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Biochemical Study of Hepcidin and Interleukin_6 in The Serum of Patients with Down Syndrome in Nineveh Governorate

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Abstract

The research included(51) cases collected from different regions of Mosul city, the cases were divided into two groups, the first group included (27) patients with down syndrome either the second group included (24) healthy person .. The study included assessment of Hepcidin hormone, lnterleukin6,Thyroid stimulating hormone TSH, Irons, Vitamin D3, Alkaline phosphatase(ALP), Calcium, Total Cholesterol, Very low density lipoprotein (VLDL-C) , High density lipoprotein (HDL-C), Triglyceride(TG), Hemoglobin, in serum of patients with down syndrome in comparison with control group. The results showed a significant increase in the levels of Hepcidin hormone, lnterleukin_6 , TSH hormone , in patient with down syndrome in comparison with control group and a significant decrease in the levels of hemoglobin(Hb), iron in serum of patient group in comparison with control group. Where there was no significant difference in the levels of Calcium, Total Cholesterol, Very low density lipoprotein (VLDL-C) , High density lipoprotein (HDL-C), Triglyceride(TG) . The results also indicate appositive correlation between Hepcidin hormone and TSH hormone ,Interleukin 6, Total Cholesterol(TC), Triglyceride (TG), High density lipoprotein (HDL-C), Very low density lipoprotein (VLDL-C), Low density lipoprotein (LDL-C) , and a negative correlation between Hepcidin hormone and Vitamin D3, Hemoglobin, lron ,Calcium, AlKalinephosphatase(ALP) . Results also showed appositive correlation between Interleukin 6 with Hepcidin hormone , Calcium, Triglyceride (TG), Very low density lipoprotein (VLDL-C) ,and a negative correlation between Interleukin 6 with TSH hormone ,Vitamin D3, Hemoglobin(Hb), lron , Alkaline phosphatase, Total Cholesterol, High _density lipoprotein(HDL-C),Low_ density lipoprotein(LDL-C).

***Keywords**: Hepcidin hormone, Interleukin 6, down syndrome, Calcium, Anemia, Iron.*

1. Introduction

Down syndrome is a genetic disorder caused by aneuploidy of human chromosome[1]. This causes physical and mental developmental delays and disabilities. They have lifelong disabilities are, affected shorten life expectancy. people with Down syndrome live fulfilling and live natural. In the case of childbearing, genetic information is passed on from both parents to their children cells contain 23 pairs of chromosomes, with one chromosome in each pair coming from the mother and the other from the father for46 chromosome These genes are carried in chromosomes. In people with Down syndrome, meiosis does not occur correctly .we get three copies of chromosome21 . This extra chromosome causes problems as the brain and physical features develop[2]. Hepcidin hormone plays a key role in the regulation of iron metabolism in humans by controlling the absorption of iron from the intestine It is mainly synthesized in the liver[3] interleukin 6 hormone Besides being an immune protein, IL-6 is also a pyrogen and is responsible for fever in autoimmune, infectious, or non-infectious diseases. IL-6 is secreted in cases of inflammation in the body. This substance interacts with interleukin-6 alpha receptor, It transcribes of inflammatory genes , IL-6 responsible for a range of diseases related to inflammation.lL_6 is to cause susceptibility to diabetes ,immune diseases mellitus rheumatoid arthritis[4] hormone TSH. is lt is secreted from the pituitary gland anterior. It works by sending a signal to the thyroid gland by decreasing or increasing the amount of the hormone it secretes. The hypothalamic-pituitary axis regulates TSH release[5]. Vitamin D3. is an important nutrient in maintaining bone health The primary role of Vitamin D3 is in bone metabolism and in increasing levels of calcium and phosphorous in the plasma vitamin D3 absorption the phosphate and calcium., balance calcium, with the parathyroid hormones balance body[6] Anemia is a lack red blood cells to carry

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oxygen to your body's tissues adequate, anemia Having[7]. Iron is an essential element an important human body for living organisms work to transport oxygen, It is involved in the synthesis of deoxyribonucleic acid (DNA), iron can form free radicals, its must regulated concentration in tissues the excess of iron in body tissue damage. iron Disorder is a common diseases from anemia to iron overload, [9]. Calcium is a metal found the hard part of bones, it is stored. Calcium removed from bone by cells called osteoclasts is added to bone by cells called osteoblasts. Calcium is essential for healthy bones and is also important for muscle contraction, heart action, and normal blood clotting's[10]. Alkaline phosphatase (ALP) is an enzyme that is present in different parts of the body, found in the liver, bones, and kidneys . An ALP test is used to determined diseases of the bones or liver[11].

