CLINICAL AND HEMATOLOGICAL STUDIES OF CHEDIAK-HIGASHI SYNDROM IN IRAQI WATER BUFFALOES (*Bubalus bubalis*)

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ABSTRACT

Chediack-Higashi syndrome (CHS) is inherited autosomal recessive disorder affected cattle and other species of animals and caused by LYST gene mutation, and characterized by oculocutaneous albinism, variations of total and differential leukocyte count , different severe infections, dysfunction of platelet**s** and a bleeding tendency.The study included 65 Iraqi water buffaloes of different ages and of both sexes which was divided as 25 black buffaloes served as controls, 25 buffaloes with patches or spotted animals and 15 white water buffaloes. The most important clinical signed showed by the animals are, white, irregular coat, unpigmented skin, hairs, eyes, with loss of appetite, emaciation, weakness, long hair than normal with tufts, anemia, photophobia with oculocutaneous depigmentation, and dullness. Animals of both sexes are affected specially those under one year of age. The results indicated a significant increases ($p<0.05$) of body temperatures, pulse and respiratory rate of diseased buffalo than in controls, However a significant decrease ($P<0.05$) has been registered in erythrocytes (RBC), hemoglobin concentration (Hb), packed cell volume (PCV) and main corpuscular hemoglobin concentration (MCHC), with no statistical differences was detected in mean corpuscular hemoglobin (MCH), whereas the mean corpuscular volume (MCV) was significantly increase ($P<0.05$). The results were

also show lymphocytosis, eosinophelia and basophelia with Nutropenia and thrombocytopenia with prolonged bleeding time.Conclusion: It has been to our knowledge that the current study is the first one in this area and the syndrome affected the Iraqi buffaloes and caused a clear clinical and hematological signs.

INTRODUCTION

Chediak-Higashi syndrome (CHS) is a genetic disease occurring in human cattle, mink, mice, cats, fox, and killer whales. CHS is manifested by oculocutaneous albinism, partial or complete hypopigmentation, a bleeding tendency, and immunologic deficiency with impaired immune cells function [1, 2, 3].CHS was firstly described in Hereford cattle and characterized by abnormal leukocytes, hypopigmentation, photophobia, increase susceptibility to infection, platelet deficiency, and large granules in the cytoplasm of leukocytes.[3,4,5,6,].

CHS is autosomal recessive gene, the lysosomal trafficking regulator gene *LYST* (CHS1) gene, this gene encodes to regulate protein membrane-associated and intracellular protein trafficking [7, 8].Studies belongs to Chediak-Higashi syndrome are very scares and little information's has been obtained therefore the aims of this study are, Registration of abnormal clinical signs among the three phenotypes of the Iraqi local buffaloes (black, patches, and white animals). Study the hematological changes through the changes in granulocytes and platelets.

MATERIALS AND METHODS

Animals: Local Iraqi buffaloes were divided into three groups as: black, partial pigmented, and white. About sixty five of local water buffaloes of both sexes with different ages were chosen as randomly in the black animals while according to its phenotypes traits in the partial pigmented and white buffaloes. The animals has grouping as (25) of black, (25) of patches, and (15) of white buffalo. All animals are subjected to complete routine clinical examinations.

Hematology and sampling: Two milliliter of jugular vein blood was collected into EDTA tubs from each animal and directly used in the hematological examinations.

Hematological Tests: Complete blood count (CBC) were done as the routine method which described [9] and include: RBC count, Hb, PCV, MCV, MCH, MCHC, total leukocytes count, platelets count and bleeding time. However, Blood smears stained with Giemza are used to evaluate Differential leukocytes count [9]

Statistical analysis: Statistical analyses were done by using SPSS statistical software version 20 (IBM SPSS Statistics 20) by using one way anova test.

