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Clinical assessment of infantile haemangioma among patients attending the dermatology department of Rapareen teaching hospital in Erbil city.

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Abstract

Background and objectives: Strawberry (capillary) haemangiomas are the most commonbenign tumors of childhood;they are present at birth in one thirdof cases. The remainder appears shortly thereafter. Sixty percentare on the head and neck, but they may occur anywhere. The aim of this study is to have a clinical evaluation of infants and children with haemangiomaand to identify risk factors associated with infantile haemangioma. **Methods:** A case control study involved 38 patients with infantile haemangioma and 38 controls matched by age and gender. Data were collected by direct interview with the patient's guardians through a questionnaire including age, gender, birth weight, any complication during pregnancy or labor and the type of complication, gestational age (full term, premature, postdate), mode of delivery (normal vaginal delivery or caesarean section), duration of the lesion, age at onset, site (head, neck, trunk, groin, upper extremity, lower extremity), size, number of the lesions, any complications and type of it, interventions and type of intervention; pharmacological, surgical or laser and family history of haemangioma. **Results:** from atotal of 76 patients and controls, 71.1% were females and 28.9% were males.Their age ranged from 1108- months.Sixty and a half percent of our patients were less than one-year age. Full term infants made 81.6% of our patients while premature infants were only18.4% of the patients. Mode of delivery was normal vaginal delivery in 55.3% of patients and 65.8% of controls while 44.7% of patients and 34.2% of controls were born by caesarean section. Hemangiomas were present since birth in 73.7%, 13.2% had their lesion in their first week, 5.3% developed the lesion during their second and fourth week of life and 2.6% developed lesion during their third week. Lesion werepresent on the head and neck in 47.4%. Minimum lesion size was 0.3cm and maximum diameter was 10.5cm. **Conclusions:** Infantile haemangioma are common in female babies, risk factors are prematurity and maternal anemia. Lesions were noticed at birth or appeared within few weeks and the majority had single lesion.

Keywords: Infantile haemangioma; Derratology; Erbil

Introduction:

Infantile haemangiomas are common, benign, vascular tumoursthat develop in early infancy and undergo spontaneous involution thereafter[1]. They are the most common benign tumors of childhood, occurring in approximately 4% of children by 1 year of age. They are more common in females (2-5:1 ratio) and in premature infants, especially those weighing less than 2,500 g. Other risk factors are Caucasian race, multiple gestation pregnancy, and maternal age greater than 30 years. Preterm infants are more likely to have multiple tumors, and the sex ratio is less skewed toward females[2]. Infantile haemangiomas is multi-factorial, with genetic factors being part of the contributing triggers. In most cases, infantile haemangiomasare sporadic[3]. The pathogenesis of infantile haemangiomas is complex. CD133+ stem cells within the haemangioma differentiate into mature blood vessels that express GLUT-1, a glucose transporter normally restricted to endothelial cells with blood tissue barrier function, as in brain and placenta. The vessel proliferates, and then involutes. Histologically, strawberry marks are composed of primitive endothelial cells similar to those found before the embryonic development of true venous channels[4]. The histopathologic composition of infantile haemangiomas varies with the age of the lesion. Early haemangiomas are highly cellular and are characterized by plump endothelial cells aligned to vascular spaces with small inconspicuous lumina. However, longstanding haemangiomas have been found to have significantly more mast cells than haemangiomas of recent origin. Regression is portrayed as progressive interstitial fibrosis and adipose metaplasia, a process without known stimulus[5]. Haemangiomas involving the papillary dermis (superficialstrawberry haemangiomas) are red; those in the reticulardermis and subcutaneous fat are blue or colorless (deep, cavernous haemangiomas). Superficial (strawberry) haemangiomas may be present atbirth but more often appear within the first 2 weeks of lifein 1% to 3% of infants. Many children have one hemangioma, but 15% to 20%have several of these lesions. The lesions begin asnodular masses or as flat, ill-

