

Contents

Subjects	Page
List of abbreviations.....	II
List of Figures	VI
List of Tables	VII
• Introduction	1
• Aim of the work	4
• Review of Literature	
♦ Chapter (1): Depression in ESRD	5
♦ Chapter (2): Anemia and Erythropoietin Resistance in ESRD Patients	34
♦ Chapter (3): Erythropoietin Resistance and Depression in ESRD	83
• Patients and Methods	90
• Results	98
• Discussion	128
• Summary and Conclusion	143
• Recommendations	150
• References	151
• Arabic Summary	

List of Abbreviations

5HT.....	(Sertonin)
A.A.....	(Amino Acids)
ACE Is.....	(Angiotensin converting enzyme inhibitors)
ADMA.....	(A symmetrical dimethyl arginine)
AL.....	(Aluminum)
APCs.....	(Antigen presenting cells)
ARBs.....	(Angiotensin Receptor blockers)
BDI.....	(Beck depression inventory)
BDNP.....	(Brain derived neutrophic factor)
BFU-E.....	(Burst forming unit- Erythroid)
BMI.....	(Body mass index)
BUN.....	(Blood urea nitrogen)
C EPO.....	(Cabamylated Erythropoietin)
CDI.....	(Children depression Inventory)
CES-D.....	(Center for epidemiology studies Depression screaning scale)
CES-DC.....	(Center for epidemiology studies Depression screaning children scale)
CFU-E.....	(Colony forming unit erythroid)
CHF.....	(Chronic heart failure)
CIs.....	(Cytokines inducible)
CKD.....	(Chronic kidney disease)

List of Abbreviations

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CNS.....	(Central nervous system)
Creat.....	(Creatinine)
CRP	(C reactive protein)
DBP	(Diastolic blood pressure)
DM	(Diabetes mellitus)
DMT1	(Divalent metal transporter)
DOPPS.....	(Dialysis outcomes and practice patterns study)
DSM III	(Diagnostic and statistical manual of mental disorders type III)
ECG	(Electrocardiogram)
EEG.....	(Electroencephalogram)
EMA	(European medicine Agency)
ENOS.....	(Endothelial nitric oxide synthetase)
EPO	(Erythropoietin)
EPOR.....	(Erythropoietin receptor)
ERI	(Erythropoietin resistant index)
ESA.....	(Erythropoietin stimulating agent)
ESRD.....	(End stage renal disease)
ET-1.....	(vasoconstrictor endothelial-1)
FDA	(Food and drug administration)
HADS	(Hamilton Anxiety depression rating scale)
Hb	(Hemoglobin)
HCP	(Hematopoietic cell phosphate)

List of Abbreviations

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HCT	(Hematocrit)
HD	(Hemodialysis)
HF-HD	(High flux hemodialysis)
HTN	(Hypertension)
INOS	(Inducible nitric oxide synthetase)
ISHD	(Ischemic heart disease)
IV	(Intravenous)
JAK2	(Janus kinase 2)
KDIGO	(Kidney disease improving global outcomes)
KDOQI	(Kidney Disease Outcomes Quality Initiative organization)
LF-HD	(Low flux hemodialysis)
MAP	(Mitogen- activated protein)
MCH	(Mean corpuscular hemoglobin)
MCHC	(Mean corpuscular hemoglobin concentration)
MCV	(Mean corpuscular volume)
MHI-S	(subscale of medical outcome study short form 36 index)
NE	(Nor Epinephrine)
NF KB	(Nuclear factor Kappa B)
NKF	(National kidney foundation)
OL-HDF	(Online hemodiafiltration)
PGF 2X	(Prostaglandin 2X)
PGI2	(Vasodilator Prostacyclin)

List of Abbreviations

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Phosph	(Phosphorus)
PI3K	(Phosphatidyl inositol 3 kinase)
PLT	(Platelets)
PTH	(Parathyroid hormone)
rhEPo	(recombinant human Erythropoietin)
RhEPO	(Recombinant human Erythropoietin)
SBP	(Systolic blood pressure)
SC	(Subcutaneous)
SNRIs	(Serotonin/Nor epinephrine reuptake inhibitors)
SOCs	(Suppressor of cytokine signaling)
SSRIs	(Selective serotonin reuptake inhibitors)
STATs	(Signal transducer and activator of transcriptions)
TCAs	(Tricyclic antidepressants)
TFR	(Transferrin receptor)
TIBC	(Total iron binding capacity)
TSAT	(Transferrin saturation)
TSH	(Thyroid stimulating hormone)
TXB2	(Thromboxane B2)
URR	(Urea reduction ratio)
WBCs	(White blood cells)
WISE	(Woman's ischemic syndrome evaluation)

List of Figures

No.	Figure	Page
<u>1</u>	Proposed schema for screening for and treating depression in a cohort of ESRD patients.	33
<u>2</u>	Schematic representation of the mechanisms underlying anemia of HD.	40
<u>3</u>	Iron metabolism and hepcidin.	67
<u>4</u>	The role of cytokines in erythropoietin resistance.	73
<u>5</u>	Iron homeostasis and the role of hepcidin.	72
<u>6</u>	Overview of erythropoietin receptor activation and intracellular pathways.	76
<u>7</u>	Sex distribution of the studied patients.	100
<u>8</u>	Causes of ESRD of the studied patients.	101
<u>9</u>	Marital status of the studied patients.	102
<u>10</u>	Education levels of the studied patients.	103
<u>11</u>	Depression grades among patients.	107
<u>12</u>	Correlation between ERI and BMI.	118
<u>13</u>	Correlation between ERI and TSAT.	119
<u>14</u>	Correlation between ERI and HCT.	120
<u>15</u>	Correlation between ERI and Ferritin.	122
<u>16</u>	Correlation between ERI and albumin.	123
<u>17</u>	Correlation between ERI and iron.	124
<u>18</u>	Correlation between ERI and CRP.	125
<u>19</u>	Correlation between ERI and BDI score.	126