RESULTS

Results indicated that the body temperatures showed significant increase ($p < 0.05$) in the CHS buffaloes (38.7867± 0.2) compared to the patches and black (control) animals while no differences between the patches and black buffaloes .Table (1). Moreover, The CHS buffaloes show a significant increase ($p < 0.01$) of the pulse rate compared to the other groups of the study. Table (1), Furthermore, it has been indicated that, there was a significant increase ($p < 0.01$), of respiratory rates in CHS group than others .Table (1)

Table (1): Body temperature, pulse and respiratory rate of all animal groups

Parameter	Black buffaloes (controls)	Patches buffaloes	White buffaloes
Body temperature C°	38.39 a ±0.07394	38.32 a ±0.12520	38.78 b ±0.20584
Pulse rate / min	84.200 a ±2.5651	88.8400 a ±2.3858	101.266 b ±4.5213
Respiratory rate / min	24.4000 a ±0.80829	30.5600 b ±0.89829	39.0667 c ±1.88090

*The different letters mean significant differences between groups.
**Values are means ± standard error of means

Age and sex: The cases of CHS in the present study are indicated in both sexes, However, the patches color in buffaloes was found .The mean of the ages of CHS buffaloes was 8.1667 months that mean the affected animals didn't pass the 1 year of age.

General Animal conditions: Buffaloes affected with Chadiak- Higashi Syndrome was non alert, dull, lazy, stolid and carless, slow movements, Since affected CHS

buffalo was slow in movements to be in the end of the rows of buffalo flocks when the animals flocking to the grazing. The CHS animals were undergone severe emaciation, in appetence, recurrent infections especially the respiratory sings. On the other hand, the patches buffalo which carry *LYST* gene show similar signs but varies in the severity, however, it is sometimes clear and some cases especially in those with occulocutineous compared to the normal (Black) animals. Furthermore, the study of hair and skin color indicated no pigmentation of the hair and skin of the CHS buffaloes as all of the body, the coat was irregular with tuft hair which was taller than of the normal animals also this signs noticed in some patches animals as compared to the control animals. Figures (1)

Figure 1: Six months CHS buffalo calf with white coat, emaciation and dullness.

Eye color and photophobia: The eyes of CHS buffalo show absences of pigmentation of the iris and the eyelashes which it is longer than in the normal eyes, as same as the periocular skin around the eyes and these animals undergo clear photophobia with pinkish color. Figure (2)The patches buffalo which carry the LYST gene also undergo hypopigmentation in the iris and occulocutaneous depigmentation especially those with non-pigmented eyelashes. Figure (3) show the normal

pigmented eyes for normal black buffalo explain the differences of the two types of LYST gene carry patches buffalo partial pigmented and non-pigmented eyes.

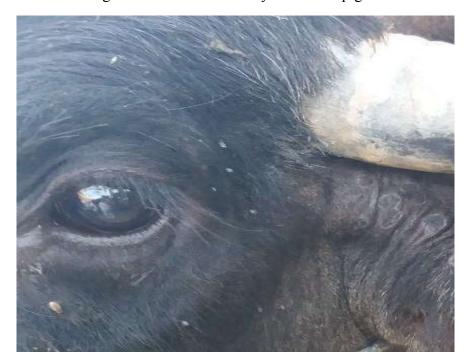Figure 2: White buffalo's eye with non-pigmentation.

Figure 3: Normal pigmented eyes and skin of buffaloes.

Hematological parameters: RBC count and Hemoglobin concentration (Hb) show a significant decrease (P<0.01) among the three buffaloes groups where there was decrease in the RBCs count of the CHS buffaloes compared to patches and control back group, also there was decrease in erythrocytes count of the patches buffaloes compared to the control black buffaloes, Further, a significant decrease (P<0.01) in the PCV of CHS buffaloes compared to the patches and black control groups, while there is no changes in the PCV values between patches and control black groups as in table (2),

On the other hand, The MCH show no differences among the CHS buffaloes and the other groups. Whereas, the mean corpuscular volume (MCV) show a significant differences (P<0.05) between the CHS buffaloes and control black buffaloes only, while there was no change between the other groups.