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defined, telangiectatic maculesthat are mistaken for bruises. Superficial haemangiomasgrow rapidly for weeks or months, forming nodular, protuberant, compressible masses of a few millimeters toseveral centimeters in diameter. In rare instances the lesionsmay almost cover an entire limb. They are bright red with well-defined borders. Vital structurescan be compressed, and rapidly growing areas may ulcerate. Larger lesions (more than 6 cm.) ulceratemore frequently. Early white discolorationof infantile haemangioma is highly suggestive of impending ulceration[6].The differential diagnosis of haemangioma includes lymphatic malformation, capillary malformation(port-wine stain), pyogenic granuloma, kaposiformhaemangi oendothelioma, tufted angioma, myofibromatosis and fibrosarcoma[7]. Ulceration is the most common complicationof infantile haemangioma. It can result in pain, infection, bleeding, and scarring and interfere with sleeping or feeding. Haemangiomas may block vision, interfere with feedingor respiration, or obstruct the external auditory canal. Recurrentbleeding may complicate ulceration. An inactive phaselasting several months is followed by fibrosis and involution. About 30% of lesions resolve by the third birthday, 50% by the fifth, and 70% by the seventh. The massshrinks and fades in color during the scarring process. Involutionbegins in most cases by age 3; lesions presentafter ages 7 to 9 infrequently undergo further regression. Regression is characterized by normal appearing skin (approximately 70% of cases) or by atrophy, scarring, telangiectasia, pigmentation changes, and deformity[6]. The aim of the study was to evaluate clinicallythe infants and children with infantile haemangiomaand to identify risk factors associated with infantile haemangioma.

Patients and methods

A case control study involved a sample of thirty-eight infants and childrenwith infantile haemangioma attending the outpatient department of dermatology at Rapareen teaching hospital for children in Erbil city. An equal number of infants and children were chosen as a control group;they were recruited from patients attending the same outpatient department having other minor dermatological problems and the absence of any angiomatous lesion. They were randomly selected and matched by age and gender with the study group.The studywas conducted within the period of October 2015 to July 2016. Data were collected by direct interview with the patient's guardians through a questionnaire.Each patient was given a number and the following data were collected: patient`s age, gender, birth weight, gestational age (full term, premature, postdate), mode of delivery (normal vaginal delivery or caesarean section), any complication during pregnancy or labor and the type of complication, duration of the lesion, age at onset, site (head, neck, trunk, groin, upper extremity, lower extremity), number of the lesions, any complications and type of it, interventions and the type of intervention whether pharmacological agent, surgical or laser and family history of haemangioma. Control subject'sguardians were interviewed and asked about age, gender, birth weight, any complication during pregnancy or labor and the type of complication, gestational age (full term, premature, postdate) and mode of delivery (normal vaginal delivery or caesarean section) and a full dermatological examination was performed for the controls.The diagnosis was made on a clinical ground by the authors based on a clear and definite clinical characteristic of haemangioma. Data were transferred into a computerized database structured SPSS software version 23 and was used for dataanalysis, Chi square test was used to test the significance of association between variables. When the expected count of more than 20% of the cells of the table was less than 5, Fisher's Exact test was used.A P- value equal or less than 0.05 was considered statistically significant.As all our patients and controls were minors, parents were informed about the purpose and the importance of the study and their permission was taken accordingly. An informed verbal consent was taken from all parents.The study was approved by the Research Ethics Committee of the College of Medicine, Hawler Medical University.

Results

The study involved 76 infants and children (38 patients and 38 controls). Females constituted 71.1% and males were 28.9% of the studied sample. Their age ranged from 1108- months for both patients and controls with a mean ± SD of 20.28 ± 25.79 months for patients and 20.52 ± 25.90 months for controls. Children less than one-year age constituted the highest proportion of our patients (60.5%), next comes the 1235- months' age (23.7%), while both 3659- and more than 60 months' age groups constituted 7.9% of our patients. Control infants less than twelve months were 55.3%, 1235- made 21.1%, 3659- were 10.5% and children sixty months' age or more were 13.1%. There was no statistically significant difference between age groups of the studied samples (P =0.471) as shown in Table 1.

Table (1): Age and gender distribution of patients and controls.