List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>1</u>	Shows drugs used in treatment of depression in hemodialysis.	28
<u>2</u>	Erythropoiesis – stimulating agents.	59
<u>3</u>	Description of personal characteristics.	99
<u>4</u>	Co-morbidities.	104
<u>5</u>	Lab results.	105
<u>6</u>	Erythropoietin dose/wk and resistance index.	106
<u>7</u>	Results of Beck Depression inventory (BDI).	106
<u>8</u>	Comparison between erythropoietin resistance groups regarding personal characteristics.	108
<u>9</u>	Comparison between erythropoietin resistance groups regarding presence of co-morbidities.	109
<u>10</u>	Comparison between erythropoietin resistance groups regarding intake of Angiotensin converting enzyme inhibitors/ angiotensin receptors blockers (ACEIs/ARBs).	110
<u>11a</u>	Comparison between erythropoietin resistance groups regarding lab results.	111
<u>11b</u>	Post hoc test results.	112
<u>12</u>	Comparison between groups regarding BDI score.	113
<u>13</u>	Comparison between erythropoietin resistance groups regarding results of BDI.	113
<u>14</u>	Relation between personal characteristics and grade of depression.	114
<u>15</u>	Comparison between degree of depression by BDI score regarding presence of co-morbidities:	115

 List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>16</u>	Relation between lab results and grade of depression.	116
<u>17</u>	Comparison between grade of depression and erythropoietin dose per week and ERI.	117
<u>18</u>	Correlation between ERI and BMI.	117
<u>19</u>	Correlation between ERI and TSAT.	119
<u>20</u>	Correlation between ERI and HCT.	120
<u>21</u>	Correlation between ERI and laboratory results.	121
<u>22</u>	Correlation between ERI and CRP.	125
<u>23</u>	Correlation between ERI and BDI score.	126
<u>24</u>	Linear regression for factors affecting ERI.	127

THE RELATIONSHIP BETWEEN DEPRESSIVE SYMPTOMS AND ERYTHROPOIETIN RESISTANCE IN HEMODIALYSIS PATIENTS

THESIS

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العلاقة بين أعراض الاكتئاب والمقاومة للإيثروبويتين في مرضى الأستسقاء الدموى المزمن

رسالة

توطئه للحصول على درجه الماجستير فى أمراض الباطنه العامه

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قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٢٢

Introduction

End stage renal disease (ESRD) has a significant impact on not only the physical but also the psychological aspects of the patient's life. Depression is generally accepted to be the commonest psychological problem encountered in patients with ESRD **(Saeed et al., 2012)**.

The prevalence of depression among dialysis patients varies from 8.1% to 65.4%. Depression was strongly associated with mortality and hospitalizations in a large cohort of prevalent hemodialysis (HD) patients maintained on dialysis for a median time of >2.4 years **(Eduardo L et al., 2012)**.

Patients on HD are thought to be highly susceptible to emotional problems because of the chronic stress-related to disease burden, dietary restrictions, functional limitations, associated chronic illnesses, adverse effects of medications, changes in self-perception and fear of death **(Kojima et al., 2010)**.

The mechanisms linking depressive symptoms with poorer outcomes in patients receiving hemodialysis are not fully understood. A proposed framework linking depressive symptoms along two pathways, one biological and one behavioral. The biological pathway involves the

inflammatory response, which can be associated with poorer nutritional stores and the development of atherosclerotic cardiovascular disease. The behavioral pathway includes the effect of depressive symptoms on adherence to treatment regimens **(Khalil et al., 2010)**.

Anemia is a common complication in hemodialysis (HD) patients, mainly due to the insufficient production of erythropoietin (EPO) by the failing kidneys. Anemia itself can worsens cardiac function, cognitive function, exercise capacity, quality of life, and it has been independently associated with increased mortality and progression of renal disease **(José et al., 2013)**.

The introduction of recombinant human EPO (rhEPO) therapy to treat anemia of chronic kidney disease (CKD) patients improves patients' quality of life. However, 5-10% of patients develop resistance to rhEPO therapy **(Gaweda et al., 2010)**.

Resistance to rhEPO therapy has been associated to inflammation, oxidative stress and “functional” iron deficiency, as major causes **(Gaweda et al., 2010)**.

Erythropoietin (Epo) has interesting properties, as a novel therapeutic agent in neuropsychiatric diseases because of its direct neurobiological actions mediated through a non-haematopoietic Epo receptor system in

the brain and several complex biochemical pathways mediate these actions (**Michael et al., 2005**).

Resistance to erythropoietin (EPO) treatment has been associated with inflammation and malnutrition in hemodialysis (HD) patients. Depression has also been associated with both inflammation and malnutrition; however, the specific relationship between depressive symptoms and EPO resistance is not known (**Afsar, 2013**).