2. Materials And Methods

This study was conducted during the period of October 2021 to February2022which is the period of case control study(27) Down syndrome patients of males and females they were compared to (24) healthy person Of the same age, sex protocol was approved by the Ethical Research Committee at the Nineveh Health in Mosul, a sample of venous blood was taken about 5 ml from drawn from the patients and the serum ofcontrol group the separated by centrifugation at a rate of (3000×g for 10 minutes(used to estimate the following clinical parameters.

1. Hepcidin hormone was measured using competitive enzyme-linked immunosorbent absorption (ELISA).BtlAB Bioassay technology Laboratory No.E0No.E0 [12]

2.lnterleukin6 hormone was measured by competitive- enzyme linked immunosorbent assay (ELISA).BtlAB bioassay technology Laboratory No E1019Hu

3. Vitamin D3 and TSHhormone were determined by Mini vids device (ltalia).

4 Total Cholesterol (TC): was determined by enzymatic colorimetric method BIOLABO Kit Cat. No.122023A1 (France).[13]

5. Triglycerides: was determined by enzymatic colorimetric method BIOLABO Kit Cat. No.122033A1 (France)[14]

6. High density lipoprotein-cholesterol (HDL-C): was estimated by precipitation method using BIOLOABO kit Cat. No.122043 (France).

7. Very low density lipoprotein –cholesterol (VLDL-C)was calculated using the equation:

VLDL-C (mol/L) =TG÷5 (mol/L) [15]

8. Calcium: was determined by CPC method using BIOLABO kit Cat. No.072006A (France).,[16]

9.Iron was determined using Colorimetric the method by the company BIOLABO Cat. No.121915A. (France).

10. Haemogobin :was determined by microhaematacrit method[17]

11.ALP was determined byenzymatic colorimetric method using BIOLABO Kitcat.No.011603B[18].

3. Results And Discussion

Hepcidin hormone: The results in table (1) showed a significant increase in hepcidin hormone levels in serum of down syndrome patients in comparison with control, Inflammation could further be a reason for the increase in hepcidin levels , Inflammatory cytokines, mainly in the form of IL-6, are released during inflammation and induce hepcidin expression in the hepatocytes[19].

Interleukin6: The results in table (1) showed a significant Increase in the levels interleukin-6 of in the serum of down syndrome patients in comparison with control group this might be the reason by The immune response pro- and anti-inflammatory cytokines expressions influenced by genetic polymorphisms[20].

Vitamin D3: The result in table (1) showed a significant decrease in serum of down syndrome patients in comparison with control group, decreased vitamin D3 bioavailability from cutaneous and dietary sources because of its deposition in body fat[21].

Thyroid stimulating hormone(TSH) hormone: The result in table (1) showed a significant increase in TSH hormone levels in serum of down syndrome patients in comparison with control group, hypothyroidism that there could be genes on chromosome 21 involved in thyroid development[22].

Iron: The result in table (1) showed a significant decrease in levels of iron in serum of patients with down syndrome in comparison with control group, people with Down syndrome have feeding difficulties (challenges with eating or with certain tastes, textures or types of food). Feeding difficulties can make it challenging for people with Down syndrome to get enough iron in their diet[23].

Hemoglobin: The result in table (1) showed a significant decrease in the levels of Hb in serum of down syndrome patients in comparison with control group .The reason for the heightened concern regarding anemia is that IDA has been associated with motor and cognitive developmental deficits in DS[24].

Total Cholesterol Triglyceride (TG) VLDL-C HDL ,LDL :The results in table (1) indicate that there is no significant difference in the levels lipids and lipoproteins in serum of patients with down syndrome in comparison with control group, this may be due to the fact that trisomy 21 does not affect pronounced general alterations in sterol lipid[25].

Alkaline phosphatase(ALP) : Interpretation of the results in table (1) There was no significant difference in ALP activity between patients with Down syndrome and the control group , as for Previous studies there is a difference in patients with down syndrome and the reason this for this is that they suffer from liver disorders[26-28]

Calcium : the results in table (1) showed that there was no significant difference in calcium levels between patients with Down syndrome and the control group, Previous studies indicate a significant decrease among patients with Down syndrome. The hormone disorder parathyroid hormone, which controls calcium levels in the blood[29-30].

Table 1: Levels of Hepcidin Hormone interleukin- 6 and other biochemical parameters in down syndrome patients in comparison with control group.