Variables		Patients No. (%)	Controls No. (%)	P- Value
Gender	Female	27 (71.1)	27 (71.1)	1.0
	Male	11 (28.9)	11 (28.9)	
Age in months	<12	23 (60.5)	21 (55.3)	0.471
	12-35	9 (23.7)	8 (21.1)	
	36-59	3 (7.9)	4 (10.5)	
	≥60	**3 (7.9)**	**5 (13.1)**	
Total		38 (100.0)	38 (100.0)	

Full term infants made 81.6% of our patients and 86.8% of the control while premature infants were only18.4% of the patients and 13.1% of controls which was statistically not significant (odds ratio: 0.671; P value 0.529). Anemia was the most common complication during pregnancy, developed in 36.8% of ourpatient'smothers and 7.9% of the controls mothers.This was statistically significant (odds ratio: 6.806; P value 0.002). Both diabetes mellitus and hypertension were present in 5.3% of patient'smothers and 2.6% and 7.9% for the controlsmothers respectively.Vaginal bleeding and facial palsy were present in 2.6% of patients mothers and none of the controlsmothers while thyrotoxicosis and vomiting were present in 2.6% and 7.9% of the controlsmothers respectively. All these complications were found to be statistically non-significant (p value >0.05) as shown in Table 2.

Table (2): Gestational age and complications during pregnancy.

Variables		Patients No. (%)	Controls No. (%)	P- Value
Gestational Age	Full term	31 (81.6)	33 (86.8)	0.529
	Premature	7 (18.4)	5 (13.1)	
Complication in pregnancy	Anemia	14 (36.8)	3 (7.9)	0.002
	Diabetes Mellitus	2 (5.3)	1 (2.6)	1.000
	Hypertension	2 (5.3)	3 (7.9)	1.000
	Vaginal bleeding	1 (2.6)	0	1.000
	Thyrotoxicosis	0	1(2.6)	1.000
	Vomiting	0	3 (7.9)	0.240
	Facial Palsy	1(2.6)	0	1.000
	No complication	18 (47.4)	27 (71.1)	
Total		**38 (100)**	**38 (100)**	

Babies were born by normal vaginal delivery in 55.3% of patients and 65.8% of controls while 44.7% of patients and 34.2% of controls were born by caesarean section. This was statistically non-significant (P value 0.348) as shown in table 3 which also shows the birth weight in kilograms.The majority of our patients, 55.3%, had a birth weight of 2.53.4- kg as also the controls (57.9%) while 15.8% of patients and 7.9% of controls had a birth weight of 1.52.4- kg.Only 2.6% patients and 10.5% controls had a birth weight of more than four kilograms.

Table (3): Mode of delivery and birth weight.

Variables		Patients No. (%)	Controls No. (%)	P- Value
Mode of delivery	Normal vaginal delivery	21 (55.3)	25 (65.8)	0.348
	Caesarean section	17 (44.7)	13 (34.2)	
Birth weight in Kg	1.5-2.4	6 (15.8)	3 (7.9)	0.674
	2.5-3.4	21 (55.3)	22 (57.9)	
	3.5-4	10 (26.3)	9 (23.7)	
	>4	1 (2.6)	4 (10.5)	
Total		**38 (100)**	**38 (100)**	

Table 4summarizes age at onset and the number ofhaemangioma lesions each patient had. Haemangioma was present since birth in 28 (73.7%) patients,5 (13.2%) had their lesion in their first week, 2 (5.3%) developed the lesion during their second week of life and the same percent had haemangioma in their fourth week while only one (2.6%) infant developed lesion during his third week. Thirty (78.9%) patients had single lesion, 4 (10.5%) patients had two lesions, 2(5.3%) had three lesions while four and five lesions were present in only one (2.6%) patient.

Table (4): Age at onset and the number ofhaemangioma lesions per patient.

Age of onset	Frequency (%)	Number of lesions/patient	Frequency (%)
Since birth	28 (73.7)	1	30 (79)
First week	5 (13.1)	2	4 (10.5)
Second week	2 (5.3)	3	2 (5.3)
Third week	1 (2.6)	4	1 (2.6)
Fourth week	2 (5.3)	5	1 (2.6)
Total	**38 (100)**		**38 (100)**

Site of the lesions are shown in table 5,lesions were present on the head and neck in 18(47.4%).
Five (13.2%) patients had a single lesion on their trunk. Upper and lower extremity lesion alone was present in 4(10.5%) and 3(7.9%) patients respectively and a single groin lesion was present in one (2.6%) patient. Multiple lesions were present on the head and trunk, head and groin, trunk and groin and head, trunk, upper extremity and mucosa each being present in one (2.6%) patient only. Three (7.9%) patients had lesions on their upper extremity and trunk.

Table (5): Site of lesions for each patient.

