## بسم الله الرحمن الرحيم

# 🖁 قال تعالى

﴿ إِنْ أُرِيدُ إِلاَّ الإِصْلاَحَ مَا اسْتَطَعْتُ وَمَا تَوْفِيقِي إِلاَّ السَّطَعْتُ وَمَا تَوْفِيقِي إِلاَّ اللهِ عَلَيْهِ تَوكُلْتُ وَإِلَيْهِ أَنِيبِ﴾.

صدق الله العظيم الأية 88} {من سورة هود

### **Dedication**

TO My parents

To My brothers

To my friends

## Acknowledgments

Firstly the grateful thanks to Almighty Allah, the lord of earth and skies for completing this research. I would like to express my thanks and appreciations to my supervisor Dr. Abdelbagi Elnagi Mohamed, College of Medical Laboratory Science, Department of Microbiology, Sudan University of Science and Technology for his unfailing patience, expert advices, supervision, guidance, efforts, suggestions and his valuable time.

Extended thanks to The staff of the College of Medical Laboratory Science, especially Dr. Mohammed Siddig, Ustaz Aboalgasim Abbas, Ustaz Yaseen.A.Omer, Ustaza Samer.M.Shareef, Ustaz Ahmed.A.Galander, Ustaza Amged Abdelkareem, Ustaza Asged.M.Mokhtar, Ustaza Maryam Abbas, Ustaza Sarah.O.Yousif, Ustaza Samia.M.Ahmed, Ustaza Altaf Suleman, Ms. Nafeesa Mohamed, Mr. Mohamed.A.Alsaied and Mr. Fawzy Ibrahim for their help and cooperation and encouragement.

A special thanks to Ms. Suhair Ramadan for her grateful efforts and valuable advices.

A lot of thanks to The Medical Laboratory staff of Omdurman Teaching Hospital, Khartoum North Renal Center and Ibn Sina Specialized Hospital for their cooperation help and support.

I would like to express a special word of thanks to my colleagues, friends and students.

My deepest appreciation to everyone who helped me in collection of my specimens, Mr. Modether.O.Abdelbaseer, Ms. Suhair Abdelsatar and those in hemodialysis units of Omdurman Teaching Hospital (in specific Youhanez and Omer), Khartoum North Renal Center and Ibn Sina Specialized Hospital.

My heartiest thanks to my parents in supporting me and who have been the source of encouragement and inspiration throughout my life.

I am also very grateful to my aunt Nora Osman, for her motivation and support.

I thank all the patients for their cooperation and participation and to whom I am greatly indebted.

#### **Abstract**

The main aim of this study was to determine the seroprevalence of human cytomegalovirus (HCMV) antibodies (IgG and IgM) using Enzyme-Linked Immunosorbent Assay (ELISA), among 160 hemodialysis patients and 40 apparently healthy control in Khartoum State. Hemodialysis patients in this study were selected from Ibn Sina Specialized Hospital, Khartoum North Renal Center and Omdurman Teaching Hospital. Of the 160 dialysis patients 107 were males (65.6%) and 53 were females (33.1%) and their ages ranged from 14 to 90 years. The subgroups of hemodialysis patients were, 110 hepatitis-negative (68.8%), 26 HBV-positive (16.3%) and 24 HCV-positive (15.0%). Out of the 40 control subjects, 19 were males (47%) and 21were females (53%) and their ages ranged from 14 to 73 years. The prevalence of CMV antibodies was high among both the hemodialysis patients (98.12%) and the control group (100%). While 157 hemodialysis patients were anti-CMV IgG positive (98.12%), only 3 were negative (1.88%). Among different hemodialysis patients subgroups, 108 hepatitis-negative (98.2%), 26 HBV-positive (100%) and 23 HCV-positive (95.5%) were positive to anti-CMV IgG and there was no significant difference (p > 0.05) between them. It was found that 105 males (98.13%) and 52females (98.11%) were anti-CMV IgG positive and there was no significant difference (p > 0.05) between both genders. In contrast, all 40 control subjects (males and females ) were positive for anti-CMV IgG (100%). Out of the 11 anti-CMV IgM positive dialysis patients (6.9%) 5 were hepatitis-negative (45.5%), 4 were HBV-positive (36.4%) and 2 were HCV-positive (18.2%) and there was no significant difference (p >0.05) between them. The study also found that 8 males (72.7%) and 3 females (27.3%) were anti-CMV IgM positive and there was no significant difference (p > 0.05) between them. In additition, out of the 11 control subjects 4 males (36.4%) and 7 females (63.6%) were anti-CMV