Hormones and some parameters	Patients Group(n=27) (Mean± Standard Deviation)	Control Group(n=24) (Mean± Standard Deviation)	Probability value
Hepcidin hormone(ng/L)	153.20±53.0331	126.61±56.2943	0.05*
Interleukin-6(pg/ml)	151.74±71.8754	97.7000±49.7697	0.05*
TSH	4.0007±1.32844	2.3346±1.01410	0.05*
Vitamin D3(ng/ml)	9.6308±1.78298	13.8417±1.89115	0.05*
Iron(ug/dl)	16.0778±4.01682	19.1667±5.26404	0.05*
Hb(g/dl)	9.4185±1.33389	13.3375±1.91874	0.05*
Total Cholesterol TC(mg/dl)	177.44±27.51497	162.53±23.77011	N.S**
Triglyceride TG(mg/dl)	148.83±60.58183	136.194±42.56185	N.S**
HDL_C(mg/dl)	46.6181±6.65031	43.9767±6.38793	N.S**
VLDL_C(mg/dl)	29.3319±11.29101	26.4796±8.88441	N.S**
LDL-C(mg/dl)	101.53±22.37327	91.3412±21.50158	N.S**
Ca(mg/dl)	2.1874±0.16097	2.1942±0.17039	N.S**
ALP(u/L)	76.8519±19.72640	74.2917±16.43559	N.S**

lt indicates that there is a significant difference at the probability value p≤0.05 Non_sigiftcant=N.S

The results in table (2) indicate appositive correlation between Hepcidin hormone and TSH hormone ,Interleukin 6, Total Cholesterol(TC), Triglyceride (TG), High density lipoprotein (HDL-C), Very low density lipoprotein (VLDL-C), Low density lipoprotein (LDL-C) , and a negative correlation between Hepcidin hormone and Vitamin D3, Hemoglobin, lron ,Calcium, AlKalinephosphatase(ALP).

Results in table (3) also showed appositive correlation between Interleukin 6 with Hepcidin hormone , Calcium, Triglyceride (TG), Very low density lipoprotein (VLDL-C) ,and a negative correlation between Interleukin 6 with TSH hormone ,Vitamin D3, Hemoglobin(Hb), lron , Alkaline phosphatase, Total Cholesterol, High _density lipoprotein(HDL-C),Low_ density lipoprotein(LDL-C).

Table 2: The correlation between Interleukin6and some parameters.

Hormone and parameters	Positive correlation	Negative correlation	Probability value
Thyroid stimulating hormone(TSH)		-0.166	0.05
Hormone hepcidin	0.155		0.05
vitaminD3		-0.111	0.05
Iron		-0.275	0.05
Hemoglobin		-0.394	0.05
Calcium	0.35		0.05
Alkaline phosphatase(ALP)		-0.054	0.05
Total cholesterol		-0.251	0.05
triglyceride	0.077		0.05
HDL_C		-0. 356	0.05
VLDL_C	0.029		0.05
LDL_C		-0.205	0.05

Table 3: The correlation between hepcidin hormone and some parameters.

Hormone and parameters	Positive Correlation	Negative Correlation	Probability value
Thyroid stimulating hormone(TSH)	0.195		0.05
Interleukin6	0.155		0.05
vitaminD3		_0.184	0.05
Iron		_0.074	0.05
Hemoglobin		_0.036	0.05
Calcium		_0.014	0.05
Alkaline phosphatase(ALP)		_0.093	0.05
Total cholesterol	0.179		0.05
triglyceride	0.136		0.05
HDL_C	0.072		0.05
VLDL_C	0.134		0.05
LDL_C	0.124		0.05

Cholesterol :
results in table (4) observed that there was a significant increase in the levels of cholesterol(182.5514±22.42179 mg/dl) in the serum of females infected with Down syndrome in Comparison with male patients and the control group , The reason for that mainly caused by eating fatty food, not exercising enough[30-31].

Low density Lipoprotein (LDL-C) : Results in table (4) observed that there was a significant increase in the levels of Low density Lipoprotein(LDL-C) (107.81±17.6550mg/dl) in the serum of females infected with Down syndrome in Comparison with male patients and the control group The reason may be that Thyroid hormones increase in female primarily play an essential role in helping the liver process and .remove excess cholesterol from the body When the thyroid gland is underactive ,the

body does not produce enough hormones, so the liver cannot process too much cholesterol ,It removes less harmful cholesterol from the blood . This can lead to high levels of LDL and total cholesterol. [32-33].

Iron: results in table (4) observed that there was moral decline the level lron(14.100±4.40492 ug/dl) in serum of females infected down syndrome Comparison with male patients ,females suffer from blood loss due to monthly menstrual cycles. causes blood loss not following a diet leads to anemia [34] .