Site	Frequency	Percent
Head and Neck	18	47.4
Head &Trunk	1	2.6
Head &Groin	1	2.6
Upper Extremity	4	10.5
Upper Extremity and Trunk	3	7.9
Lower Extremity	3	7.9
Trunk	5	13.2
Groin	1	2.6
Trunk & Groin	1	2.6
Head, Trunk, Upper Extremity &Mucosa	1	2.6
Total	**38**	**100**

Out of the eighteen patients whose heamangioma were located in the head region, 60% were located in the scalp, 22.2% on the forehead and 5.6% for each of these areas,periorbital, ear and temple, table 6.A positive family history of haemangioma was obtained in 12(31.6%) while 26(68.4%) had no family history.Complication in the form of ulceration developed in two (5.3%) patients only and both were in the groin area.For both topical antibiotics and corticosteroids has been used. Topical corticosteroids have been used for one patient with upper extremity lesion of 1.5cm size. Minimum lesion size was 0.3cm and maximum diameter was 10.5cm. Significant association was found between size and site of the lesion (P -value 0.03). The larger lesions were in the extremities and the smaller lesions were in the head and neck and groin areas.

Table (6): Location of the lesions in head

Location	Number	Percent
Scalp	11	61
Forehead	4	22.2
Periorbital	1	5.6
Temple	1	5.6
Ear	1	5.6
Total	**18**	**100**

Discussion

Hemangiomas are benign, vascular proliferations that rapidly enlarge during the first year of life and slowly spontaneously involute by age 5 to 10 years. Lesions present soon after birth during the first few weeks of life8.They are principally composed of highly proliferative hyperplastic endothelial cells and the majority causes no clinical issue, require no investigation and can be left alone to involute with time. IH infantile haemangioma typically present as a small lesion 26- weeks after birth. They undergo a period of rapid proliferation in the first 12–18 months of life followed by a phase of involution. Most appear as bright red exophytic lesions of the skin, though deep-seated lesions can cause no discolouration[9]. Females constituted the majority (71.1%) of our patients which is comparable with the literature as infantile haemangioma is more common in female babies[1,2]. Our youngest infant was one month age and the oldest was nine years old. About 60.5% of our patients were less than a year old and children older than five years constituted 7.9% only which is due to the fact that infantile haemangioma regress spontaneously. Infantile haemangiomas arise during the first year of life and are the most common tumor of infancy. They develop in 4–5% of infants, with the majority of lesions noted within the first several weeks of life. Involution of infantile haemangiomas may begin as early as the firstyear of life and continues for several years. Natural history studies of untreated haemangiomas demonstrate that 30% of lesions involute fully by 3 years of age, 50% by 5 years, 70% by 7 years, and over 90% by 9 years. Some haemangiomasinvolutes completely, while others may leave atrophic, fibrofatty or telangiectatic residua[10]. Premature infant's constituted 18.4% while full term infants were the majority 81.6%, in comparison with controls, premature were 13.1% and full term infants were 86.8% which was statistically insignificant. This is concordant with the literature as prematurity is a risk factor for infantile haemangioma[1,2,6]. A role for hypoxia in the pathogenesis of haemangiomas is supported bytheir association with hypoxic placental changes, prematurity, lowbirthweight (often caused by placental insufficiency), and retinopathy ofprematurity[10]. More than half of our patients were born by normal vaginal delivery; this was in accordance with other studies in which 60.2% had a vaginal delivery[11]. There was a statistically significant difference between patients and controls concerning complications their mother developed during pregnancy. Complications during pregnancy were found in 52.6% of our patient's mothers. Anemia was the most common complication; it was found in 36.8% of mothers. Both diabetes mellitus and hypertension were found in 5.3% of mother and one mother had vaginal bleeding. In a similar research hypertension was found in 1.5%,diabetes was found in 1% and vaginal bleeding in 10.912%. Higher percentages were reported by other investigators, they found diabetes and hypertension as the most common medical conditions, accounting for 7.1% and 9.3% respectively[11]. Low birth weight has been considered potential risk factors for developing haemangiomas[1,3,4]. We found that more than half of our patients had a birth weight of 2.5-3.4 kg and 15.8% had a birth weight of 1.5–2.4 kg. In another research low birth weight was found in 9.113%. Haemangiomas were present since birth in a considerable number of our patients (73.7%). In a prospective study of 34 haemangioma-type lesions, 8.8% were detected at birth, 38.1% were detected at 1 month, and 52.8%were detected at 3 months[14]. Other investigators noted haemangiomas on examination immediately after birth in 915%. Lesions usually become apparent during the first few weeks of life, although the proportion of haemangiomas that were "congenital" in published series has ranged from 15% to 60%. Reports of significant numbers of haemangiomas being noted at birth probably included precursor lesions. Telangiectasias surrounded by a vasoconstricted halo, areas of pallor, pink macules, and blue bruise-like patches are the most common precursor lesions[10]. Lesion appeared during the first week in 13.1% of our infants. Although haemangiomas may be present at birth, they usually delay appearance until the second week of life5. More than two thirds of our patients had a single lesion. Similar results were found by other investigators, in which the vast majority of their patients had a single lesion[13,16]. Lesions were most commonly located in the headand neck area,next comes the trunk and extremities. These were concordant with other studies in which the most commonlocation for infantile haemangiomas was the headand neck (60%), trunk (25%), and extremities (15%).Multiple cutaneous haemangiomas were seen in 10%-25% of cases, with more than one lesion found in 31% of cases[17]. Among our patients,the most common location in the head was the scalp. Facialhaemangiomas have a nonrandom distribution. The distribution of focal lesions localized to one of twenty-twoclusters which each corresponded to margins of embryonic fusion planes known as facial placodes. Most focal lesions occurred in the central face (60%). Diffuse