IgM positive (27.0%) and there was no significant difference (p>0.05) between them. Furthermore, this study found that the main risk factor for primary or past infection of CMV was aging and for secondary infection or reinfection or reactivation of virus was blood transfusion. However, hepatitis viruses, sex,the marital status, chronicity of hemodialysis, multiple hemodialysis, blood transfusion, and the crowdness were not risk factors for CMV infections.

الهدف الرئيسي من هذه الدراسة هو تحديد الإنتشار المصلي للأجسام المضادة من النمط (gGI) والنمط (gMI) لفيروس مضخم الخلاد بالستخدام الختبا اللالايزا ل 160 مريض يخضعون للإستصفاء الدموي و 40 شخص سليم ظاهريًا كضابط الختبار في ولاية الخرطوم تم الختيار المرضى الذين يخضعون للإستصفاء الدموي لهذه الدراسة من مستشفى ابن سينا التخصصي و مركز بحري لأمراض وزراعة الكلى و مستشفى أمدرمان التعليمي. من بين 160 مريض يخضعون للإستصفاء الدموي , 107 منهم كانوا ذكورا ( 65.6%) و 53 كانوا إناثا (33.1٪) وتترواح أعمارهم ما بين 14 الى 90 سنة. وتشمل مجموعات المرضى الذين يخضعون للإستصفاء الدموي: 110 مريضاً لا يعانون من فيروسات إلتهاب الكبد الوبائي (68.8٪) و 26 مريضاً يعانون من فيروس التهاب الكبد الوبائي (ب) (16.3٪) و 24 مريضاً يعانون من فيروس التهاب الكبد الوبائي (ج) ( 15.0٪). أما لأفراد ضابط إلى الختبار , 19 منهم كانوا ذكوراً (47.0٪) و 21 منهم كانوا إناثاً (53.0٪) وتترواح أعمارهم ما بين 14 الى 73 سنة. وجد أن معدل إنتشارالأجسام المضادة لفيروس مضخم الخلايا كان عالياً بين المرضى الذين يخضعون للإستصفاء الدموي (98.12٪) و المجموعة الضابط للا الختبار (100٪) معا. وجد أن 157 مريضا يخضعورللا استصفاء الدموي كانت لديهم أجسام مضادة من النمط (IgG) لفيروس مضخم الخلايا بنسبة 98.12 ٪ و 3 عينات فقط أعطت نتيجة سلبية بنسبة 1.88٪ . وكانت النسبة موزعة بين مجموعات المرضى الذين يخضعون للإستصفاء الدموي كالآتي: 108 مريضاً لا يعانون من فيروسات إلتهاب الكبد الوبائي (98.2٪) و 26 مريضاً يعانون منفيروس التهاب الكبد الوبائي ب (100٪) و 23 مريضاً يعانون من فيروس التهاب الكبد الوبائي (ج)

(95.5%) لديهم أجسام مضادة من النمط (gGI) للفيروس المضخم للخلايا. كما لا توجد أي فرو قات ذات دلالة الحصائية بينهم (الاقيم اللاحتمالية أكبر من 0.05). وجد أن: 105 من الذكور (98.13%) و 52 من الإناث (98.13%) كانت لديهم أجسام مضادة من النمط (gGI) لفيروس مضخم الخلايا, ولا توجد أي فرو قات ذات دلالة الحصائية بينهما (الاقيم الله الحتمالية أكبر من 0.05). بالم قارنة وجد أن كل أفراد المجموعة الضابطة (ذكوراً وإناثاً) لديهم أجسام مضادة من النمط (gGI) للفيروس المضخم للخلايا (100%). وجد أن 11 مريضاً يخضعون للإستصفاء الدموي (6.9%) كانت لديهم أجسام مضادة من النمط (IgM) منهم 5 مرضى لا يعانون من فيروسات إلتهاب الكبد الوبائي (45.5%) و 4 من