Results, was also indicate a significant differences (P>0.05) of MCHC among the three groups of buffalo's in the present study except the significant decrease (P<0.05) of the MCHC of the CHS buffaloes compared to the control black buffaloes as in table (2). This results were indicated the white buffaloes was affected with macrocytic hypochromic anemia compared with other groups.

Table (2) Hematological parameters of all animals groups

Parameter	Black buffaloes (controls)	Patches buffaloes	White buffaloes
RBCs X10^6	9.6888 a ±0.39840	8.0432 b ±0.36727	6.3060 c ±0.57995
Hb mg/dl	12.5840 a ±0.17801	11.7200 b ±0.24604	9.1933 c ±0.51293
PCV %	38.5200 a ±0.76620	38.3200 a ±0.81388	30.5333 b ±1.41039
MCV fL	41.7440 a ±2.31843	50.8244 ab ±3.32770	57.7773 b ±7.68968
MCH pg	13.6316 a ±0.72878	15.2916 a ±0.73614	16.2153 a ±1.69974
MCHC g/dl	32.8428 a ±0.52345	31.2940 ab ±0.9.859	30.1793 b ±1.25450

*The different letters mean significant differences between groups.
**Values are means ± standard error of means

Results was also indicated that total and percentage monocytes values show no significant difference among all buffalo groups , However, results show a significant Lymphocytopenia,Basophelia and Esinophelia with a significant Neutropenia table(2)

Table (3) Total and percentage differential leukocytes counts of all groups

Parameter	Black buffaloes(controls)	Patches buffaloes	White buffaloes
WBC X 10^3	7172.400 a ±739.2774	8677.600 a ±544.6985	7539.333 a ±390.0677
Lymphocytes%	47.3200 a ±2.27502	54.6400 b ±1.54043	59.4667 b ±2.42971
Monocytes%	5.2400 a ±0.71480	6.1600 a ±0.90126	5.2667 a ±0.70011
Neutrophils%	41.5200 a ±1.77118	32.0800 b ±1.51649	23.7333 c ±1.37483
Basophils %	1.1600 a ±0.27495	1.0800 a ±0.26407	2.2667 b ±0.44150
Eosinophils%	4.7600 a ±0.55462	5.9600 a ±1.07313	9.3333 b ±1.27117

*The different letters mean significant differences between groups.
**Values are means ± standard error of means

Results was indicated that the CHS buffalo groups have a significant decrease (P<0.01) of platelets counts compared with the controls, Moreover, bleeding time was only show a significant decrease (P<0.01) in white buffalo than in other groups Table (4)

Table (4) Platelets count and bleeding time parameters of all groups

Parameter	Black buffaloes (controls)	Patches buffaloes	White buffaloes
Bleeding time / min	6.3333 ± a ±0.69121	8.3333 ± a ±0.35746	23.4000 ± b ±1.16619
Platelets x10^3	463.7200 ± a ±17.14706	317.2000 ± b ±11.24174	257.1333 ± c ±13.16050

*The different letters mean significant differences between groups.
**Values are means ± standard error of means

DISCUSSION

The increase in the body temperatures, pulse rate and respiratory rate may be due to the recurrent bacterial infection in the affected CHS buffaloes and this results [10,11,12] especially the respiratory infection such as the calf diphtheria and pulmonary abscesses, while [13] refers to impairment of leukocytes functions that make the

bacterial recurrent infection more easy then lead to increase of the vital signs as in the present results.

The age shortness of the affected CHS buffaloes is agree with the results of [11,14,15,] and [16,17,18,19] whose reported the CHS is a lethal disease and cause hemophagocytic lymphohistiocytosis (HLH) as accelerated face. The dullness,weakness, photophopia and audiopathy results which reported in the present study are agreed with that results reported. [20,21,22,23, 24] were they reported that the CHS cases show peripheral and central nervous systemic impairments and disturbances, but the emaciation of the CHS buffaloes may due to anemia and the nervous system disturbances were the previous studies show a histological changes in the neurons with the central and peripheral nervous system especially the brain.

