SCIENCES**

PENERBIT
USM

OM-17

THE STUDY OF SERUM MAGNESIUM LEVEL IN ACUTE CORONARY SYNDROME PATIENTS

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* Department of Emergency Medicine, ** Department of Chemical Pathology, *** Cardiac Unit, Department of Medicine, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150 Kota Bharu, Kelantan

PURPOSE :

There is a need to know the state of serum magnesium in Acute Coronary Syndrome (ACS), which consists of STEMI, UA and NSTEMI in our population. Our aim in this study is to determine the serum magnesium in ACS. Knowledge on this will serve as a guide on future investigations, studies and treatment of the disease.

METHOD :

The serum magnesium level of 420 patients with chest pain was taken at the Emergency Department. Upon confirmation based on WHO criteria, 255 were confirmed case of Acute Coronary Syndrome (64 STEMI, 155 UA and 37 were confirmed as NSTEMI). 95 healthy control samples (age range from late teen to elderly) were taken as comparison.

RESULTS :

Mean serum magnesium in ACS group (0.88 ± 0.15) is still within the normal range but there is a significant difference as compared to the control group ($p = 0.038$). The lower level of serum Magnesium was mainly found in NSTEMI patients. Hypomagnesemia was found in 12.5% of STEMI ($p = 0.00$), 9.7% of UA ($p = 0.039$), 29.7 % of NSTEMI ($p = 0.00$) and 3.2% of control patients. 9.4% of STEMI patients actually had hypermagnesemia. The Odd's Ratio for developing ACS in the presence of hypomagnesemia in symptomatic patients is 4.559 times compared to normal control. (95% Confidence Interval between 1.364 and 15.236); $p = 0.00$.

CONCLUSIONS :

Serum magnesium of ACS patients is within the normal range but tends to be at the lower level. Compared to the control healthy population, there is a significant proportion of hypomagnesemia in ACS group and within the subgroups. NSTEMI has the highest proportion of hypomagnesemia There is 4.6 folds risk of developing ACS in patients with hypomagnesemia presenting with chest pain compared to normal healthy population.

Best Oral Communication in CLINICAL SCIENCES (MEDICAL-BASED)



was awarded to

Dr Alzamani Mohammad Idrose

for the presentation entitled

The study of serum magnesium level in acute coronary syndrome patients

Authors: Alzamani MI, Rashidi A, Hasenan N, Zurkurnai Y

at the


11th National Conference on Medical Sciences

"in rhythm with nature"

20 - 21 May 2006

Organised by:
Health Campus
Universiti Sains Malaysia
Kelantan, Malaysia


Prof. Dr. Abdul Aziz Baba
Dean
School of Medical Sciences
Universiti Sains Malaysia


Prof. Dr. Nor Hayati Othman
Chairperson
11th National Conference on
Medical Sciences



ACADEMY OF MEDICINE OF MALAYSIA



ACADEMY OF MEDICINE, SINGAPORE

Certificate of Attendance

This is to certify that

Alzamani Bin Mohammad Idrose

participated in the

**40th Malaysia-Singapore
Congress of Medicine**

held on

24 to 27 August 2006

at

**Sunway Pyramid Convention Centre
Petaling Jaya, Malaysia**

PROF CHAN YOO KUEN

**SURAT PEMAKLUMAN
PENGHANTARAN LAPORAN AKHIR
KE BHG PENYELIDIKAN**

DR ALZAMANI MOHAMMAD IDROSE
(BAGI PIHAK PROFESOR MADYA DR ZURKURNAI YUSOF)
NO 11 Jalan 14/1 Taman Tun Abdul Razak
Ampang Jaya 68000 Selangor

Kepada:

Pn. Che Merah Ismail
Pen. Pegawai Tadbir
Pejabat Pengurusan dan Kreativiti Penyelidikan (RCMO)
Aras 6, Bangunan Canselori
Universiti Sains Malaysia
11800 Pulau Pinang.

Tarikh: 29 Julai 2007

Puan,

LAPORAN AKHIR GERAN PENYELIDIKAN USM JANGKA PENDEK

Tajuk: Study of Serum Magnesium in Acute Coronary Syndrome Patients
No: Akaun: 304/PPSP/6131370
Tarikh Mula: 1 April 2005
Tarikh Tamat (Berdasarkan kelulusan RCMO) : 1 April 2007

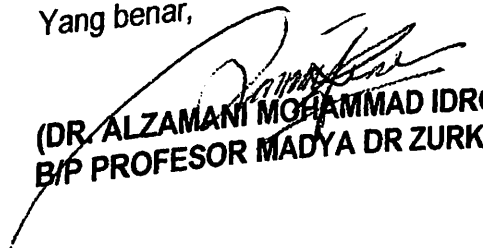
Dengan segala hormatnya perkara di atas adalah dirujuk.

Untuk makluman puan, laporan akhir projek penyelidikan jangka pendek yang bertajuk seperti di atas telah dihantar kepada Bahagian Penyelidikan & Inovasi, Pusat Pengajian Sains Perubatan, Kampus Kesihatan USM untuk tindakan selanjutnya.

Sekian, harap maklum.

"BERSAING DIPERINGKAT DUNIA: KOMITMEN KITA"

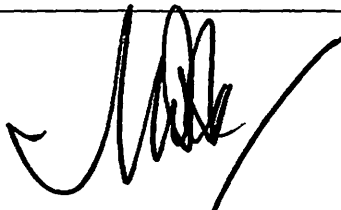
Yang benar,


(DR. ALZAMANI MOHAMMAD IDROSE)
B/P PROFESOR MADYA DR ZURKURNAI YUSOF

s.k- En. Halim Othman
Bhg. Penyelidikan & Inovasi , PPSP

Komen Jawatankuasa Penyelidikan Pusat Pengajian/Pusat
Comments by the Research Committees of Schools/Centres

suggest submit paper
manuscript to any journal



ASSOC. PROF. MUSTAFFA MUSA
Chairman of Research Committee
School of Medical Sciences
Health Campus

TANDATANGAN PENGERUSI
JAWATANKUASA PENYELIDIKAN
PUSAT PENGAJIAN/PUSAT
Signature of Chairman
[Research Committee of School/Centre]

21/10/07

Tarikh
Date