Hemoglobin: results in table (4) showed a significant decrease in the level Hb(8.8143±1.67773 g/dl) in the serum of females infected down syndrome in Comparison with male patients and the control group , iron deficiency is the most common cause of anemia worldwide. Since there are no significant physiological mechanisms to regulate iron loss[35-36]

hepcidin hormone: results in table (4) observed that there was a significant increase in the levels of hepcidin hormone levels (167.15±50.2136ng/l) in the serum of males infected Down syndrome in comparison with females patients and the control group ,The reason may be Low testosterone levels in males Down's syndrome patients testosterone-induced increase is associated with suppression of the iron regulatory peptide hepcidin[37-38]

Vitamin D3: results in Table (4) observed that there was a significant decrease in the levels of Vitamin D3 (9.5250±1.76691ng/ml) in the serum of males infected Down syndrome in comparison with females patients and the control group The reason may be spend more time indoors and less of their skin is exposed to the sun. This fact may explain the high percentage of DS individuals showing a vitamin D deficiency[39]

Thyroid stimulating hormone (TSH): results in Table (4) observed that there was a significant increase in the level hormone TSH(4.4929±0.64316) in the serum of females infected down syndrome in comparison with male patients and the control group The reason may be reason for the prevalence of thyroid disorders in women is that there is an interplay between thyroid hormones and the hormones that fluctuate during the menstrual cycle[40]

Interleuk-6 : results in Table (4) observed that there was a significant increase in the levels of Interleuk-6(206.3714±14.95646 pg/ml) in females with Down syndrome compared to males Patients and control group Our findings indicate the presence of an early and evolving neuroinflammatory[41-42].

Similar significance in the same column indicates that there are no significant differences Different letters in the same column indicate significant differences between the transactions.

4. Conclusions

Through the results of our study, we noticed that :

1-There was significant increase in the levels of the hepcidin hormone and lnterleukin6 in down syndrome patients.

2-hepcidin hormone and lnterleukin6 plays an important role in the development of anemia in down syndrome patients

3. Benefits : We learned about the role of hepcidin Interleukin 6 in down syndrome and its relationship with the rest of the Biochemical parameters, and this gives us an idea about the metabolism of this hormone and its mechanism of action in down syndrome.

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Table 4: Comparsion of some biochemical parameters between down syndrome patients with gender and the control group.

Sick		cholesterol	TG	HDL	VLDL	LDL	iron	ALP	TSH	Ca	vitD3	Hepcidin	Interleuk6	Hb
Male patient	Mean	175.6545 ab	143.34 a	47.2785 a	29.0820 a	99.3315 ab	16.7700 ab	77.3500 a	3.9965 a	2.2005 a	9.5250 b	167.15 a	132.6250 b	9.6300 b
	Std. Deviation	29.39822	63.2584	6.61632	12.0865	23.8106	3.74252	22.3990	1.38603	.16462	1.76691	50.2136	74.25981	1.16804
	N	20	20	20	20	20	20	20	20	20	20	20	20	20
Male control	Mean	166.9513 ab	132.74 a	44.0075 a	25.4188 a	96.4344 ab	20.3125 a	73.8125 a	2.3119 b	2.2006 a	13.5125 a	142.09ab	78.1062 c	13.6375 a
	Std. Deviation	26.56440	45.6304	6.35076	9.54429	22.6361	4.52723	17.5013	1.05559	.17210	1.72776	60.9912	41.94608	1.52310
	N	16	16	16	16	16	16	16	16	16	16	16	16	16
Female patient	Mean	182.5514 a	164.54 a	44.7314 a	30.0457 a	107.81 a	14.10 00 b	75.4286 a	4.4929 a	2.1500 a	9.7714 b	113.34 b	206.3714 a	8.8143 b
	Std. Deviation	22.42179	53.3267	6.88616	9.43623	17.6550	4.40492	9.71008	.64316	.15578	1.87413	41.2439	14.95646	1.67773
	N	7	7	7	7	7	7	7	7	7	7	7	7	7
Female control	Mean	153.6838 c	143.08 a	3.9150 a	28.6012 a	81.1550 b	16.8750 ab	75.2500 a	2.3800 b	2.1812 a	14.5000 a	95.6500 b	136.8875 b	12.7375 a
	Std. Deviation	14.49925	37.5379	6.90242	7.51222	15.5944	6.17454	15.1540	.99388	.17788	2.14742	28.2545	41.66466	2.55116
	N	8	8	8	8	8	8	8	8	8	8	8	8	8
Total	Mean	170.4243	142.88	45.3751	27.9896	96.7347	17.5314	75.6471	3.2825	2.1906	11.5902	140.69	126.3118	11.2627
	Std. Deviation	26.64785	52.7486	6.59860	10.2308	22.3458	4.85401	18.1183	1.44673	.16383	2.80273	55.6773	67.58711	2.55374
	N	51	51	51	51	51	51	51	51	51	51	51	51	51

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