The results of skin, hair, eyes color and photophobia is agree with the results reported by [19,25,26,27,28,29] where they explained the failure of lysosomal function of the melanocytes to transport the melanin satin to the correct and suitable sites the clumped it inside the melanocyte leading to hypopigmentation and impairment of pigment where the melanin granules.The study revealed hematology changes represented by significant decrease of RBC, Hb, and PCV parameters which agreed with [14,30,31] that refer to anemia which may be caused by the in appetence which reported in the CHS animals and cause the emaciation and dullness. Moreover, [32,33] revealed to impairment of bone marrow functions.

The normal MCH and increase of MCV with decrease of the MCHC of the CHS buffaloes indicated macrocytic-hypochromic anemia agree with [35] and it may be due to malnutrition of affected animals for the nervous disturbances and recurrent infections as explained above. Results indicated machrocytic hypochromic anemia.

The results of leukocytes parameters are agree with results of [13,28,34,35,36] where the neutropenia is the major important result of the leukocytes change and that explain the recurrent bacterial infection The prolong bleeding time and the significant decrease of the platelets counts are agree with results that reported by [6,19, 37,38,39, 40, 41])and refers to the defect in the platelets functions and decrease in numbers of platelets due to the defect of the coagulative system which include the serotonin, dense granules of platelets and the defect of second stage of the coagulation process as reported by the previous references .

دراسة سريرية ودمية لمتلازمة شيديك-هيغاشي في جاموس الماء العراقي

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الخلاصـة

متلازمة شيديك-هيغاشي والتي تنتقل وراثيا كصفة متنحية وتم تسجيلها في الابقار وبعض فصائل الحيوانات الاخرى وتنتج عن طفرة وراثية في اللايست جين وتتصف بفقدان التصبغ الجلدي الكلي او الجزئي وتغيرات في العدد الكلي والتفريقي لخلايا الدم البيض وخمجات امراضية مختلفة مع تناقص في العدد الكلي للصفائح الدموية والميل للنزف.تمت دراسة ٦٥ جاموسة مختلفة الاعمار ومن كلا الجنسين تم تقسيمها الى ثلاث مجاميع: ٢٥ حيوان اسود كمجموعة سيطرة للمقارنه، ٢٥ مرقط و ١٥ جاموسة ذات لون ابيض .اطهرت الدراسة تسجيل بعض العلامات السريرية ومنها علامات اللون الابيض، كسوة غير منظمة، ، فقدان تصبغ الجلد والعين والشعر، فقدان شهية، الهزال ، الضعف العام ، تكتل الشعر وطول الشعر نسبيا، علامات فقر الدم ، رهاب الضوء، عدم تصبغ الجلد حول العين، والخمول. المتلازمة تم تسجيلها في كلا الجنسين وسجلت بأعمار اقل من سنه.اظهرت الدراسة ارتفاعا معنويا (0.05>p) في درجات حرارة الجسم والنبض والتنفس ونقصان محسوس (P<0.05) في العدد الكلي لكريات الدم الحمر وتركيز صباغ الدم و حجم كريات الدم المرصوصة ومعدل تركيز الصباغ الكريي بينما لم تضهر اختلافا معنويا في الضباغ الكريي واضهرت الدراسه زيادة معنوية (P<0.05) معدل الحجم الكريي. لم تشر الدراسة الى تغيير معنوي (P>0.05) في العدد الكلي لكريات الدم البيض و الخلايا وحيدة النواة، بينما اضهرت زيادة معنوية واضحة (P<0.01) في عد الخلايا اللمفية و الحمضات والقعدات ،كما لوحظ انخفاضا معنويا (P<0.01) في العدلات وكذلك الصفيحات الدموية وطول زمن النزيف. وبهذا فان متلازمة شيديك- هيغاشي ممكن ان تصيب الجاموس العراقي وتضهر علامات واضحة وتغييرات دمية كما اثبتتها الدراسة الحالية.

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