المرضى الذين لديهم فيروس إلتهاب الكبد الوبائي (ب) (4.36.%) و 2 من المرضى الذين لديهم في روس إلتهاب الكبد الوبائي (ج) (1.82%). ولا توجد فرو قات ذات دلالة الحصائيةيين المجموعات الثلاث (الاقيم المالات أكبر من 0.05). كما وجد من هذه الدراسة أيضاً أن 8 من الذكور (72.7%) و 3 من الإناث (27.3%) كانت لديهم أجسام مضدادة من النمط (IgM) ولا توجد بينهما فرو قات ذات دلالة الحصائية (الاقيمة الساحتمالية أكبر من 0.05). وبالأضافة لذك , وجد أن 11 فرد من المجموعة الضابطة منهم 4 ذكور بنسبة 4.36% و 7 إناث بنسبة 6.66% لديهم أجسام مضادة من النمط (MgI) ولا توجد بينهما فرو قات ذات دلالة الحصائية (الاقيم المالات الرئيسي اللها من 0.05). وبالأولية أو إصابة ساب قة بفيروس مضخم الخلايا و عمليات نقل الدم هي عامل الخطورة الأولية أو إصابة متكررة بنفس الفيروس أو نشاط الفيروس مرة أخرى. كما لوحظ أيضاً أن : فيروسات إلتهاب الكبد الوبائي و الجنس و الحال المالجتماعية والفترة الزمنية للإستصفاء الدموي و عدد مرات الإستصفاء الدموي وعمليات نقل الدم و الإزدهام لا تمثل عوامل خطورة للإصابة بأمراض الفيروس المضخم للخلايا.

### **Table of contents**

No.	Subjects	Page
		No.
الآدة	<u>'</u>	I
Dedication		II
Acknowl	Acknowledgments	
Abstract,	English	IV
Abstract,	Arabic	VI
Tables of		VIII
List of ta		XI
List of fig	gures	XII
Abbrevia	tions	XIII
	Chapter one: Introduction	
1.1	Background	1
1.2	Rationale	2
1.3	Objectives	3
1.3.1	General objective	3
1.3.2	Specific objectives	3
	Chapter two: Literature review	
2.1	Introduction to herpesviruses	4
2.2	History	4
2.3	Classification	4
2.4	Structure of virus	5
2.5	Properties of CMV	7
2.6	Replication of CMV	7
2.7	Routes of infection	8
2.8	Epidemiology	9
2.9	Pathogenesis	10
2.10	Pathogenicity	11
2.10.1	Infection of mothers and babies	11
2.10.2	Infection in children	12
2.10.3	Infection in adults	12
2.10.4	Infection in immunocompromised patients	13
2.11	Immunity	14
2.12	Laboratory diagnosis	14
2.12.1	Collection of specimen	14
2.12.2	Isolation of virus	15
2.12.3	Serology	18

2.12.4	Polymerase Chain Reaction and Antigen Detection	19
	Assay	
2.13	Treatment	19
2.14	Prevention and control	20
2.15	Prevalence of CMV in hemodialysis patients	20
	Chapter three: Materials and methods	
3.1	Methods	22
3.1.1	Study approach	22
3.1.2	Study area	22
3.1.3	Study duration	22
3.1.4	Study design	22
3.1.5	Study population	22
3.1.6	Inclusion criteria	22
3.1.7	Exclusion criteria	22
3.1.8	Sample size	22
3.1.9	Sampling technique	23
3.1.10	Method of data collection	23
3.1.11	Ethical consideration	23
3.1.12	Specimen collection	23
3.1.13	Laboratory tests	24
3.1.13.1	Enzyme-Linked Immunosorbent Assay (ELISA)	24
3.1.13.1.1		24
3.1.13.1.1	1.1 Principle	24
3.1.13.1.1	1.2 Procedure	24
3.1.13.1.1	1.3 Calculation and interpretation of the results	25
3.1.13.1.2	2 ELISA for detection of CMV IgM antibodies	25
3.1.13.1.2	2.1 Principle	25
3.1.13.1.2	2.2 Procedure	25
3.1.13.1.2	2.3 Calculation and interpretation of the results	26
3.1.14	Data analysis	26
	Chapter four: Results	
4	Results	27
4.1	Hepatitis sero-reactivity among hemodialysis patients	27
4.2	Detection of anti-CMV IgG positive cases among the	27
	hemodialysis patients and the control group	
4.3	Detection of anti-CMV IgM positive subjects among	27
	the hemodialysis patients and the control group	
4.1	Association of HBV and HCV antibodies with CMV	27
	antibodies among hemodialysis patients	