haemangiomas were localized within areas marked by embryonal facial placodes of the frontonasal, maxillary, and mandibular areas or segments[18]. Another study, in contrast, found that the majority of lesions occur on the trunk, following the natural body surface area proportional distribution found in infants[15]. Haemangiomas of infancy that are present in certain locations may be associated with other anomalies or may have an increased risk of developing particular complications. Most complications arise duringthe proliferative phase of growth,and prompt recognition and interventionmay be required in orderto prevent permanent sequelae. Haemangiomas that arepresent in the following areas areof particular concern and requirecloser follow-up, additional evaluation,specialized therapy, or referralto pediatric subspecialistsfor further management: periorbital,pelvic and perineal, lumbosacral,and facial[19]. History of having a family member with hemangioma was present in 31.6% of our patients. A positive family history was obtained in 10% by another investigator16 and haemangiomas were present in first-degree relatives in 12.3% in another research[20]. This finding support spreviously published data that hereditary character istics account for 10–32% of haemangiomas[12,15]. Ulceration is the most common infantile haemangioma complication;it has developed in the groinareain a minority (5.3%) of our patients. In one large series ulceration occurred in 16%of patients; riskfactors include larger lesions,segmental infantile haemangioma, and distribution inthe head, neck, perioral, andperineal or perianal locations[21]. The pathogenesis of ulceration is unknown, three factors that may play a role, sites oftrauma (maceration or friction or both), local factorssuch as bacteria (either infection or colonization), and tissue hypoxia such thatulcerationoccurswhenahaemangioma"outgrows its blood supply[22]. None of our patients needed any sort of intervention except for the patient who developed ulceration and another patient with an extremity lesion. Lesions which lead to remarkable deformity and malformation need earlier and faster treatment. These lesions are usually located on forehead, glabella, or central face >0.5cm in diameter, Nasal tip (Cyrano deformity), pinna, eyebrow and eyelid, any superficial thick haemangiomas of an area that is not easily covered by clothing, lip and perioral (may ulcerate and scar), and neck fold (may ulcerate and scar)[23]. A significant association was found between the location and size of the haemangioma.Lesion size ranged from 0.3-10.5cm, the larger lesions were found on the extremities.In a study of size analysis, the mean size of segmental haemangiomas was 10 times that of localized haemangiomas, the largest increase in size occurred inthe early prolife rative stage. By 5 months of age,the average haemangioma had already achieved 80% ofits final size[24].

Conclusions

We demonstrated that risk factors for infantile haemangioma are female gender, prematurity and maternal anemia during pregnancy. Lesions were present at birth or appeared soon after delivery. Haemangioma were mostly single. Head and neck was the commonest site. Location of the lesion is a significant factor for complication. Although ulceration is the most common complication of infantile haemangioma; it has developed in a minority of our patients.

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