4.2	Sero-detection of CMV antibodies among hemodialysis	27
	patients according to age incidence	
4.3	Sero-detection of CMV antibodies among hemodialysis	28
	patients according to sex incidence	
4.4	Association of crowdness with CMV antibodies among	28
	hemodialysis patients	
4.5	Association of marital status with CMV antibodies	28
	among hemodialysis patients	
4.6	Association of multiple hemodialysis with CMV	28
	antibodies	
4.7	Association of chronicity of hemodialysis with CMV	28
	antibodies	
4.8	Association of blood transfusion with CMV antibodies	28
	among hemodialysis patients	
4.9	Sero-detection of CMV IgM antibodies among control	28
	group subjects according to sex incidence	
4.10	Sero-detection of CMV IgM antibodies among control	29
	group subjects according to age incidence	
4.11	Association of marital status with CMV IgM antibodies	29
	among control group subjects	
4.12	Association of crowdness with CMV IgM antibodies	29
	among control group subjects	
	Chapter five: Discussion	
5	Discussion	38
	Conclusion	42
	Recommendations	42
	References	43
	Appendices	47

## **List of tables**

Table No.	Legend	Page No.
4.1	Association of HBV and HCV antibodies with CMV	32
	antibodies among hemodialysis patients	
4.2	Sero-detection of CMV antibodies among hemodialysis	32
	patients according to age incidence	
4.3	Sero-detection of CMV antibodies among hemodialysis	33

	patients according to sex incidence	
4.4	Association of crowdness with CMV antibodies among	33
	hemodialysis patients	
4.5	Association of marital status with CMV antibodies	34
	among hemodialysis patients	
4.6	Association of multiple hemodialysis with CMV	34
	antibodies	
4.7	Association of chronicity of hemodialysis with CMV	35
	antibodies	
4.8	Association of blood transfusion with CMV antibodies	35
	among hemodialysis patients	
4.9	Sero-detection of CMV IgM antibodies among control	36
	group subjects according to sex incidence	
4.10	Sero-detection of CMV IgM antibodies among control	36
	group subjects according to age incidence	
4.11	Association of marital status with CMV IgM antibodies	36
	among control group subjects	
4.12	Association of crowdness with CMV IgM antibodies	37
	among control group subjects	

# List of figures

Figure	Legend	Page
No.		No.
2.1	Virion of CMV	6
2.2	The CPE of CMV in cell culture	16
2.3	The inclusion bodies of CMV	17
4.1	Hepatitis sero-reactivity among hemodialysis patients	30
4.2	Detection of anti-CMV IgG positive cases among the	31
	hemodialysis patients and the control group	
4.3	Detection of anti-CMV IgM positive subjects among the	31

hemodialysis patients and the control group

### **Abbreviations**

**AIDS** Acquired immunodeficiency syndrome

**CMID** Cytomegalic inclusion disease

**CMV** Cytomegalovirus

**CPE** Cytopathic effect

**D**+ Seropositive donor

**DNA** Deoxyribonucleic acids

**EIA** Enzyme immunoassays

**ELISA** Enzyme-Linked Immunosorbent Assay

Fc Fragment crystallizable

**H&E stain** Hematoxylin and Eosin stain

**HBV** Hepatitis B virus

**HCMV** Human cytomegalovirus

**HCV** Hepatitis C virus

**HIV** Human immunodeficiency virus

**HHV-5** Human herpes Virus 5

**HHV-6** Human herpes Virus 6

**HHV-7** Human herpes Virus 7

**HSV** Herpes simplex virus

**IgA** Immunoglobulin A

**IgG** Immunoglobulin G

**IgM** Immunoglobulin M

**mRNA** messenger RNA

**O.D** Optical density

**PCR** Polymerase chain reaction

**R**- Seronegative recipient

**RNA** Ribonucleic acids

**US** United States